CHEMICAL BASIS OF LIFE

SUBCELLULAR ORGANELLES AND CELL MEMBRANES

1. Mitochondria

Definition:
Mitochondria are double membrane bound cytoplasmic organelles known as the "power house of the cell".

Structure:

- Outer membrane – smooth and permeable
- Inner membrane – folded into cristae
- Matrix – contains enzymes of Tricarboxylic acid cycle, mitochondrial Deoxyribonucleic acid and ribosomes
- Intermembrane space present

Functions:

- Adenosine triphosphate production by oxidative phosphorylation
- Tricarboxylic acid cycle
- Beta oxidation of fatty acids
- Apoptosis
- Calcium storage
- Heat production in brown fat

2. Describe the fluid mosaic model of cell membrane with a neatly labeled diagram.

Fluid Mosaic Model:
Proposed by Singer and Nicolson in 1972.

Features:

- Cell membrane is a phospholipid bilayer
- Proteins are embedded within lipid bilayer
- Membrane is fluid in nature
- Proteins are arranged in a mosaic pattern
- Cholesterol maintains membrane fluidity
- Glycoproteins and glycolipids help in cell recognition

Functions:

- Selective permeability
- Transport of substances
- Cell signaling
- Cell recognition

Diagram:

REFER DIAGRAM SECTION

3. Mitochondria – structure & functions

Structure:

- Double membrane organelle
- Outer membrane smooth
- Inner membrane forms cristae
- Matrix contains enzymes, mitochondrial Deoxyribonucleic acid and ribosomes

Functions:

- Adenosine triphosphate synthesis
- Electron transport chain
- Oxidative phosphorylation
- Beta oxidation
- Tricarboxylic acid cycle
- Apoptosis
- Calcium homeostasis

4. Fluid mosaic model

Definition:
The cell membrane is composed of a fluid phospholipid bilayer with proteins arranged in a mosaic pattern.

Features:

- Proposed by Singer and Nicolson
- Lipids and proteins move laterally
- Membrane is dynamic and selectively permeable
- Cholesterol stabilizes membrane

5. Active transport

Definition:
Transport of substances across membrane against concentration gradient using energy.

Features:

- Requires Adenosine triphosphate
- Carrier mediated
- Specific and saturable

Examples:

- Sodium potassium pump
- Calcium pump
- Proton pump

6. Peroxisome

Definition:
Peroxisomes are single membrane bound organelles containing oxidative enzymes.

Functions:

- Beta oxidation of very long chain fatty acids
- Detoxification of hydrogen peroxide by catalase
- Synthesis of plasmalogens

7. Golgi complex

Structure:
Stack of flattened membranous sacs.

Functions:

- Protein modification
- Glycosylation
- Packaging and secretion
- Lysosome formation

8. Ribosomes

Definition:
Ribonucleoprotein particles responsible for protein synthesis.

Types:

- 80S in eukaryotes
- 70S in prokaryotes

Functions:

- Protein synthesis

9. Endoplasmic reticulum

Types:

1. Rough endoplasmic reticulum
2. Smooth endoplasmic reticulum

Functions:

- Protein synthesis by rough endoplasmic reticulum
- Lipid synthesis by smooth endoplasmic reticulum
- Detoxification
- Intracellular transport

10. Lysosomes

Definition:
Membrane bound organelles containing hydrolytic enzymes.

Functions:

- Intracellular digestion
- Autophagy

- Removal of damaged organelles

AMINOACIDS AND PROTEINS

SHORT ESSAYS

1. Sources biochemical functions and deficiency manifestations of thiamine

Sources:

- Cereals
- Pulses
- Liver
- Yeast
- Nuts

Biochemical functions:
Thiamine acts as Thiamine pyrophosphate.

Functions:

- Oxidative decarboxylation of alpha keto acids
- Transketolase reaction in Hexose monophosphate shunt
- Carbohydrate metabolism

Deficiency manifestations:

1. Dry beriberi – peripheral neuropathy
2. Wet beriberi – cardiac failure and edema
3. Wernicke Korsakoff syndrome
4. Infantile beriberi

2. Classify proteins based on their functions giving suitable examples.

Functional classification of proteins:

1. Structural proteins

- Collagen
- Keratin

2. Catalytic proteins

- Enzymes

3. Transport proteins

- Hemoglobin
- Transferrin

4. Storage proteins

- Ferritin
- Casein

5. Regulatory proteins

- Insulin
- Growth hormone

6. Contractile proteins

- Actin
- Myosin

7. Protective proteins

- Immunoglobulins

3. Describe the structural organization of proteins

Protein structure is organized into four levels.

1. Primary structure:
Sequence of amino acids linked by peptide bonds.

2. Secondary structure:
Local folding of polypeptide chain.
Examples:

- Alpha helix
- Beta pleated sheet

3. Tertiary structure:
Three dimensional folding of protein.
Stabilized by:

- Hydrogen bonds
- Hydrophobic interactions
- Ionic bonds
- Disulfide bonds

4. Quaternary structure:
Association of two or more polypeptide chains.
Example:

- Hemoglobin

SHORT ANSWERS

4. Isoelectric pH and its significance.

Definition:
Isoelectric pH is the pH at which a protein carries no net charge.

Significance:

- Minimum solubility at isoelectric pH
- Used in protein separation
- Important in electrophoresis

5. Explain the Quarternary structure of proteins with example.

Definition:
Arrangement of two or more polypeptide chains to form a functional protein.

Features:

- Stabilized by non covalent interactions
- Seen in oligomeric proteins

Example:
Hemoglobin consists of two alpha and two beta chains.

6. Secondary structure of protein

Definition:
Regular arrangement of polypeptide chain due to hydrogen bonding.

Types:

- Alpha helix
- Beta pleated sheet
- Triple helix

7. Essential amino acids

Amino acids which cannot be synthesized in the body and must be supplied in diet.

Examples:

- Leucine
- Isoleucine
- Lysine
- Methionine
- Phenylalanine
- Threonine
- Tryptophan
- Valine
- Histidine

8. Why heat coagulation is an irreversible process

Heat causes denaturation and aggregation of proteins resulting in coagulation which cannot return to original state.

9. Primary structure of protein

Sequence of amino acids in a polypeptide chain linked by peptide bonds.

10. Keratin

Keratin is a fibrous protein rich in cysteine.

Types:

- Alpha keratin
- Beta keratin

Functions:

- Structural support in hair, nails and skin

11. Biologically important peptides

- Glutathione
- Oxytocin
- Vasopressin
- Bradykinin
- Angiotensin

12. Nutritional classification of protein with examples

1. Complete proteins – contain all essential amino acids
   Example: Egg protein
2. Partially complete proteins
   Example: Wheat protein
3. Incomplete proteins
   Example: Gelatin

13. Define Peptide bonds. Enumerate two biochemically important peptides and their significance.

Peptide bond:
Bond formed between alpha carboxyl group of one amino acid and alpha amino group of another amino acid.

Examples:

1. Glutathione – antioxidant
2. Oxytocin – uterine contraction

14. Definition and characteristics of denaturation

Definition:
Loss of native conformation of protein without breaking peptide bonds.

Characteristics:

- Loss of biological activity
- Decreased solubility
- Coagulation
- Secondary and tertiary structures destroyed

15. Protein denaturation

Causes:

- Heat
- Acids
- Alkalis
- Heavy metals

Effects:

- Loss of biological activity
- Coagulation

16. Classify amino acids based on its metabolic fate

1. Glucogenic amino acids
2. Ketogenic amino acids
3. Both glucogenic and ketogenic amino acids

17. Non covalent bonds responsible for protein structure

- Hydrogen bonds
- Hydrophobic interactions
- Ionic bonds
- Van der Waals forces

18. Name the factors affecting BMR

- Age
- Sex

- Body surface area
- Hormones
- Fever
- Pregnancy
- Nutrition

19. Formation and characteristics of peptide bond

Formation:
Condensation reaction between amino and carboxyl groups.

Characteristics:

- Rigid and planar
- Partial double bond character
- Usually trans configuration

20. Functional classification of proteins

- Structural
- Catalytic
- Transport
- Storage
- Regulatory
- Contractile
- Protective

21. Heat coagulation

Heat denatures proteins causing aggregation and precipitation.
Example: Boiling of egg albumin.

22. Define isoelectric pH. state properties of protein and its isoelectric pH

Definition:
pH at which protein has no net charge.

Properties:

- Minimum solubility
- No migration in electric field
- Maximum precipitation

23. Alpha helix

A right handed helical structure stabilized by hydrogen bonds.

Features:

- 3.6 amino acids per turn
- Present in keratin

ENZYMOLOGY: GENERAL CONCEPTS, ENZYME KINETICS, ISOENZYMES & CLINICAL ENZYMOLOGY

LONG ESSAYS

1. Explain various ways by which enzyme activity is regulated in human body. Give suitable examples.

Mechanisms of enzyme regulation:

1. Allosteric regulation

- Modulator binds at allosteric site
- Example: Aspartate transcarbamoylase

2. Covalent modification

- Phosphorylation and dephosphorylation
- Example: Glycogen phosphorylase

3. Induction and repression

- Regulation of enzyme synthesis
- Example: Cytochrome P450 induction

4. Feedback inhibition

- End product inhibits first enzyme

- Example: Cholesterol inhibits Hydroxymethylglutaryl coenzyme A reductase

5. Compartmentalization

- Different pathways occur in different organelles

6. Proteolytic activation

- Activation of zymogens
- Example: Trypsinogen to trypsin

2. a) Define and classify enzymes giving one example each.

b) Enumerate the factors affecting enzyme activity

c) Describe the different types of enzyme inhibition with appropriate examples.

a) Definition:
Enzymes are biological catalysts produced by living cells.

Classification:

1. Oxidoreductases – Lactate dehydrogenase
2. Transferases – Alanine transaminase
3. Hydrolases – Lipase
4. Lyases – Aldolase
5. Isomerases – Phosphohexose isomerase
6. Ligases – Pyruvate carboxylase

b) Factors affecting enzyme activity:

- Temperature
- pH
- Enzyme concentration
- Substrate concentration
- Product concentration
- Inhibitors

c) Types of inhibition:

1. Competitive inhibition
   Example: Malonate inhibits succinate dehydrogenase
2. Non competitive inhibition
   Example: Cyanide inhibits cytochrome oxidase
3. Uncompetitive inhibition
4. Suicide inhibition
   Example: Allopurinol inhibits xanthine oxidase

3. Define Enzyme, what are the factors affecting enzyme activity. Explain various mechanism of enzyme regulation.

Definition:
Enzymes are biological catalysts.

Factors affecting enzyme activity:

- Temperature
- pH
- Enzyme concentration
- Substrate concentration
- Inhibitors

Mechanisms of regulation:

- Allosteric regulation
- Covalent modification
- Feedback inhibition
- Induction and repression
- Proteolytic activation

4. Write IUMB classification of enzymes with examples and describe the factors affecting the enzyme activity

IUBMB Classification:

1. Oxidoreductases – Lactate dehydrogenase
2. Transferases – Transaminases
3. Hydrolases – Lipase

4. Lyases – Aldolase
5. Isomerases – Racemase
6. Ligases – Carboxylases

Factors affecting activity:

- Temperature
- pH
- Substrate concentration
- Enzyme concentration
- Inhibitors

5. Define enzyme inhibition. Explain the different types of enzyme inhibitions. Mention significance of enzyme inhibitors.

Definition:
Decrease in enzyme activity due to a substance called inhibitor.

Types:

1. Competitive inhibition
2. Non competitive inhibition
3. Uncompetitive inhibition
4. Suicide inhibition

Significance:

- Therapeutic drugs
- Regulation of metabolism
- Poisoning
- Antibiotic action

6. Define enzyme. Classify with suitable examples. Discuss the various types of enzyme inhibitions with clinical examples.

Definition:
Enzymes are biological catalysts.

Classification:
Same as IUBMB classification.

Types of inhibition:

- Competitive – Statins
- Non competitive – Cyanide
- Suicide inhibition – Allopurinol

7. Define enzymes. Classify enzymes according to IUB System with one example each. Mention three enzymes commonly estimated after myocardial infarction

Definition:
Enzymes are biological catalysts.

IUB Classification:

1. Oxidoreductases – Lactate dehydrogenase
2. Transferases – Alanine transaminase
3. Hydrolases – Lipase
4. Lyases – Aldolase
5. Isomerases – Mutase
6. Ligases – Synthetase

Enzymes estimated after myocardial infarction:

- Creatine kinase MB
- Lactate dehydrogenase
- Aspartate transaminase

SHORT ESSAYS

8. What is competitive enzyme inhibition. Mention the salient features and clinical relevance of competitive enzyme inhibition with the help of at least four examples.

Definition:
Inhibitor competes with substrate for active site.

Features:

- Reversible
- Km increases

- Vmax unchanged
- Can be overcome by increasing substrate concentration

Examples:

1. Malonate and succinate dehydrogenase
2. Sulfonamides and Para amino benzoic acid
3. Methotrexate and dihydrofolate reductase
4. Statins and Hydroxymethylglutaryl coenzyme A reductase

9. What are isoenzymes? Explain the clinical significance of the isoenzymes of CPK.

Isoenzymes:
Different molecular forms of same enzyme catalyzing same reaction.

Creatine phosphokinase isoenzymes:

- CK BB – brain
- CK MB – cardiac muscle
- CK MM – skeletal muscle

Clinical significance:

- CK MB increases in myocardial infarction
- Helps in diagnosis of cardiac muscle damage

10. Explain the effect of Temperature and Substrate concentration on enzyme activity

Temperature:

- Activity increases up to optimum temperature
- High temperature causes denaturation
- Optimum around 37 degree Celsius in humans

Substrate concentration:

- Activity increases with substrate concentration till maximum velocity is reached

11. Enumerate three important Isoenzymes having clinical significance

1. Creatine kinase
2. Lactate dehydrogenase
3. Alkaline phosphatase

12. What are the different types of enzyme inhibition. Explain with suitable examples

Types:

1. Competitive inhibition – Malonate
2. Non competitive inhibition – Cyanide
3. Uncompetitive inhibition
4. Suicide inhibition – Allopurinol

13. Competitive Inhibition of enzymes

Inhibitor resembles substrate and competes for active site.

Examples:

- Sulfonamides
- Methotrexate
- Statins

14. Define competitive inhibition. Describe the features of competitive inhibition Give three examples.

Definition:
Reversible inhibition where inhibitor competes for active site.

Features:

- Km increased
- Vmax unchanged
- Reversible

Examples:

- Malonate
- Sulfonamides
- Methotrexate

15. Name four therapeutically important enzymes and their significance

1. Streptokinase – thrombolysis
2. Asparaginase – leukemia treatment
3. Hyaluronidase – increases drug diffusion
4. Trypsin – wound debridement

16. Describe the salient features of any two types of enzyme inhibition with suitable examples

Competitive inhibition:

- Active site competition
- Reversible
- Example: Malonate

Non competitive inhibition:

- Inhibitor binds at separate site
- Vmax decreases
- Example: Cyanide

17. What are isoenzymes? Discuss diagnostic importance of isoenzymes.

Definition:
Isoenzymes are different forms of same enzyme.

Diagnostic importance:

- CK MB in myocardial infarction
- Lactate dehydrogenase isoenzymes in cardiac disease
- Alkaline phosphatase isoenzymes in liver and bone disease

18. What are enzymes? Explain briefly the factors affecting the velocity of enzyme catalyzed reactions

Definition:
Enzymes are biological catalysts.

Factors affecting velocity:

- Temperature
- pH
- Substrate concentration
- Enzyme concentration
- Inhibitors

19. Diagnostic significance of serum enzymes

- Alanine transaminase and Aspartate transaminase in liver disease
- CK MB in myocardial infarction
- Amylase and lipase in pancreatitis
- Alkaline phosphatase in obstructive jaundice

SHORT ANSWERS

20. Name the enzymes that help in the diagnosis of

a) Liver disease b) Pancreatic disease

a) Liver disease:

- Alanine transaminase
- Aspartate transaminase
- Alkaline phosphatase
- Gamma glutamyl transferase

b) Pancreatic disease:

- Amylase
- Lipase

21. Describe the Biochemical basis of - Difluoromethyl ornithine (DFMO) is effective against trypanosomiasis.

Difluoromethyl ornithine inhibits ornithine decarboxylase required for polyamine synthesis in Trypanosomes.

22. What is Allosteric inhibition of enzymes. Give one example.

Allosteric inhibitor binds at site other than active site and decreases enzyme activity.

Example:
ATP inhibits phosphofructokinase.

23. Km value and its significance

Km:
Substrate concentration at half maximal velocity.

Significance:

- Indicates affinity between enzyme and substrate
- Lower Km means higher affinity

24. Classification of enzymes with suitable examples.

1. Oxidoreductases – Lactate dehydrogenase
2. Transferases – Transaminases
3. Hydrolases – Lipase
4. Lyases – Aldolase
5. Isomerases – Mutase
6. Ligases – Carboxylase

25. Write briefly on Covalent modification of enzymes with two suitable examples.

Enzyme activity regulated by reversible phosphorylation and dephosphorylation.

Examples:

1. Glycogen phosphorylase
2. Glycogen synthase

26. Give 2 examples for therapeutic use of enzymes

1. Streptokinase in myocardial infarction
2. Asparaginase in leukemia

27. Define isoenzymes. Discuss the clinical significance of different isoenzyme variants of creatine kinase

Definition:
Different molecular forms of same enzyme.

Variants:

- CK BB
- CK MB
- CK MM

Clinical significance:
CK MB elevated in myocardial infarction.

28. Isoenzymes and its diagnostic importance

- CK MB in myocardial infarction
- Lactate dehydrogenase isoenzymes in cardiac disease
- Alkaline phosphatase isoenzymes in liver and bone disease

29. Isoenzymes and their clinical significance

Clinical significance:

- Diagnosis of myocardial infarction

- Differentiation of liver and bone diseases
- Detection of tissue damage

30. Suicide inhibition? Explain with one example

Irreversible inhibition where inhibitor permanently inactivates enzyme.

Example:
Allopurinol inhibits xanthine oxidase.

31. Diagnostic importance of enzymes

- Liver diseases
- Myocardial infarction
- Pancreatitis
- Bone diseases

32. Non competitive inhibition

Inhibitor binds at site other than active site.

Features:

- Vmax decreases
- Km unchanged

Example:
Cyanide inhibition of cytochrome oxidase.

33. List two examples of competitive inhibition with its clinical significance

1. Statins – hypercholesterolemia treatment
2. Methotrexate – cancer chemotherapy

34. Types of specificity of enzymes with examples

1. Absolute specificity – Urease
2. Group specificity – Hexokinase
3. Optical specificity – L amino acid oxidase
4. Bond specificity – Lipase

35. Isoenzymes of creatine phosphokinase

- CK BB – brain
- CK MB – cardiac muscle
- CK MM – skeletal muscle

36. Name four enzymes of diagnostic significance of liver disease

- Alanine transaminase
- Aspartate transaminase
- Alkaline phosphatase
- Gamma glutamyl transferase

37. Define Km value and its significance

Km:
Substrate concentration at half maximum velocity.

Significance:

- Measures enzyme affinity
- Low Km indicates high affinity

38. Pro-enzymes

Inactive precursor forms of enzymes.

Examples:

- Trypsinogen
- Pepsinogen

39. Michaelis menten constant

Michaelis Menten constant is substrate concentration at which reaction velocity is half of maximum velocity.

40. Allosteric enzymes

Enzymes regulated by binding of modulators at allosteric site.

Example:
Phosphofructokinase.

41. Iso-enzymes

Different molecular forms of same enzyme catalyzing same reaction.

42. Enzyme markers of myocardial infarction

- CK MB
- Lactate dehydrogenase
- Troponins
- Aspartate transaminase

43. Covalent modification

Regulation of enzyme activity by reversible covalent changes like phosphorylation.

CHEMISTRY OF CARBOHYDRATES

SHORT ESSAYS

1. Composition, location and functions of mucopolysaccharides

Definition:
Mucopolysaccharides are glycosaminoglycans composed of repeating disaccharide units.

Composition:

- Amino sugar
- Uronic acid

Examples and location:

1. Hyaluronic acid – connective tissue
2. Chondroitin sulfate – cartilage
3. Keratan sulfate – cornea
4. Heparin – mast cells

Functions:

- Structural support
- Lubrication
- Anticoagulant action
- Water binding

2. Define and classify Polysaccharides with examples. Write clinical applications of any three polysaccharides

Definition:
Polysaccharides are polymers of monosaccharides.

Classification:

1. Homopolysaccharides

- Starch
- Glycogen
- Cellulose

2. Heteropolysaccharides

- Hyaluronic acid
- Chondroitin sulfate

Clinical applications:

1. Heparin – anticoagulant
2. Dextran – plasma expander
3. Hyaluronic acid – ophthalmic surgery

3. Classify carbohydrates with suitable examples. What are epimers ?

Classification:

1. Monosaccharides – glucose
2. Disaccharides – sucrose
3. Oligosaccharides
4. Polysaccharides – glycogen

Epimers:
Sugars differing in configuration around one carbon atom.

Examples:

- Glucose and galactose
- Glucose and mannose

SHORT ANSWERS

4. What are glycosaminoglycans. Give four examples and mention their functions.

Definition:
Long unbranched heteropolysaccharides containing amino sugars and uronic acids.

Examples:

- Hyaluronic acid
- Chondroitin sulfate
- Heparin
- Keratan sulfate

Functions:

- Structural support
- Lubrication
- Anticoagulant action

5. Invert sugar

Mixture of glucose and fructose formed by hydrolysis of sucrose.

6. What are mucopolysaccharides. Give examples.

Mucopolysaccharides are glycosaminoglycans made of repeating disaccharide units.

Examples:

- Hyaluronic acid
- Heparin
- Chondroitin sulfate

7. Compare and contrast amylose and amylopectin.

Feature	Amylose	Amylopectin
Structure	Linear	Branched
Bond	Alpha 1,4	Alpha 1,4 and alpha 1,6
Solubility	Less soluble	More soluble
Iodine test	Blue	Violet

8. Dietary fibre

Non digestible plant carbohydrates.

Functions:

- Prevents constipation
- Lowers cholesterol
- Reduces colon cancer risk

9. Why sucrose is a non reducing sugar ?

Both anomeric carbons of glucose and fructose are involved in glycosidic bond, so free aldehyde or keto group is absent.

10. Importance of dietary fibre

- Prevents constipation
- Reduces cholesterol
- Helps control diabetes mellitus
- Prevents colon cancer

11. Isomerism of carbohydrates

Types:

1. Structural isomerism
2. Stereoisomerism
    - Enantiomers
    - Epimers
    - Anomers

Examples:

- Glucose and fructose are structural isomers
- Glucose and galactose are epimers

12. Epimers

Epimers are sugars differing in configuration around one carbon atom other than the anomeric carbon.

Examples:

- Glucose and galactose
- Glucose and mannose

13. Differentiate between starch and glycogen

Feature	Starch	Glycogen
Source	Plant storage polysaccharide	Animal storage polysaccharide
Branching	Less branched	Highly branched
Components	Amylose and amylopectin	Glycogen only
Iodine test	Blue color	Red brown color

14. mutarotation

Change in optical rotation due to interconversion of alpha and beta forms of sugar in solution.

15. What are glycosaminoglycans? List two examples with its function

Definition:
Glycosaminoglycans are long unbranched heteropolysaccharides composed of repeating disaccharide units.

Examples with functions:

1. Hyaluronic acid – lubrication of joints
2. Heparin – anticoagulant action

CHEMISTRY OF LIPIDS

SHORT ESSAYS

1. Structure and functions of phospholipid

Structure:
Phospholipids contain:

- Glycerol backbone
- Two fatty acids
- Phosphoric acid
- Nitrogenous base

Types:

- Lecithin
- Cephalin
- Sphingomyelin

Functions:

- Components of cell membrane
- Lung surfactant formation
- Lipid transport
- Signal transduction
- Formation of lipoproteins

2. Classify phospholipids and enumerate their functions

Classification:

1. Glycerophospholipids

- Lecithin
- Cephalin
- Cardiolipin

2. Sphingophospholipids

- Sphingomyelin

Functions:

- Structural components of membrane
- Lung surfactant
- Lipid absorption
- Cell signaling
- Blood coagulation

3. Functions of phospholipids

- Structural components of cell membrane
- Formation of lipoproteins
- Lung surfactant action
- Absorption and transport of lipids
- Signal transduction
- Source of arachidonic acid

4. What are essential fatty acids. Enumerate them. List two functions and one deficiency manifestation

Definition:
Essential fatty acids cannot be synthesized in the body and must be supplied in diet.

Essential fatty acids:

- Linoleic acid
- Linolenic acid
- Arachidonic acid

Functions:

1. Component of cell membrane
2. Formation of eicosanoids

Deficiency manifestation:
Phrynoderma.

SHORT ANSWERS

5. List any four phospholipids with their significance.

1. Lecithin – lung surfactant
2. Cephalin – blood coagulation
3. Cardiolipin – inner mitochondrial membrane
4. Sphingomyelin – myelin sheath formation

6. Lung Surfactant.

Lung surfactant reduces surface tension in alveoli.

Main component:
Dipalmitoyl phosphatidylcholine.

Functions:

- Prevents alveolar collapse
- Helps lung expansion

7. Micelles

Micelles are aggregates of amphipathic lipids formed in aqueous solution.

Function:
Help in absorption of lipids in intestine.

8. Liposomes.

Liposomes are vesicles composed of phospholipid bilayers.

Uses:

- Drug delivery
- Gene therapy

9. Give reason: " Premature infants have higher incidence of Respiratory Distress Syndrome"

Premature infants have deficient lung surfactant due to immature lungs causing alveolar collapse.

10. Trans fatty acids

Unsaturated fatty acids with trans configuration.

Sources:
Hydrogenated vegetable oils.

Effects:
Increase risk of coronary artery disease.

11. Functions of phospholipids

- Membrane structure
- Lipoprotein formation
- Lung surfactant
- Cell signaling

12. What are amphipathic lipids. Add a note on its significance

Definition:
Lipids containing both hydrophilic and hydrophobic regions.

Significance:

- Formation of cell membranes
- Formation of micelles and liposomes
- Lipid transport

13. Name two phospholipids and their functions

1. Lecithin – lung surfactant
2. Cephalin – coagulation process

14. Essential fatty acids

- Linoleic acid
- Linolenic acid
- Arachidonic acid

Functions:

- Membrane integrity
- Eicosanoid synthesis

15. Name the lung surfactant and mention its components

Lung surfactant:
Dipalmitoyl phosphatidylcholine.

Components:

- Phospholipids
- Surfactant proteins
- Cholesterol

16. Classification of glycolipids

1. Cerebrosides
2. Sulfatides
3. Gangliosides

GENERAL METABOLISM

OVER VIEW OF METABOLISM

1. Metabolic changes in the body during brief fasting

- Glycogenolysis increases
- Gluconeogenesis starts
- Lipolysis increases
- Blood glucose maintained
- Insulin decreases and glucagon increases

2. Role of Liver in integration of metabolism

- Maintains blood glucose
- Glycogen storage
- Gluconeogenesis
- Lipid metabolism
- Protein synthesis
- Urea formation

- Detoxification

METABOLIC PATHWAYS OF GLUCOSE

LONG ESSAYS

1. A 2-year-old child presented with liver enlargement and complaints of weakness, sweating and pallor which disappeared on eating food. Mother revealed that milestones were delayed. On investigation, blood glucose: 50mg/dl, uric acid: 10 mg/dl, lactic acid: 15 mg/dl, cholesterol: 300 mg/dl, and presence of ketone bodies.

a) What is the likely diagnosis

b) Name the enzyme defect

c) Discuss the pathways that lead to elevated levels of uric acid, lactic acid, and cholesterol

d) Discuss the reason for liver enlargement

e) Give the normal reference range for serum cholesterol and Fasting blood glucose.

Diagnosis:
Von Gierke's disease.

Enzyme defect:
Glucose 6 phosphatase deficiency.

Biochemical basis:

- Glucose 6 phosphate accumulates
- Increased glycolysis causes lactic acidosis
- Excess lactate reduces uric acid excretion causing hyperuricemia
- Excess acetyl coenzyme A increases cholesterol synthesis

Reason for hepatomegaly:
Excess glycogen accumulation in liver.

Normal values:

- Fasting blood glucose: 70–110 mg/dl
- Serum cholesterol: 150–200 mg/dl

2. Define gluconeogenesis. Name the substrates for gluconeogenesis. Trace the pathway of gluconeogenesis from pyruvate to glucose. Add a note on its regulation.

Definition:
Formation of glucose from non carbohydrate precursors.

Substrates:

- Lactate
- Alanine
- Glycerol
- Propionate

Pathway:
Pyruvate → Oxaloacetate → Phosphoenolpyruvate → Fructose 1,6 bisphosphate → Fructose 6 phosphate → Glucose 6 phosphate → Glucose.

Key enzymes:

1. Pyruvate carboxylase
2. Phosphoenolpyruvate carboxykinase
3. Fructose 1,6 bisphosphatase
4. Glucose 6 phosphatase

Regulation:

- Glucagon stimulates
- Insulin inhibits

- Fructose 2,6 bisphosphate inhibits gluconeogenesis

3. A 2-year-old child presented with complaints of on and off vomiting and lethargy for past two months. On examination child had a massive liver enlargement. Blood investigation reports were as follows: Blood sugar: 50mg%, Uric acid:10mg%, lactic acid:15mg%, Total cholesterol:300mg%. Liver biopsy demonstrated the mosaic pattern of enlarged hepatocytes, exhibiting abundant clear cytoplasm containing glycogen and lipid vacuoles.

a) What is the diagnosis

b) Name other glycogen storage disorders

c) Explain how glycogen is metabolized in the body

d) Explain the hormonal regulation of glycogen metabolism

Diagnosis:
Von Gierke's disease.

Other glycogen storage disorders:

- Pompe disease
- Cori disease
- Andersen disease
- McArdle disease
- Hers disease

Glycogen metabolism:

- Glycogenesis forms glycogen
- Glycogenolysis breaks glycogen

Hormonal regulation:

- Insulin stimulates glycogenesis
- Glucagon and adrenaline stimulate glycogenolysis

4. Explain the pathways by which glycogen is synthesized and broken down in the body. Describe how these pathways are regulated

Glycogenesis:
Glucose → Glucose 6 phosphate → Glucose 1 phosphate → Uridine diphosphate glucose → Glycogen.

Key enzymes:

- Glycogen synthase
- Branching enzyme

Glycogenolysis:
Glycogen → Glucose 1 phosphate → Glucose 6 phosphate.

Key enzymes:

- Glycogen phosphorylase
- Debranching enzyme

Regulation:

- Insulin activates glycogen synthase
- Glucagon activates glycogen phosphorylase

5. Trace the pathway of gluconeogenesis starting from alanine. Mention the key enzymes and how they are regulated

Alanine → Pyruvate → Oxaloacetate → Phosphoenolpyruvate → Glucose.

Key enzymes:

- Alanine transaminase
- Pyruvate carboxylase
- Phosphoenolpyruvate carboxykinase
- Fructose 1,6 bisphosphatase

- Glucose 6 phosphatase

Regulation:

- Stimulated by glucagon and cortisol
- Inhibited by insulin

6. Explain the reactions of glycogenesis and glycogenolysis with flow diagrams. Describe how these processes are regulated

Glycogenesis:
Glucose → Glucose 6 phosphate → Glucose 1 phosphate → Uridine diphosphate glucose → Glycogen.

Glycogenolysis:
Glycogen → Glucose 1 phosphate → Glucose 6 phosphate → Glucose.

Regulation:

- Insulin stimulates glycogenesis
- Glucagon and epinephrine stimulate glycogenolysis

7. Explain in detail glycogenesis and glycogenolysis. Mention the enzyme defects in any two of glycogen storage disorders

Glycogenesis:
Synthesis of glycogen from glucose.

Glycogenolysis:
Breakdown of glycogen to glucose.

Glycogen storage disorders:

1. Von Gierke disease – glucose 6 phosphatase deficiency
2. McArdle disease – muscle glycogen phosphorylase deficiency

8. Describe by a flow diagram the reactions of glycolysis giving names of enzymes involved. Explain its regulation and add a note on the energetics in aerobic and anaerobic conditions

Definition:
Glycolysis is conversion of glucose to pyruvate.

Pathway:
Glucose → Glucose 6 phosphate → Fructose 6 phosphate → Fructose 1,6 bisphosphate → Glyceraldehyde 3 phosphate → Pyruvate.

Key regulatory enzymes:

1. Hexokinase
2. Phosphofructokinase 1
3. Pyruvate kinase

Regulation:

- Insulin stimulates glycolysis
- ATP and citrate inhibit phosphofructokinase

Energetics:

- Aerobic glycolysis: 8 Adenosine triphosphate
- Anaerobic glycolysis: 2 Adenosine triphosphate

SHORT ESSAYS

9. What is gluconeogenesis. Name the substrates of this pathway. Describe the reactions catalyzed by the key regulatory enzyme of gluconeogenesis.

Definition:
Formation of glucose from non carbohydrate precursors.

Substrates:

- Lactate
- Alanine
- Glycerol

Key regulatory enzyme:
Fructose 1,6 bisphosphatase converts fructose 1,6 bisphosphate to fructose 6 phosphate.

10. Write down the steps involved in conversion of glycerol to glucose.

Glycerol → Glycerol 3 phosphate → Dihydroxyacetone phosphate → Fructose 1,6 bisphosphate → Glucose.

11. What are the reactions that form NADPH. List any FOUR reactions where NADPH is utilised.

Formation of NADPH:

- Glucose 6 phosphate dehydrogenase reaction
- 6 phosphogluconate dehydrogenase reaction
- Malic enzyme reaction

Utilization:

1. Fatty acid synthesis
2. Cholesterol synthesis
3. Glutathione reduction
4. Cytochrome P450 reactions

12. Describe HMP shunt pathway. Add a note on the significance of the pathway.

Definition:
Alternative pathway of glucose oxidation producing NADPH and ribose 5 phosphate.

Phases:

1. Oxidative phase
2. Non oxidative phase

Significance:

- NADPH production
- Ribose synthesis
- Maintenance of reduced glutathione

13. Glucose transporters

Types:

- GLUT 1 – erythrocytes
- GLUT 2 – liver and pancreas
- GLUT 3 – brain
- GLUT 4 – muscle and adipose tissue
- GLUT 5 – fructose transport

14. Explain glycolysis, regulation and its energetics

Definition:
Breakdown of glucose to pyruvate.

Regulation:

- Hexokinase
- Phosphofructokinase
- Pyruvate kinase

Energetics:

- Aerobic: 8 Adenosine triphosphate
- Anaerobic: 2 Adenosine triphosphate

15. Cori's cycle and its significance

Lactate formed in muscle is transported to liver and converted to glucose.

Significance:

- Prevents lactic acidosis
- Maintains blood glucose

16. Glycogenolysis and its regulation

Breakdown of glycogen to glucose 1 phosphate.

Regulation:

- Glucagon and epinephrine stimulate
- Insulin inhibits

17. Gluconeogenesis

Formation of glucose from non carbohydrate precursors.

Site:
Liver and kidney.

Key enzymes:

- Pyruvate carboxylase
- Phosphoenolpyruvate carboxykinase
- Fructose 1,6 bisphosphatase
- Glucose 6 phosphatase

18. Mention the major functions of HMP shunt pathway. Explain its importance in erythrocytes.

Functions:

- NADPH generation
- Ribose synthesis

Importance in erythrocytes:
NADPH maintains reduced glutathione protecting erythrocytes from oxidative damage.

19. Glycogen storage diseases

Inherited disorders due to defects in glycogen metabolism.

Examples:

- Von Gierke disease
- Pompe disease
- Cori disease
- McArdle disease

20. Discuss the regulation of glycogen metabolism

- Insulin stimulates glycogenesis
- Glucagon stimulates glycogenolysis
- Covalent modification regulates glycogen synthase and phosphorylase

21. Explain the digestion and absorption of carbohydrates

Digestion:

- Salivary amylase acts in mouth
- Pancreatic amylase acts in intestine
- Disaccharidases act at brush border

Absorption:

- Glucose and galactose by Sodium glucose linked transporter 1
- Fructose by GLUT 5

SHORT ANSWERS

22. Enumerate the different types of Glucose transporters and their locations. Add a note on glucose absorption in GIT.

Transporters:

- GLUT 1 – erythrocytes
- GLUT 2 – liver
- GLUT 3 – brain
- GLUT 4 – muscle and adipose tissue
- GLUT 5 – intestine

Glucose absorption:
Glucose absorbed by Sodium glucose linked transporter 1 in intestine.

23. Give reason - 2,3 BPG concentration in RBCs increases in hypoxic conditions.

In hypoxia, increased 2,3 bisphosphoglycerate decreases hemoglobin affinity for oxygen facilitating oxygen release to tissues.

24. Cori's cycle

Lactate produced in muscle is converted to glucose in liver.

25. Give the differences between hexokinase and glucokinase.

Feature	Hexokinase	Glucokinase
Site	Most tissues	Liver and pancreas
Km	Low	High
Specificity	Broad	Specific for glucose
Inhibition	Inhibited by glucose 6 phosphate	Not inhibited

26. Essential pentosuria

Rare disorder due to L xylulose reductase deficiency causing excretion of pentose sugars in urine.

27. What is Von Gierkes disease. Name the enzyme involved.

Glycogen storage disease due to glucose 6 phosphatase deficiency.

28. Fate of pyruvate

- Conversion to acetyl coenzyme A
- Conversion to lactate
- Conversion to oxaloacetate
- Transamination to alanine

29. Von Gierke's disease

Glycogen storage disease type I caused by glucose 6 phosphatase deficiency.

Features:

- Severe hypoglycemia
- Hepatomegaly
- Lactic acidosis

30. Products of HMP shunt pathway

- NADPH
- Ribose 5 phosphate
- Carbon dioxide

31. Describe the digestion and absorption of carbohydrates

- Salivary and pancreatic amylase digest starch
- Brush border enzymes digest disaccharides
- Glucose absorbed by Sodium glucose linked transporter 1

32. Significance of HMP shunt pathway

- NADPH production
- Ribose synthesis
- Reduced glutathione maintenance

33. Lactose intolerance

Deficiency of lactase enzyme causing inability to digest lactose.

Symptoms:

- Diarrhea
- Flatulence
- Abdominal pain

34. Uronic acid pathway

Alternative oxidative pathway of glucose producing glucuronic acid.

Functions:

- Detoxification
- Vitamin C synthesis in animals

35. Substrate level phosphorylation

Formation of Adenosine triphosphate directly from high energy substrate.

Examples:

- Phosphoglycerate kinase reaction
- Pyruvate kinase reaction

36. Enumerate the clinical significance of HMP pathway

- Prevents hemolysis in erythrocytes
- Required for fatty acid synthesis
- Required for steroid synthesis

37. Formation of 2,3 BPG

Formed from 1,3 bisphosphoglycerate by Rapaport Luebering shunt in erythrocytes.

38. Rapaport Leubering pathway

Pathway in erythrocytes producing 2,3 bisphosphoglycerate.

Function:
Facilitates oxygen release from hemoglobin.

39. Mention the significance of hexose monophosphate shunt pathway

- NADPH generation
- Ribose synthesis
- Maintenance of reduced glutathione

40. Enumerate irreversible steps of glycolysis with the enzymes involved

1. Glucose → Glucose 6 phosphate – Hexokinase
2. Fructose 6 phosphate → Fructose 1,6 bisphosphate – Phosphofructokinase
3. Phosphoenolpyruvate → Pyruvate – Pyruvate kinase

41. Define gluconeogenesis. Name the gluconeogenic substrates

Definition:
Formation of glucose from non carbohydrate sources.

Substrates:

- Lactate
- Glycerol
- Alanine
- Propionate

42. Pyruvate dehydrogenase complex

Complex converting pyruvate to acetyl coenzyme A.

Coenzymes:

- Thiamine pyrophosphate
- Lipoic acid
- Coenzyme A
- Flavin adenine dinucleotide
- Nicotinamide adenine dinucleotide

43. Name three glycogen storage disease and its biochemical defect

1. Von Gierke disease – glucose 6 phosphatase deficiency
2. Pompe disease – acid maltase deficiency
3. McArdle disease – muscle glycogen phosphorylase deficiency

44. Digestion of carbohydrates

- Salivary amylase digests starch
- Pancreatic amylase acts in intestine
- Brush border enzymes form monosaccharides

45. What is glucose alanine cycle and mention its significance

Alanine transports amino groups from muscle to liver.

Significance:

- Gluconeogenesis
- Nitrogen transport

46. Lactose intolerance

Deficiency of lactase enzyme causing osmotic diarrhea after milk intake.

47. Gluconeogenesis

Formation of glucose from lactate, glycerol and amino acids.

48. Two co-enzyme roles of NADPH

1. Fatty acid synthesis
2. Reduced glutathione formation

49. Glucose transporters

- GLUT 1 – erythrocytes
- GLUT 2 – liver
- GLUT 3 – brain
- GLUT 4 – muscle and adipose tissue
- GLUT 5 – intestine

REGULATION OF BLOOD GLUCOSE, INSULIN AND DIABETES MELLITUS

LONG ESSAYS

1. A 51 years male came to medical OPD with complaints of feeling weak and tired for past 2 months. He had polyuria, polydipsia and felt hungry in between meals. He also has family history of Diabetes. His lab reports are : Fasting blood glucose: 176 mg/dl, Postprandial blood glucose: 410 mg/dl, Blood urea: 27mg/dl, HbA1c- 14%, Urine: albumin - nil, Sugar +++, Ketone bodies - nil.

a) What is the probable diagnosis

b) Enumerate the diagnostic criteria for Diabetes Mellitus as per American Diabetes Association (ADA).

c) Discuss lab investigations done to diagnose Diabetes Mellitus with their normal levels

Diagnosis: Type 2 Diabetes Mellitus.

ADA diagnostic criteria:

1. Fasting plasma glucose ≥126 mg/dl
2. Post glucose value ≥200 mg/dl during oral glucose tolerance test
3. Random blood glucose ≥200 mg/dl with symptoms
4. HbA1c ≥6.5%

Investigations and normal values:

- Fasting blood glucose: 70–110 mg/dl
- Postprandial blood glucose: <140 mg/dl
- Random blood glucose: <140 mg/dl
- HbA1c: <5.7%
- Urine sugar: absent

2. Mention the normal glucose levels in fasting, post prandial and random samples and HbA1c levels. Explain the homeostasis of Blood glucose levels in well fed condition and during starvation.

Normal values:

- Fasting blood glucose: 70–110 mg/dl
- Postprandial glucose: <140 mg/dl
- Random blood glucose: <140 mg/dl
- HbA1c: <5.7%

Well fed state:

- Insulin secretion increases
- Glycolysis and glycogenesis increase
- Lipogenesis increases

Starvation:

- Glucagon increases
- Glycogenolysis and gluconeogenesis increase
- Lipolysis and ketogenesis increase

3. A 45-year-old man complains of increased appetite, thirst, and frequent micturition.His random blood sugar is 346 mg/dl

• What is the diagnosis.What are the diagnostic criteria

• Discuss the relevant investigations that can be done for further monitoring of the patient

• How is blood glucose regulated

• What is the renal threshold for Glucose

Diagnosis: Type 2 Diabetes Mellitus.

Diagnostic criteria:

- Fasting plasma glucose ≥126 mg/dl
- Random blood glucose ≥200 mg/dl with symptoms
- HbA1c ≥6.5%

Monitoring investigations:

- Fasting and postprandial glucose
- HbA1c
- Urine sugar and ketones
- Lipid profile
- Renal function tests

Regulation of blood glucose:

- Insulin lowers blood glucose
- Glucagon increases blood glucose
- Cortisol and epinephrine increase glucose

Renal threshold for glucose:
Approximately 180 mg/dl.

4. A 45-year-old bank manager visits the OPD with increased frequency of urination (Polyuria), Increased thirst (Polydipsia) and increased hunger (Polyphagia). He also gives the history of weight loss. On general examination, there were no significant findings. The laboratory investigations were as follows:

Test | Result | Biological reference interval

Random blood glucose level | 316 mg/dl | 70-140 mg/dl

Urine sugar | ++++ | NIL

Answer the following questions using the above data:

• What is the diagnosis.

• Mention various methods for estimation of glucose

• What are WHO criteria for diagnosis of this disorder

• Why urine sugar was positive in this patient

• Describe the various factors that regulate blood glucose level

Diagnosis: Type 2 Diabetes Mellitus.

Methods for glucose estimation:

- Glucose oxidase method
- Hexokinase method
- Orthotoluidine method

WHO criteria:

- Fasting plasma glucose ≥126 mg/dl
- Two hour post glucose ≥200 mg/dl
- Random blood glucose ≥200 mg/dl with symptoms

Reason for glycosuria: Blood glucose exceeds renal threshold causing glucose excretion in urine.

Factors regulating blood glucose:

- Insulin
- Glucagon
- Cortisol
- Growth hormone
- Epinephrine

5. 23-year-old female was brought to casualty with the complaints of dizziness, weakness and fainting attack. History revealed that she had skipped her breakfast and lunch with intention of losing weight Random blood glucose was 40 mg/dl.

All other investigations were normal.

• What is the probable diagnosis

• What is the normal blood glucose level

• Describe the regulation of blood glucose.

• Add a note on glucose tolerance test.

Diagnosis: Hypoglycemia.

Normal blood glucose: 70–110 mg/dl fasting.

Regulation of blood glucose:

- Insulin decreases blood glucose
- Glucagon, cortisol and epinephrine increase blood glucose

Glucose tolerance test: Used to diagnose diabetes mellitus.

Procedure:

- Fasting blood sample collected
- 75 g glucose given orally
- Blood glucose measured after 2 hours

SHORT ESSAYS

6. Describe metabolic changes in fed state

Hormonal status: High insulin and low glucagon.

Carbohydrate metabolism:

- Glycolysis increases
- Glycogenesis increases

Lipid metabolism:

- Lipogenesis increases
- Fatty acid synthesis increases

Protein metabolism:

- Protein synthesis increases

7. A ten-year-old boy presented with a history of fever since 3 days, disturbance

of consciousness, accompanied by thirst, fruity odour of breath and deep laboured breathing. On examination pulse: 120/min, blood pressure: 90/50 mmHg, temperature: 38°C, respiratory rate: 30 breaths/min, Blood glucose: 407 mg/dL and ketone bodies present in urine.

a) What is the probable diagnosis

b) Explain how ketone bodies are formed and utilised in the body

Diagnosis: Diabetic ketoacidosis.

Formation of ketone bodies: Occurs in liver mitochondria from acetyl coenzyme A.

Acetyl coenzyme A → Acetoacetate → Beta hydroxybutyrate and acetone.

Utilization: Ketone bodies converted to acetyl coenzyme A in extrahepatic tissues and oxidized for energy.

8. A 49-year-old woman was admitted to hospital. She had polyuria, lost weight, had a fruity odour in breath. The following were her lab reports.Blood glucose= 450 mg/dl, Urine glucose 4+, Urine Rothera's test= positive, Urine pH= 5.5.

a) What is the probable diagnosis.

b) Explain the clinical features of the disorder.

c) Write briefly about ketogenesis.

Diagnosis: Diabetic ketoacidosis.

Clinical features:

- Polyuria
- Polydipsia
- Weight loss
- Fruity breath odor
- Kussmaul respiration

Ketogenesis: Occurs in liver from excess acetyl coenzyme A producing acetoacetate, beta hydroxybutyrate and acetone.

9. Glucose Tolerance Test – give two indications. Explain the different responses seen

Indications:

1. Suspected diabetes mellitus
2. Gestational diabetes mellitus

Responses:

- Normal curve
- Diabetic curve
- Impaired glucose tolerance curve

10. Define obesity. What are the metabolic changes and complications of obesity

Definition: Excess accumulation of body fat.

Metabolic changes:

- Insulin resistance
- Hyperlipidemia
- Increased free fatty acids

Complications:

- Type 2 diabetes mellitus
- Hypertension
- Coronary artery disease
- Fatty liver

11. Absorption of carbohydrates.

- Monosaccharides absorbed in small intestine
- Glucose and galactose by Sodium glucose linked transporter 1
- Fructose by GLUT 5
- Glucose exits by GLUT 2

12. Regulation of blood glucose level

- Insulin lowers glucose
- Glucagon raises glucose
- Cortisol and epinephrine raise glucose
- Liver maintains glucose homeostasis

SHORT ANSWERS

13. Biochemical basis of- "Adding KCl to Insulin while treating DKA"

Insulin drives potassium into cells causing hypokalemia. Potassium chloride supplementation prevents severe hypokalemia.

14. Hormones regulating blood glucose level

- Insulin
- Glucagon
- Epinephrine
- Cortisol
- Growth hormone

15. Hypoglycemia

Blood glucose less than normal level.

Symptoms:

- Sweating
- Tremors
- Weakness
- Confusion

16. Renal glycosuria.

Presence of glucose in urine due to decreased renal threshold despite normal blood glucose.

17. Diagnosis of diabetes mellitus

- Fasting plasma glucose
- Postprandial glucose
- Oral glucose tolerance test
- HbA1c estimation

18. Monitoring of diabetes mellitus

- Blood glucose estimation
- HbA1c
- Urine sugar and ketones
- Lipid profile

19. What is HbA1c and mention its clinical importance

HbA1c: Glycated hemoglobin formed by non enzymatic glycation.

Clinical importance: Reflects average blood glucose over previous 2–3 months.

20. Discuss the primary structure of human insulin

Human insulin consists of:

- A chain with 21 amino acids
- B chain with 30 amino acids

Chains connected by disulfide bonds.

21. Explain why blood is collected in fluoride for glucose estimation

Sodium fluoride inhibits glycolysis preserving blood glucose level.

22. Ketosis

Definition:
Ketosis is the accumulation of ketone bodies in blood due to increased ketogenesis.

Ketone bodies:

- Acetoacetate
- Beta hydroxybutyrate
- Acetone

Causes:

- Uncontrolled diabetes mellitus
- Starvation
- Prolonged fasting
- High fat low carbohydrate diet

Clinical features:

- Fruity odor of breath
- Ketonuria
- Nausea and vomiting
- Metabolic acidosis

Significance:
Occurs when carbohydrate utilization is decreased and fat oxidation is increased, leading to excess production of ketone bodies.

METABOLIC PATHWAYS OF CARBOHYDRATES OTHER THAN GLUCOSE

SHORT ANSWERS

1. A 2-year-old baby was brought to the pediatrics department by her mother with complaints of vision problems. On examination baby was jaundiced and had cataract in both eyes. Abdomen examination showed hepatomegaly. Blood investigation showed serum bilirubin: 6.4 mg/dL and plasma glucose: 45 mg/dL

a) What is your probable diagnosis

b) What are the types, biochemical defect, clinical features and their basis, diagnosis and treatment of this disorder

Diagnosis: Galactosemia.

Types and defects:

1. Classical galactosemia – galactose 1 phosphate uridyl transferase deficiency
2. Galactokinase deficiency
3. Epimerase deficiency

Clinical features:

- Jaundice
- Cataract
- Hepatomegaly
- Hypoglycemia

Basis: Accumulation of galactose and galactitol.

Diagnosis:

- Reducing sugar in urine
- Enzyme assay

Treatment: Galactose and lactose restricted diet.

2. Galactosemia

Definition

Galactosemia is an inherited disorder of galactose metabolism caused commonly by deficiency of galactose-1-phosphate uridyl transferase.

Enzyme defect

- Classical galactosemia – deficiency of galactose-1-phosphate uridyl transferase (GALT)
- Galactokinase deficiency – causes cataract
- UDP galactose-4-epimerase deficiency – rare

Biochemical defect

Accumulation of:

- Galactose
- Galactose-1-phosphate
- Galactitol

Clinical features

- Vomiting and refusal of feeds
- Failure to thrive
- Jaundice
- Hepatomegaly
- Cataract
- Mental retardation
- Hypoglycemia
- Aminoaciduria
- E. coli sepsis

Diagnosis

- Reducing substances in urine
- Increased blood galactose
- Enzyme assay

Treatment

- Elimination of lactose and galactose from diet
- Soy milk substitution

3. Name three glycosaminoglycans and their functions

Glycosaminoglycan	Function
Hyaluronic acid	Lubrication in synovial fluid, ground substance of connective tissue
Chondroitin sulfate	Structural component of cartilage, bone and tendons
Heparin	Anticoagulant action

Other examples:

- Dermatan sulfate – skin and blood vessels
- Keratan sulfate – cornea and cartilage
- Heparan sulfate – basement membrane

4. Mention the enzyme defective in galactosemia. Add a note on the clinical features of galactosemia.

Defective enzyme

Classical galactosemia is due to deficiency of galactose-1-phosphate uridyl transferase.

Clinical features

- Symptoms appear after milk feeding
- Vomiting and diarrhea
- Failure to thrive
- Jaundice and hepatomegaly
- Cataract due to galactitol accumulation
- Mental retardation
- Hypoglycemia
- Aminoaciduria
- Renal tubular damage
- Increased susceptibility to E. coli infection

Treatment

Withdrawal of lactose and galactose from diet.

METABOLISM OF FATTY ACIDS

LONG ESSAYS

1. What are the types of fatty acid oxidation. Explain in detail the oxidation of palmitic acid and its regulation

Types of fatty acid oxidation

1. Beta oxidation
2. Alpha oxidation
3. Omega oxidation
4. Peroxisomal oxidation

Beta oxidation of palmitic acid

Definition

Beta oxidation is the process by which fatty acids are oxidized at the beta carbon atom with removal of two carbon units as acetyl CoA.

Site

Mitochondrial matrix.

Steps

1. Activation of palmitic acid

Palmitic acid + CoA + ATP → Palmitoyl CoA
Enzyme: Acyl CoA synthetase (thiokinase)
ATP equivalent used = 2 ATP.

2. Transport into mitochondria – Carnitine shuttle

- Carnitine palmitoyl transferase I forms acyl carnitine
- Translocase transfers it into mitochondria
- Carnitine palmitoyl transferase II reforms acyl CoA

3. Beta oxidation spiral

Each cycle has four reactions:

(i) Dehydrogenation

Acyl CoA → Trans enoyl CoA
Enzyme: Acyl CoA dehydrogenase
Coenzyme: FAD → FADH2

(ii) Hydration

Trans enoyl CoA → Beta hydroxy acyl CoA
Enzyme: Enoyl CoA hydratase

(iii) Dehydrogenation

Beta hydroxy acyl CoA → Beta keto acyl CoA
Enzyme: Beta hydroxy acyl CoA dehydrogenase
Coenzyme: NAD+ → NADH

(iv) Thiolysis

Beta keto acyl CoA → Acetyl CoA + Acyl CoA shortened by 2 carbons
Enzyme: Thiolase

Palmitic acid (16 carbons) undergoes 7 cycles producing:

- 8 acetyl CoA
- 7 NADH
- 7 FADH2

Energetics of palmitic acid oxidation

- 8 acetyl CoA × 10 ATP = 80 ATP
- 7 NADH × 2.5 ATP = 17.5 ATP
- 7 FADH2 × 1.5 ATP = 10.5 ATP
  Total = 108 ATP
  Minus 2 ATP used for activation
  Net ATP = 106 ATP

Regulation of beta oxidation

1. Carnitine palmitoyl transferase I

Rate limiting enzyme.
Inhibited by malonyl CoA.

2. Hormonal regulation

- Glucagon and epinephrine stimulate lipolysis
- Insulin inhibits lipolysis

3. Availability of carnitine

Required for transport of long chain fatty acids.

4. High NADH/NAD ratio

Inhibits beta hydroxy acyl CoA dehydrogenase.

5. High acetyl CoA concentration

Inhibits thiolase.

2. Describe the breakdown of triglycerides, the mobilization of fatty acids. Discuss the beta oxidation of palmitic acids. Add a note on its energetics

Breakdown of triglycerides

Triglycerides are hydrolysed by lipases into glycerol and fatty acids.

Lipases involved

- Hormone sensitive lipase
- Lipoprotein lipase
- Pancreatic lipase

Hormonal regulation

Stimulated by:

- Glucagon
- Epinephrine
- ACTH

Inhibited by insulin.

Mobilization of fatty acids

- Fatty acids released from adipose tissue enter blood.
- Transported bound to albumin.
- Taken up by tissues for oxidation.

Energetics

Net ATP yield = 106 ATP.

3. What are ketone bodies. How are they formed in the body. Describe the role of ketone bodies in starvation and uncontrolled diabetes mellitus.

Ketone bodies

1. Acetoacetate
2. Beta hydroxybutyrate
3. Acetone

Site of formation

Liver mitochondria.

Ketogenesis

Steps

1. Two acetyl CoA condense to form acetoacetyl CoA
   Enzyme: Thiolase
2. Acetoacetyl CoA + acetyl CoA → HMG CoA
   Enzyme: HMG CoA synthase
3. HMG CoA → Acetoacetate
   Enzyme: HMG CoA lyase
4. Acetoacetate may:

- Form beta hydroxybutyrate
- Decarboxylate to acetone

Role in starvation

- Brain adapts to ketone body utilization
- Protein breakdown decreases
- Provides energy to muscle and brain
- Conserves glucose

Role in uncontrolled diabetes mellitus

- Increased lipolysis due to insulin deficiency
- Excess acetyl CoA formed
- Increased ketogenesis
- Ketone bodies accumulate causing ketosis and ketoacidosis
- Fruity odor due to acetone
- Severe acidosis may lead to coma

4. Define Beta oxidation. Enumerate the steps and add a note on its regulation. Explain the energetics for palmitic acid.

Definition

Beta oxidation is the oxidation of fatty acids at the beta carbon atom with release of acetyl CoA.

Steps

1. Activation
2. Carnitine shuttle transport
3. Dehydrogenation
4. Hydration
5. Dehydrogenation
6. Thiolysis

Regulation

- Carnitine palmitoyl transferase I inhibited by malonyl CoA
- Hormonal control by insulin and glucagon
- Availability of carnitine
- Product inhibition by NADH and acetyl CoA

Energetics of palmitic acid

Net ATP yield = 106 ATP.

5. Name the ketone bodies. Describe their synthesis and catabolism. Write the causes of ketosis.

Ketone bodies

1. Acetoacetate
2. Beta hydroxybutyrate
3. Acetone

Synthesis (Ketogenesis)

Occurs in liver mitochondria.

Steps

1. 2 Acetyl CoA → Acetoacetyl CoA
2. Acetoacetyl CoA + Acetyl CoA → HMG CoA
3. HMG CoA → Acetoacetate
4. Acetoacetate forms beta hydroxybutyrate or acetone

Catabolism (Ketolysis)

Occurs in extrahepatic tissues.

Steps

1. Beta hydroxybutyrate → Acetoacetate
2. Acetoacetate + Succinyl CoA → Acetoacetyl CoA
   Enzyme: Thiophorase
3. Acetoacetyl CoA → 2 Acetyl CoA

Liver cannot utilize ketone bodies because thiophorase is absent.

Causes of ketosis

- Starvation
- Uncontrolled diabetes mellitus
- Low carbohydrate diet
- Pregnancy and lactation
- Vomiting

6. What is β oxidation. Describe the process of β oxidation of even chain fatty acids with energetics.

Definition

Beta oxidation is oxidation of fatty acids at the beta carbon atom.

Site

Mitochondrial matrix.

Process

1. Activation
2. Transport through carnitine shuttle
3. Four recurring reactions:

- Dehydrogenation
- Hydration
- Dehydrogenation
- Thiolysis

Example – Palmitic acid

7 cycles produce:

- 8 acetyl CoA
- 7 NADH
- 7 FADH2

Energetics

Net ATP = 106 ATP.

7. Name the site where betaoxidation of fatty acid occurs. Describe the steps involved in beta oxidation of fatty acids. Explain how much energy is released in betaoxidation of one molecule of palmitic acid

Site

Mitochondrial matrix.

Steps

1. Activation
2. Carnitine shuttle
3. Dehydrogenation
4. Hydration
5. Dehydrogenation
6. Thiolysis

Energy released from one molecule of palmitic acid

Net ATP generated = 106 ATP.

8. Explain the oxidation of palmitate in mitochondria. Describe how the process is regulated. Mention the number of high energy phosphate bonds generated in palmitate oxidation

Oxidation of palmitate

Occurs through beta oxidation in mitochondrial matrix.

Steps

- Activation
- Carnitine shuttle transport
- Repeated cycles of:
    - FAD linked oxidation
    - Hydration
    - NAD linked oxidation
    - Thiolysis

Regulation

- CPT I inhibited by malonyl CoA
- Hormonal regulation by insulin and glucagon
- Product inhibition by NADH and acetyl CoA

High energy phosphate bonds generated

Net ATP = 106 ATP.
Traditional value = 129 ATP.

9. Define β-Oxidation. Explain the reactions of β-oxidation of palmitic acid. Add a note on its energies

Definition

Beta oxidation is oxidation of fatty acids at beta carbon atom.

Reactions

1. Activation of palmitate
2. Carnitine shuttle
3. Acyl CoA dehydrogenase reaction
4. Enoyl CoA hydratase reaction
5. Beta hydroxy acyl CoA dehydrogenase reaction
6. Thiolase reaction

Energies

Net ATP yield = 106 ATP.

SHORT ESSAYS

10. Describe how ketone bodies are formed and degraded in the human body

Formation

Occurs in liver mitochondria.

Steps:

1. 2 Acetyl CoA → Acetoacetyl CoA
2. Formation of HMG CoA
3. HMG CoA → Acetoacetate
4. Acetoacetate forms beta hydroxybutyrate and acetone

Degradation

Occurs in extrahepatic tissues.

Steps:

1. Beta hydroxybutyrate → Acetoacetate
2. Acetoacetate activated by thiophorase
3. Acetoacetyl CoA split into 2 acetyl CoA

11. Define Beta Oxidation. Explain the steps, regulation & energetics.

Definition

Beta oxidation is oxidation of fatty acids at beta carbon atom.

Steps

1. Activation
2. Carnitine shuttle
3. Dehydrogenation
4. Hydration
5. Dehydrogenation
6. Thiolysis

Regulation

- CPT I inhibited by malonyl CoA
- Hormonal regulation
- Product inhibition

Energetics

Net ATP from palmitate = 106 ATP.

12. Explain the steps of β-oxidation of palmitic acid, giving energetics.

Steps

1. Activation of palmitate
2. Transport by carnitine shuttle
3. Repeated beta oxidation spiral:

- FAD linked oxidation
- Hydration
- NAD linked oxidation
- Thiolysis

Products from palmitate

- 8 acetyl CoA
- 7 NADH
- 7 FADH2

Energetics

Net ATP = 106 ATP.

13. How are dietary triglycerides absorbed and transported in plasma. Briefly explain the transport of dietary triglyceride from intestine to liver.

Absorption of dietary triglycerides

1. Emulsification by bile salts
2. Hydrolysis by pancreatic lipase
3. Formation of micelles
4. Absorption into intestinal mucosal cells
5. Re-esterification to triglycerides
6. Formation of chylomicrons

Transport in plasma

- Chylomicrons carry dietary triglycerides.
- Enter lymphatics and then blood.
- Lipoprotein lipase hydrolyses triglycerides.
- Chylomicron remnants taken up by liver.

Transport from intestine to liver

Intestinal mucosal cells → Chylomicrons → Lymph → Thoracic duct → Blood → Liver.

14. Describe the reactions of Beta oxidation in the mitochondrial matrix. Add a note on ATP yield from palmitate.

Reactions

1. Dehydrogenation – FAD dependent
2. Hydration
3. Dehydrogenation – NAD dependent
4. Thiolysis

ATP yield from palmitate

Net ATP = 106 ATP.

15. Describe the denovosynthesis of fatty acid. Add a note on its regulation

De novo synthesis of fatty acids

Site

Cytoplasm of liver, adipose tissue and lactating mammary gland.

Requirements

- Acetyl CoA
- ATP
- NADPH
- Biotin

Key enzyme

Acetyl CoA carboxylase.

Steps

1. Formation of malonyl CoA
2. Fatty acid synthase complex reactions:

- Condensation
- Reduction
- Dehydration
- Reduction

Final product: Palmitate.

Regulation

Stimulated by

- Insulin
- Citrate
- High carbohydrate diet

Inhibited by

- Glucagon
- Epinephrine
- Palmitoyl CoA

16. How are lipids digested and absorbed. Add a note on the associated disorders

Digestion of lipids

In stomach

Lingual and gastric lipases.

In intestine

- Emulsification by bile salts
- Hydrolysis by pancreatic lipase
- Formation of micelles

Absorption

- Micelles enter mucosal cells
- Re-esterification of fatty acids
- Chylomicron formation
- Entry into lymphatics

Associated disorders

- Steatorrhea
- Pancreatic insufficiency
- Obstructive jaundice
- Abetalipoproteinemia
- Malabsorption syndrome

17. Ketone body metabolism.

Ketogenesis

Occurs in liver mitochondria.

Steps:

1. Formation of acetoacetyl CoA
2. Formation of HMG CoA
3. Formation of acetoacetate
4. Formation of beta hydroxybutyrate and acetone

Ketolysis

Occurs in extrahepatic tissues.

Steps:

1. Beta hydroxybutyrate → Acetoacetate
2. Acetoacetate activated by thiophorase
3. Formation of acetyl CoA

Significance

- Alternative fuel during starvation
- Excess causes ketoacidosis

18. Describe the steps of beta oxidation. Calculate the energetics from palmitic acid.

Steps

1. Activation

2. Carnitine shuttle
3. Dehydrogenation
4. Hydration
5. Dehydrogenation
6. Thiolysis

Energetics

- 8 acetyl CoA = 80 ATP
- 7 NADH = 17.5 ATP
- 7 FADH2 = 10.5 ATP
  Total = 108 ATP
  Minus 2 ATP activation
  Net = 106 ATP.

19. Formation and utilization of ketone bodies

Formation

Occurs in liver mitochondria through ketogenesis.

Steps:

1. Acetyl CoA → Acetoacetyl CoA
2. HMG CoA formation
3. Acetoacetate formation
4. Formation of beta hydroxybutyrate and acetone

Utilization

Occurs in extrahepatic tissues.

Steps:

1. Beta hydroxybutyrate → Acetoacetate
2. Acetoacetate activated by thiophorase
3. Formation of acetyl CoA for TCA cycle

20. Explain the steps of beta oxidation of fatty acids

Steps

1. Activation of fatty acid
2. Carnitine shuttle transport
3. First oxidation – FAD dependent
4. Hydration
5. Second oxidation – NAD dependent
6. Thiolysis

Repeated until complete conversion to acetyl CoA.

21. Define carnitine and explain its role in oxidation of fatty acids

Definition

Carnitine is a beta hydroxy gamma trimethyl amino butyrate required for transport of long chain fatty acids into mitochondria.

Role

- Forms acyl carnitine by CPT I
- Transported into mitochondria
- CPT II regenerates acyl CoA
- Essential for beta oxidation of long chain fatty acids

Clinical importance

Carnitine deficiency causes muscle weakness and hypoglycemia.

22. Name the ketone bodies. Describe the process of ketogenesis. List the condition that lead to ketoacidosis

Ketone bodies

1. Acetoacetate
2. Beta hydroxybutyrate
3. Acetone

Ketogenesis

Occurs in liver mitochondria.

Steps:

1. Formation of acetoacetyl CoA
2. Formation of HMG CoA
3. Formation of acetoacetate
4. Formation of beta hydroxybutyrate and acetone

Conditions leading to ketoacidosis

- Uncontrolled diabetes mellitus
- Starvation
- Prolonged vomiting
- Alcoholism

23. Fatty acid synthase complex

Definition

A multienzyme complex responsible for de novo synthesis of fatty acids.

Components

- Acetyl transacylase
- Malonyl transacylase
- Ketoacyl synthase
- Ketoacyl reductase
- Dehydratase
- Enoyl reductase
- Thioesterase
- Acyl carrier protein (ACP)

Function

Synthesizes palmitate from acetyl CoA and malonyl CoA.

SHORT ANSWERS

24. Give reason - Presence of brown adipose tissue in newborns and hibernating animals.

Brown adipose tissue produces heat by non shivering thermogenesis.
It contains abundant mitochondria with thermogenin (uncoupling protein).
Present in newborns and hibernating animals for maintenance of body temperature.

25. Mention the causes of fatty liver and name the lipotropic factors.

Causes of fatty liver

- Excess fat mobilization
- Alcoholism
- Diabetes mellitus
- Starvation
- Protein deficiency
- Toxins

Lipotropic factors

- Choline
- Methionine
- Inositol
- Betaine
- Vitamin B12
- Folic acid

26. Lipotropic factors

Lipotropic factors prevent accumulation of fat in liver.

Examples:

- Choline
- Methionine
- Inositol
- Betaine
- Folic acid
- Vitamin B12

27. Explain the role of Carnitine in fatty acid oxidation.

Carnitine transports long chain fatty acids into mitochondria.

Steps

1. CPT I forms acyl carnitine
2. Translocase transports it across inner membrane
3. CPT II reforms acyl CoA
4. Carnitine returns to cytosol

Essential for beta oxidation.

28. Adipose tissue is an endocrine organ. Explain

Adipose tissue secretes adipokines.

Hormones secreted

- Leptin
- Adiponectin
- TNF alpha
- Resistin

Functions

- Regulation of appetite
- Insulin sensitivity
- Energy balance
- Inflammation

29. Describe any two Shuttle mechanisms across mitochondrial membrane.

1. Carnitine shuttle

Transports long chain fatty acids into mitochondria.

2. Malate aspartate shuttle

Transfers reducing equivalents from cytosol to mitochondria.

Other example:
Glycerol phosphate shuttle.

30. Explain the transport of dietary lipids from intestine

Dietary lipids are transported as chylomicrons.

Steps

1. Lipid absorption in intestine
2. Re-esterification to triglycerides
3. Chylomicron formation
4. Entry into lymphatics
5. Entry into blood
6. Triglycerides hydrolysed by lipoprotein lipase
7. Remnants taken up by liver

31. Fatty liver and lipotropic factors

Fatty liver

Accumulation of triglycerides in liver.

Causes

- Alcoholism
- Diabetes mellitus
- Starvation
- Protein deficiency

Lipotropic factors

- Choline
- Methionine
- Inositol
- Betaine

32. Name the ketone bodies and describe their synthesis

Ketone bodies

1. Acetoacetate

2. Beta hydroxybutyrate
3. Acetone

Synthesis

Occurs in liver mitochondria.

Steps

1. 2 Acetyl CoA → Acetoacetyl CoA
2. Formation of HMG CoA
3. HMG CoA → Acetoacetate
4. Formation of beta hydroxybutyrate and acetone

33. Tests for detection of ketone bodies in the urine

1. Rothera's test
2. Gerhardt's ferric chloride test
3. Dipstick method

34. Enzyme defect in the methyl malonyl aciduria and refsum's disease

Methyl malonyl aciduria

Deficiency of methyl malonyl CoA mutase.

Refsum's disease

Defect in alpha oxidation due to deficiency of phytanic acid oxidase.

35. Brown adipose tissue

Brown adipose tissue contains numerous mitochondria and produces heat by non shivering thermogenesis.

Features

- Rich blood supply
- Contains thermogenin
- Found in newborns

Function

Maintenance of body temperature.

36. Fat is burnt under the fire of carbohydrates. Justify this statement.

Oxaloacetate derived from carbohydrates is required for complete oxidation of acetyl CoA in TCA cycle.

In carbohydrate deficiency:

- Oxaloacetate decreases
- Acetyl CoA accumulates
- Ketone bodies formed

Hence fat burns completely only in presence of carbohydrates.

37. Role of carnitine in fatty acid oxidation with the help of a diagram.

Role

Carnitine transports long chain fatty acids into mitochondria.

REFER DIAGRAM SECTION

38. Carnitine shuttle

Function

Transport of long chain fatty acids into mitochondria.

Steps

1. CPT I forms acyl carnitine
2. Translocase transports it
3. CPT II reforms acyl CoA
4. Carnitine recycled

Importance

Required for beta oxidation.

39. Causes of fatty liver

- Alcoholism
- Diabetes mellitus
- Starvation
- Obesity
- Protein deficiency
- Toxins
- Impaired lipoprotein synthesis

40. Bile salts

Bile salts are sodium or potassium salts of conjugated bile acids.

Functions

- Emulsification of fats
- Micelle formation
- Absorption of lipids
- Absorption of fat soluble vitamins
- Activation of pancreatic lipase

41. Name different lipases involved in lipid metabolism and mention its functions

Lipase	Function
Lingual lipase	Digestion of milk fat
Gastric lipase	Digestion of triglycerides
Pancreatic lipase	Hydrolysis of dietary triglycerides
Lipoprotein lipase	Hydrolysis of triglycerides in chylomicrons and VLDL
Hormone sensitive lipase	Mobilization of stored fat

42. Carnitine deficiency

Causes

- Nutritional deficiency
- Genetic defects
- Renal loss

Features

- Muscle weakness
- Hypoglycemia
- Cardiomyopathy
- Reduced beta oxidation

43. Bile salts and functions

Bile salts

- Sodium glycocholate
- Sodium taurocholate

Functions

- Emulsification of fats
- Micelle formation
- Fat absorption
- Absorption of vitamins A, D, E and K

44. Enumerate primary and secondary bile acids

Primary bile acids

1. Cholic acid
2. Chenodeoxycholic acid

Secondary bile acids

1. Deoxycholic acid
2. Lithocholic acid

CHOLESTEROL AND LIPOPROTEINS

LONG ESSAYS

1. A man of 45 years of age is overweight with a sedentary lifestyle underwent an annual health Test checkup Following are the details of the investigations.

Given values

- Fasting blood glucose – 115 mg/dL
- Total cholesterol – 250 mg/dL
- Triglycerides – 269 mg/dL
- HDL cholesterol – 24 mg/dL
- LDL cholesterol – 172 mg/dL

Investigation findings

- Fasting blood glucose – 115 mg/dL
- Total cholesterol – 250 mg/dL
- Triglycerides – 269 mg/dL
- HDL cholesterol – 24 mg/dL
- LDL cholesterol – 172 mg/dL

What is the probable diagnosis

The probable diagnosis is Hyperlipidaemia.

Mention the causes for the above condition

Primary causes

1. Familial hypercholesterolemia
2. Genetic defects of apoproteins
3. Lipoprotein lipase deficiency

Secondary causes

1. Obesity
2. Sedentary lifestyle
3. Diabetes mellitus
4. Hypothyroidism
5. Nephrotic syndrome
6. Alcoholism
7. High fat diet
8. Liver disease

Briefly describe chylomicron metabolism

Formation

- Formed in intestinal mucosal cells.
- Contain triglycerides, cholesterol and Apo B48.

Metabolism

1. Chylomicrons enter lymph and blood.
2. Receive Apo CII and Apo E from HDL.
3. Lipoprotein lipase activated by Apo CII hydrolyzes triglycerides.
4. Fatty acids enter adipose tissue and muscle.
5. Chylomicron remnants taken up by liver through Apo E receptors.

Briefly describe hyperlipidemia

Hyperlipidemia is elevation of plasma cholesterol, triglycerides or both.

Classification

1. Primary hyperlipidemia
2. Secondary hyperlipidemia

Complications

1. Atherosclerosis
2. Coronary artery disease
3. Pancreatitis
4. Xanthomas

Management

1. Diet control
2. Exercise
3. Weight reduction
4. Statins
5. Fibrates

SHORT ESSAYS

2. Discuss the metabolism of chylomicrons

Definition

Chylomicrons are lipoproteins that transport dietary triglycerides from intestine to tissues.

Formation

- Synthesized in intestinal mucosal cells.
- Main apoprotein is Apo B48.

Composition

- Rich in triglycerides.
- Contain cholesterol and phospholipids.

Metabolism

1. Enter lymphatics and blood.
2. Obtain Apo CII and Apo E from HDL.
3. Lipoprotein lipase hydrolyzes triglycerides.
4. Fatty acids utilized by tissues.
5. Glycerol transported to liver.
6. Chylomicron remnants formed.
7. Remnants taken up by liver via Apo E receptor mediated endocytosis.

Functions

Transport dietary lipids.

Clinical significance

Defect causes hyperchylomicronemia.

3. Describe the role of lipoproteins in cholesterol transport

Lipoproteins

Complexes of lipids and proteins responsible for lipid transport.

Types and roles

Chylomicrons

Transport dietary triglycerides from intestine.

Very low density lipoprotein

Transport endogenous triglycerides from liver.

Low density lipoprotein

- Carries cholesterol to peripheral tissues.
- Called bad cholesterol.
- Promotes atherosclerosis.

High density lipoprotein

- Removes cholesterol from tissues.
- Carries cholesterol to liver.
- Called good cholesterol.

Reverse cholesterol transport

HDL transports excess cholesterol from tissues to liver.

SHORT ANSWERS

4. What is reverse cholesterol transport

Reverse cholesterol transport is transport of excess cholesterol from peripheral tissues to liver by HDL.

Steps

1. HDL collects cholesterol from tissues.
2. Lecithin cholesterol acyl transferase esterifies cholesterol.
3. Cholesteryl esters transported to liver.
4. Liver excretes cholesterol in bile.

5. Classification of Lipoproteins

Based on density

1. Chylomicrons
2. Very low density lipoprotein
3. Intermediate density lipoprotein
4. Low density lipoprotein
5. High density lipoprotein

6. Functions of apolipoproteins.

1. Structural components of lipoproteins
2. Act as enzyme cofactors
3. Act as receptor ligands
4. Help in lipoprotein assembly
5. Regulate lipid metabolism

7. Functions of cholesterol

1. Component of cell membrane
2. Precursor of bile acids
3. Precursor of steroid hormones
4. Precursor of vitamin D
5. Maintains membrane fluidity

8. Lipoproteins

Lipoproteins are complexes of lipids and proteins that transport lipids in blood.

Types

1. Chylomicrons
2. Very low density lipoprotein
3. Intermediate density lipoprotein
4. Low density lipoprotein
5. High density lipoprotein

9. Compounds derived from cholesterol

1. Bile acids
2. Steroid hormones
3. Vitamin D
4. Bile salts

10. Functions and significance of Low density lipoproteins

Functions

- Transport cholesterol from liver to tissues.

Significance

- Called bad cholesterol.
- Elevated levels cause atherosclerosis.
- Increased risk of coronary artery disease.

11. Which is good cholesterol and why it is called so?

High density lipoprotein is called good cholesterol.

Reason

- Removes cholesterol from peripheral tissues.
- Carries cholesterol to liver for excretion.
- Protects against atherosclerosis.

12. Mention the rate limiting step and the inhibitors of cholesterol synthesis

Rate limiting step

Conversion of HMG CoA to mevalonate.

Enzyme

HMG CoA reductase.

Inhibitors

1. Statins
2. Cholesterol
3. Glucagon
4. Fasting

13. Regulation of cholesterol synthesis

Key enzyme

HMG CoA reductase.

Regulation

1. Feedback inhibition by cholesterol
2. Insulin activates enzyme
3. Glucagon inhibits enzyme
4. Statins inhibit enzyme
5. Thyroxine increases synthesis

14. LDL receptors

LDL receptors are cell surface receptors that bind LDL particles.

Functions

1. Mediate uptake of LDL cholesterol.
2. Maintain cholesterol homeostasis.

Clinical significance

Defect causes familial hypercholesterolemia.

CARDIOVASCULAR DISEASES, BIOMARKERS OF CVD AND HYPERLIPIDEMIAS

SHORT ESSAYS

1. Enumerate the cardiac biomarkers and give an account of their pattern of elevation in myocardial infarction.

Cardiac biomarkers

1. Cardiac troponin I
2. Cardiac troponin T
3. Creatine kinase MB
4. Myoglobin
5. Lactate dehydrogenase
6. Aspartate aminotransferase

Pattern of elevation

Marker	Rise	Peak	Returns to normal
Myoglobin	1–2 hours	6–8 hours	24 hours
CK-MB	4–6 hours	24 hours	2–3 days
Troponin I	3–6 hours	24–48 hours	7–10 days
Troponin T	3–6 hours	24–48 hours	10–14 days
LDH	12–24 hours	48–72 hours	7–10 days

Importance

Troponins are most sensitive and specific markers of myocardial infarction.

SHORT ANSWERS

2. Cardiac biomarkers

1. Cardiac troponin I
2. Cardiac troponin T
3. CK-MB
4. Myoglobin
5. LDH
6. AST

3. Isoenzymes as Cardiac Markers

1. CK-MB
2. LDH1

Importance

Used in diagnosis of myocardial infarction.

4. List the cardiac markers

1. Troponin I
2. Troponin T
3. CK-MB

4. Myoglobin
5. LDH
6. AST

MCFA, PUFA, PROSTAGLANDINS AND COMPOUND LIPIDS

SHORT ESSAYS

1. Function and therapeutic role of prostaglandins

Functions of prostaglandins

1. Mediate inflammation
2. Produce pain and fever
3. Regulate blood pressure
4. Control gastric secretion
5. Stimulate uterine contraction
6. Regulate platelet aggregation
7. Bronchial smooth muscle action

Therapeutic roles

1. Induction of labor
2. Medical termination of pregnancy
3. Treatment of peptic ulcer
4. Treatment of glaucoma
5. Maintenance of patent ductus arteriosus

SHORT ANSWERS

2. PUFA (Poly Unsaturated Fatty Acids)

PUFA are fatty acids containing more than one double bond.

Examples

1. Linoleic acid
2. Linolenic acid
3. Arachidonic acid

Functions

1. Essential for growth
2. Maintain membrane fluidity
3. Precursor of prostaglandins
4. Lower plasma cholesterol

3. Functions of prostaglandins

1. Inflammation
2. Pain sensation
3. Fever production
4. Regulation of blood pressure
5. Gastric protection
6. Uterine contraction
7. Platelet aggregation regulation

GENERAL AMINO ACID METABOLISM: UREA CYCLE AND ONE-CARBON METABOLISM

LONG ESSAYS

1. Enumerate the reactions of urea cycle and explain its regulation. Add a note on disorders of the urea cycle.

Urea cycle

Site: Liver.

Steps

1. Formation of carbamoyl phosphate

- Ammonia + CO_2 + 2 ATP → Carbamoyl phosphate
- Enzyme: Carbamoyl phosphate synthetase I
- Occurs in mitochondria

2. Formation of citrulline

- Carbamoyl phosphate + Ornithine → Citrulline
- Enzyme: Ornithine transcarbamylase

3. Formation of argininosuccinate

- Citrulline + Aspartate → Argininosuccinate
- Enzyme: Argininosuccinate synthetase

4. Formation of arginine

- Argininosuccinate → Arginine + Fumarate
- Enzyme: Argininosuccinate lyase

5. Formation of urea

- Arginine → Urea + Ornithine
- Enzyme: Arginase

Regulation of urea cycle

1. Carbamoyl phosphate synthetase I is rate limiting enzyme.
2. Activated by N-acetyl glutamate.
3. High protein diet increases enzyme synthesis.
4. Starvation increases urea cycle activity.

Disorders of urea cycle

1. Hyperammonemia type I

- Deficiency of carbamoyl phosphate synthetase I

2. Hyperammonemia type II

- Deficiency of ornithine transcarbamylase

3. Citrullinemia

- Deficiency of argininosuccinate synthetase

4. Argininosuccinic aciduria

- Deficiency of argininosuccinate lyase

5. Hyperargininemia

- Deficiency of arginase

Clinical features

1. Hyperammonemia
2. Vomiting
3. Convulsions
4. Mental retardation
5. Coma

2. 11-month-old infant was brought to the out-patient department with complaints of vomiting, refusal to feeds failure to gain weight and lethargy for past few weeks. He is born of non-consanguineous marriage and pregnancy was uneventful. Parents also complained of delayed milestones. His laboratory investigations is as follows: Plasma glucose random: 84 mg/dL, Serum urea: 6 mg/dL, Plasma ammonia: Elevated, Plasma citrulline: decreased

a) What is your probable diagnosis

b) Why ammonia is toxic to the body

c) Explain detoxification of ammonia and the regulation of the process

d) Enumerate any TWO ways of reducing plasma ammonia levels

a) Probable diagnosis

Hyperammonaemia type II due to ornithine transcarbamylase deficiency.

b) Why ammonia is toxic to the body

1. Ammonia depletes alpha ketoglutarate.
2. Decreased alpha ketoglutarate inhibits citric acid cycle.
3. ATP production decreases.
4. Increased glutamine causes cerebral edema.
5. Neurotransmitter imbalance occurs.
6. Leads to encephalopathy and coma.

c) Detoxification of ammonia and regulation

Detoxification

1. Urea synthesis in liver.
2. Formation of glutamine by glutamine synthetase.
3. Transport as alanine from muscle.
4. Renal excretion as ammonium ion.

Urea cycle steps

1. Carbamoyl phosphate formation.
2. Citrulline formation.
3. Argininosuccinate formation.
4. Arginine formation.
5. Urea formation.

Regulation

1. Carbamoyl phosphate synthetase I is activated by N-acetyl glutamate.
2. High protein diet increases enzyme synthesis.
3. Starvation increases urea formation.

d) Two ways of reducing plasma ammonia levels

1. Low protein diet.
2. Administration of sodium benzoate or sodium phenylbutyrate.
3. Hemodialysis.
4. Lactulose therapy.

3. Explain the formation and disposal of Ammonia. Add a note on the urea cycle disorders

Formation of ammonia

1. Oxidative deamination of glutamate.
2. Deamination of amino acids.
3. Intestinal bacterial action.
4. Purine and pyrimidine metabolism.
5. Catabolism of amines.

Disposal of ammonia

1. Urea synthesis in liver.
2. Glutamine formation.
3. Excretion as ammonium salts in kidney.

Urea cycle disorders

1. Carbamoyl phosphate synthetase deficiency.
2. Ornithine transcarbamylase deficiency.
3. Citrullinaemia.
4. Argininosuccinic aciduria.
5. Hyperargininaemia.

Clinical features

1. Hyperammonaemia.
2. Vomiting.
3. Convulsions.
4. Mental retardation.
5. Coma.

4. Describe the pathway for synthesis of urea. Add a note on the regulation of the pathway. Name two conditions in which blood urea is increased giving the biochemical basis or enzyme defect

Urea synthesis

Occurs in liver.

Steps

1. Carbamoyl phosphate formation.
2. Citrulline formation.
3. Argininosuccinate formation.
4. Arginine formation.
5. Urea formation.

Regulation

1. Carbamoyl phosphate synthetase I is rate limiting.
2. Activated by N-acetyl glutamate.
3. Increased by high protein diet and starvation.

Conditions with increased blood urea

1. Renal failure – decreased excretion of urea.
2. Dehydration – decreased renal perfusion.

SHORT ESSAYS

5. Explain how proteins are digested and absorbed in the body

Digestion of proteins

In stomach

1. Hydrochloric acid denatures proteins.
2. Pepsin converts proteins to proteoses and peptones.

In intestine

Pancreatic enzymes:

1. Trypsin
2. Chymotrypsin
3. Elastase
4. Carboxypeptidase

These convert proteins into oligopeptides.

Intestinal enzymes

1. Aminopeptidases
2. Dipeptidases

Convert peptides into amino acids.

Absorption

1. Amino acids absorbed by active transport.
2. Sodium dependent carriers involved.
3. Small peptides also absorbed.
4. Amino acids enter portal circulation.

6. Describe the urea cycle and add a note on its regulation.

Urea cycle

1. Carbamoyl phosphate formation.
2. Citrulline formation.
3. Argininosuccinate formation.
4. Arginine formation.
5. Urea formation.

Regulation

1. Rate limiting enzyme – Carbamoyl phosphate synthetase I.
2. Activated by N-acetyl glutamate.
3. High protein diet increases enzyme synthesis.
4. Starvation increases urea formation.

7. Describe in detail the reactions of transamination and oxidative deamination. Add a note on the significance of these reactions

10. Transamination

Transfer of amino group from an amino acid to a keto acid.

Examples

1. Alanine + alpha ketoglutarate form pyruvate + glutamate.
2. Aspartate + alpha ketoglutarate form oxaloacetate + glutamate.

Enzyme

Transaminases.

Coenzyme

Pyridoxal phosphate.

Oxidative deamination

Removal of amino group from glutamate as ammonia.

Reaction

Glutamate forms alpha ketoglutarate + ammonia.

Enzyme

Glutamate dehydrogenase.

Significance

1. Synthesis of nonessential amino acids.
2. Formation of glutamate.
3. Ammonia production for urea cycle.
4. Interconversion of amino acids and keto acids.

8. Describe the reactions of urea cycle. Discuss the diagnostic significance of blood urea.

Reactions of urea cycle

1. Carbamoyl phosphate formation.
2. Citrulline formation.
3. Argininosuccinate formation.
4. Arginine formation.
5. Urea formation.

Diagnostic significance of blood urea

Increased blood urea

1. Renal failure.
2. Dehydration.
3. Shock.
4. High protein diet.

Decreased blood urea

1. Liver disease.
2. Low protein diet.

9. Discuss the detoxification of ammonia in the body. Mention two inborn errors associated with it.

Detoxification of ammonia

1. Urea synthesis in liver.
2. Glutamine formation.
3. Alanine transport from muscle.
4. Excretion as ammonium ion by kidney.

Inborn errors

1. Ornithine transcarbamylase deficiency.
2. Citrullinaemia.

10.Transamination

Transamination is the transfer of amino group from an amino acid to a keto acid.

General reaction

Amino acid + Keto acid ↔ New amino acid + New keto acid

Enzyme

Transaminases.

Coenzyme

Pyridoxal phosphate.

Examples

1. Alanine + alpha ketoglutarate form pyruvate + glutamate.
2. Aspartate + alpha ketoglutarate form oxaloacetate + glutamate.

Importance

1. Amino acid synthesis.
2. Amino acid catabolism.
3. Formation of glutamate.

11. Define transamination and explain by giving two examples

Transamination is the transfer of amino group from an amino acid to a keto acid.

Examples

1. Alanine + alpha ketoglutarate form pyruvate + glutamate.
2. Aspartate + alpha ketoglutarate form oxaloacetate + glutamate.

Enzyme

Transaminases.

Coenzyme

Pyridoxal phosphate.

12. Mention the normal blood urea level. Explain how urea is synthesized in the body

Normal blood urea level

20–40 mg/dL.

Urea synthesis

1. Carbamoyl phosphate formation.
2. Citrulline formation.
3. Argininosuccinate formation.
4. Arginine formation.
5. Urea formation.

Occurs in liver.

13. Describe the reactions of urea cycle. Discuss the interrelationship between urea cycle and citric acid cycle

Reactions of urea cycle

1. Carbamoyl phosphate formation.
2. Citrulline formation.
3. Argininosuccinate formation.
4. Arginine formation.
5. Urea formation.

Interrelationship with citric acid cycle

Krebs bicycle.

1. Fumarate formed in urea cycle enters citric acid cycle.
2. Fumarate forms malate and oxaloacetate.
3. Oxaloacetate undergoes transamination to form aspartate.
4. Aspartate re-enters urea cycle.

SHORT ANSWERS

14. Describe the Biochemical basis of - Proteolytic enzymes of GIT are secreted as zymogens.

Proteolytic enzymes are secreted as inactive zymogens to prevent autodigestion of tissues.

Examples

1. Pepsinogen.
2. Trypsinogen.
3. Chymotrypsinogen.

They are activated only in gastrointestinal lumen.

15. Describe the Biochemical basis of: Ammonia Toxicity

1. Ammonia depletes alpha ketoglutarate.
2. Citric acid cycle activity decreases.
3. ATP production decreases.
4. Increased glutamine causes cerebral edema.
5. Neurotoxicity leads to coma.

16. Transamination reactions

1. Alanine + alpha ketoglutarate form pyruvate + glutamate.
2. Aspartate + alpha ketoglutarate form oxaloacetate + glutamate.

Enzyme

Transaminases.

Coenzyme

Pyridoxal phosphate.

17. What is transamination. Mention clinical importance of any two transaminases

Transamination

Transfer of amino group from amino acid to keto acid.

Clinical importance

1. Alanine aminotransferase increases in liver disease.
2. Aspartate aminotransferase increases in myocardial infarction and liver disease.

18. What is transamination. Explain the diagnostic significance of any one serum transaminase

Transamination

Transfer of amino group from amino acid to keto acid.

Alanine aminotransferase

1. Present mainly in liver.
2. Increased in hepatitis.
3. Marker of hepatocellular injury.

19. Orotic aciduria

Orotic aciduria is a disorder due to deficiency of enzymes involved in pyrimidine synthesis.

Enzyme defects

1. Orotate phosphoribosyl transferase deficiency.
2. Orotidine monophosphate decarboxylase deficiency.

Features

1. Megaloblastic anemia.
2. Growth retardation.
3. Increased urinary orotic acid.

Treatment

Uridine administration.

20. Decarboxylation of amino acids

Decarboxylation removes carboxyl group from amino acids producing amines.

Examples

1. Histidine forms histamine.
2. Glutamate forms gamma amino butyric acid.
3. DOPA forms dopamine.

Coenzyme

Pyridoxal phosphate.

21. Sources of ammonia

1. Oxidative deamination of amino acids.
2. Intestinal bacterial action.
3. Purine and pyrimidine metabolism.
4. Catabolism of amines.

22.Transamination

Transamination is transfer of amino group from amino acid to keto acid.

Enzyme

Transaminases.

Coenzyme

Pyridoxal phosphate.

Examples

1. Alanine transaminase reaction.
2. Aspartate transaminase reaction.

METABOLISM OF ALIPHATIC AMINO ACIDS

SHORT ESSAYS

1. Give an account of formation of specialized products from glycine and their clinical importance.

Specialized products formed from glycine

1. Heme

Glycine combines with succinyl CoA to form delta amino levulinic acid.

Clinical importance:

- Defect causes porphyrias.

2. Creatine

Glycine participates in creatine synthesis.

Clinical importance:

- Creatinine used to assess renal function.

3. Purines

Glycine contributes carbon and nitrogen atoms in purine ring.

Clinical importance:

- Excess purine catabolism causes gout.

4. Glutathione

Glycine forms part of glutathione.

Clinical importance:

- Important antioxidant.

5. Hippuric acid

Glycine conjugates with benzoic acid.

Clinical importance:

- Detoxification reaction in liver.

6. Bile salts

Glycine conjugates with bile acids.

Clinical importance:

- Helps fat digestion and absorption.

7. Serine

Glycine converted to serine.

Clinical importance:

- Important in one carbon metabolism.

2. Explain Homocystinurias in detail, with clinical presentations and lab tests.

Definition

Homocystinuria is an inherited disorder of methionine metabolism characterized by accumulation of homocysteine in blood and urine.

Causes / Enzyme defects

1. Deficiency of cystathionine β-synthase (most common)
2. Defect in methylcobalamin formation
3. Defect in methylene tetrahydrofolate reductase

Metabolic defect

Methionine metabolism is blocked leading to:

- Increased homocysteine
- Increased methionine
- Decreased cysteine

Clinical features

1. Mental retardation
2. Ectopia lentis (downward displacement of lens)
3. Skeletal abnormalities resembling Marfan syndrome
    - Long limbs
    - Arachnodactyly
    - Kyphosis
4. Osteoporosis
5. Thromboembolic episodes
6. Fair complexion
7. Developmental delay

Laboratory findings

1. Increased plasma homocysteine
2. Increased methionine in blood
3. Homocystine in urine
4. Cyanide nitroprusside test positive
5. Enzyme assay confirms diagnosis
6. Genetic studies

Treatment

1. Pyridoxine supplementation
2. Low methionine diet
3. Folate and vitamin B12 supplementation
4. Betaine therapy
5. Cysteine supplementation

Complications

- Vascular thrombosis
- Stroke
- Myocardial infarction

3. Outline the metabolism of glycine under following heads. Synthesis of glycine, synthesis of biologically important compounds from glycine.

Glycine metabolism

Synthesis of glycine

1. From serine

- Enzyme: Serine hydroxymethyl transferase
- Coenzyme: Tetrahydrofolate

2. From threonine

- Via threonine aldolase

3. From glyoxylate

- By transamination

Catabolism of glycine

1. Conversion to serine
2. Oxidative cleavage by glycine cleavage system
3. Formation of glyoxylate

Biologically important compounds synthesized from glycine

1. Creatine
2. Heme
3. Purines
4. Glutathione
5. Hippuric acid
6. Bile salts
7. Oxalate

Clinical importance

- Defect causes primary hyperoxaluria
- Non-ketotic hyperglycinemia due to glycine cleavage defect

4. Important compounds derived from glycine.

1. Heme

- Glycine + succinyl CoA form δ-aminolevulinic acid

2. Creatine

- Glycine combines with arginine and methionine

3. Purine ring

- Glycine contributes carbon and nitrogen atoms

4. Glutathione

- Tripeptide containing glutamate, cysteine and glycine

5. Hippuric acid

- Glycine conjugates with benzoic acid

6. Bile salts

- Glycocholic acid

7. Oxalate

- Produced from glyoxylate

SHORT ANSWERS

5. Synthesis of biogenic amines and their biological role.

Biogenic amine	Parent amino acid	Function
Histamine	Histidine	Allergy, gastric secretion
Serotonin	Tryptophan	Neurotransmitter

Biogenic amine	Parent amino acid	Function
Dopamine	Tyrosine	Neurotransmitter
Epinephrine	Tyrosine	Hormone
GABA	Glutamate	Inhibitory neurotransmitter
Tyramine	Tyrosine	Vasopressor action

Biogenic amines are formed mainly by decarboxylation reactions.

6. Homocystinuria

- Inborn error of methionine metabolism
- Usually due to cystathionine β-synthase deficiency

Clinical features

1. Mental retardation
2. Lens dislocation
3. Skeletal deformities
4. Thrombosis

Laboratory findings

- Increased homocysteine in plasma and urine
- Cyanide nitroprusside test positive

Treatment

- Pyridoxine
- Low methionine diet
- Folate and vitamin B12

7. Write briefly on the biologically important compounds synthesized from Glycine.

1. Heme
2. Creatine
3. Purines
4. Glutathione
5. Hippuric acid
6. Bile salts

8. Describe the synthesis of any two compounds of biomedical importance synthesized from glycine.

1. Creatine synthesis

- Glycine + arginine → guanidinoacetate
- Guanidinoacetate methylated by S-adenosyl methionine to form creatine

2. Heme synthesis

- Glycine + succinyl CoA → δ-aminolevulinic acid
- Enzyme: ALA synthase
- Pyridoxal phosphate required

9. Transmethylation reaction

Transfer of methyl group from one compound to another.

Active methyl donor

S-adenosyl methionine.

Examples

1. Norepinephrine → Epinephrine
2. Guanidinoacetate → Creatine
3. Phosphatidyl ethanolamine → Lecithin

10. What is glutathione and mention its importance in body.

Definition

Glutathione is a tripeptide containing glutamate, cysteine and glycine.

Functions

1. Antioxidant action
2. Detoxification
3. Maintains red cell membrane integrity
4. Participates in amino acid transport
5. Reduces hydrogen peroxide by glutathione peroxidase

11. Formation and functions of nitric oxide.

Formation

Arginine is converted to nitric oxide by nitric oxide synthase.

Functions

1. Vasodilation
2. Neurotransmission
3. Bactericidal action by macrophages
4. Inhibits platelet aggregation

12. GABA

Formation

Glutamate is decarboxylated by glutamate decarboxylase.

Functions

1. Major inhibitory neurotransmitter in central nervous system
2. Regulates neuronal excitability
3. Deficiency causes seizures

13. Primary hyperoxaluria

Inherited disorder due to deficiency of alanine glyoxylate aminotransferase.

Features

1. Increased oxalate formation
2. Renal stones
3. Nephrocalcinosis
4. Renal failure

14. Glutathione peroxidase

Function

Reduces hydrogen peroxide and organic peroxides.

Reaction

$2\ GSH + H_2O_2 \rightarrow GSSG + 2H_2O$

Importance

Protects cells from oxidative damage.

Cofactor

Selenium.

15. What is active methionine? Mention two examples of transmethylation reaction.

Active methionine

S-adenosyl methionine.

Examples

1. Guanidinoacetate → Creatine
2. Norepinephrine → Epinephrine

16. Active methionine

Active methionine is S-adenosyl methionine formed from methionine and ATP.

Functions

Acts as methyl group donor in transmethylation reactions.

17. Glucose alanine cycle

Alanine transports amino groups from muscle to liver.

Steps

1. Pyruvate in muscle forms alanine
2. Alanine transported to liver
3. Alanine converted back to pyruvate
4. Pyruvate used for gluconeogenesis

Importance

- Transport of nitrogen
- Maintains blood glucose

18. Mention three examples of transmethylation reactions

1. Guanidinoacetate → Creatine
2. Norepinephrine → Epinephrine
3. Ethanolamine → Choline

19. Importance of glutamine

1. Transport form of ammonia
2. Fuel for intestinal mucosa
3. Important in acid-base balance in kidney
4. Used for nucleotide synthesis
5. Forms glucosamine

AROMATIC AND HETEROCYCLIC AMINO ACIDS

LONG ESSAYS

1. Explain in detail Phenylalanine metabolism with a note on inborn errors associated with and relevant biochemical investigations for them.

Metabolism of phenylalanine

Phenylalanine is an essential amino acid.

Conversion to tyrosine

Phenylalanine is hydroxylated to tyrosine.

- Enzyme: Phenylalanine hydroxylase
- Cofactor: Tetrahydrobiopterin

Fate of tyrosine

Tyrosine forms:

1. Catecholamines
2. Melanin
3. Thyroxine

Catabolism

Tyrosine → p-hydroxyphenylpyruvate → homogentisic acid → fumarate + acetoacetate

Phenylalanine is both glucogenic and ketogenic.

Inborn errors

1. Phenylketonuria

- Deficiency of phenylalanine hydroxylase
- Increased phenylalanine and phenyl ketones
- Mental retardation, seizures, hypopigmentation

2. Alkaptonuria

- Deficiency of homogentisate oxidase
- Urine turns black on standing
- Ochronosis

3. Albinism

- Deficiency of tyrosinase
- Defective melanin synthesis

Laboratory investigations

1. Plasma phenylalanine estimation
2. Ferric chloride test
3. Guthrie bacterial inhibition test
4. Tandem mass spectrometry
5. Urinary homogentisic acid

2. Mother noticed that her child didn't attain milestone for the age. Mother also noticed hypopigmentation.

• Name the amino acid involved
• What is the diagnosis
• What is the metabolism of the amino acid. Mention the inborn errors associated with its metabolism
• Enumerate the laboratory investigations aiding in the diagnosis.
• Name two specialized compounds formed from tyrosine and discuss their formation in brief

Amino acid involved

Phenylalanine / Tyrosine.

Diagnosis

Phenylketonuria.

Metabolism

Phenylalanine → Tyrosine by phenylalanine hydroxylase.

Tyrosine further forms:

- Catecholamines
- Melanin
- Thyroxine

Inborn errors

1. Phenylketonuria
2. Alkaptonuria
3. Albinism
4. Tyrosinemia

Laboratory investigations

1. Elevated blood phenylalanine
2. Phenylpyruvate in urine
3. Ferric chloride test positive
4. Guthrie test
5. Tandem mass spectrometry

Specialized products from tyrosine

1. Catecholamines

Tyrosine → DOPA → Dopamine → Norepinephrine → Epinephrine

2. Melanin

Tyrosine converted to DOPA and melanin by tyrosinase.

3. A 50 years old man with 3 years history of hypertension and occasional panic attacks reported to hospital with episode of throbbing headache, associated with excessive sweating. He gave history of similar attacks earlier. On examination, his BP was 180/100 mm Hg and pulse was 82/min. urine examination revealed very high levels of 24 hrs VMA.

• What is the probable diagnosis ?
• Name the aromatic amino acids
• Describe the biochemical basis of symptoms and urinary finding
• Describe the synthesis of any two biochemically important compounds from the parent amino acid

Probable diagnosis

Pheochromocytoma.

Aromatic amino acids

1. Phenylalanine
2. Tyrosine
3. Tryptophan

Biochemical basis

Tumor secretes excess catecholamines causing:

- Hypertension
- Sweating
- Tachycardia
- Headache

Catecholamines degraded to vanillyl mandelic acid (VMA), hence increased urinary VMA.

Synthesis of catecholamines

Tyrosine → DOPA → Dopamine → Norepinephrine → Epinephrine

Synthesis of melanin

Tyrosine converted to DOPA and then melanin by tyrosinase.

4. What are biologically important compounds derived from tyrosine. Explain the catabolism of tyrosine and name three inborn errors associated with tyrosine metabolism.

Compounds derived from tyrosine

1. Catecholamines
2. Melanin
3. Thyroxine
4. Tyramine

Catabolism of tyrosine

Tyrosine → p-hydroxyphenylpyruvate → homogentisate → maleylacetoacetate → fumarylacetoacetate → fumarate + acetoacetate.

Inborn errors

1. Alkaptonuria
2. Tyrosinemia
3. Albinism

5. Discuss in detail the metabolism of phenylalanine. Name four biologically important compounds synthesized from phenylalanine. State two metabolic disorders associated and indicate the defective enzymes.

Metabolism

Phenylalanine converted to tyrosine by phenylalanine hydroxylase.

Tyrosine degraded to fumarate and acetoacetate.

Biologically important compounds

1. Catecholamines
2. Melanin
3. Thyroxine
4. Tyramine

Disorders

Disorder	Defective enzyme
Phenylketonuria	Phenylalanine hydroxylase
Alkaptonuria	Homogentisate oxidase

6. Discuss the metabolism of phenylalanine

Phenylalanine is hydroxylated to tyrosine by phenylalanine hydroxylase using tetrahydrobiopterin.

Tyrosine undergoes transamination and oxidation to finally form fumarate and acetoacetate.

Important products:

- Catecholamines
- Melanin
- Thyroxine

Disorders:

- Phenylketonuria
- Alkaptonuria
- Albinism

SHORT ESSAYS

7. What is Phenylketonuria. Describe the catabolism of Phenyl Alanine.

Definition

Phenylketonuria is an inherited disorder due to deficiency of phenylalanine hydroxylase.

Clinical features

1. Mental retardation
2. Convulsions
3. Hypopigmentation
4. Musty odor of urine

Catabolism

Phenylalanine → Tyrosine → p-hydroxyphenylpyruvate → homogentisate → fumarate + acetoacetate.

Investigations

1. Ferric chloride test
2. Guthrie test
3. Elevated blood phenylalanine

8. A child was brought to the Pediatric OPD of the hospital, mother gave history of convulsions, delayed milestones and mental retardation. On examination child was dull and had a blank look, there was mousy odour of the body and urine.

a) What could be your probable diagnosis
b) Mention the enzyme defect
c) Explain the Biochemical basis for the clinical manifestations mentioned in the above case.
d) Mention any two Diagnostic tests done in this case

a) Diagnosis

Phenylketonuria.

b) Enzyme defect

Phenylalanine hydroxylase deficiency.

c) Biochemical basis

- Increased phenylalanine causes brain damage
- Decreased melanin causes hypopigmentation
- Phenylacetate causes mousy odor

d) Diagnostic tests

1. Ferric chloride test
2. Guthrie bacterial inhibition test

9. Describe the steps by which catecholamines are synthesized. Outline the pathway of their degradation.

Synthesis

Tyrosine → DOPA → Dopamine → Norepinephrine → Epinephrine.

Enzymes

1. Tyrosine hydroxylase
2. DOPA decarboxylase
3. Dopamine β-hydroxylase
4. Phenylethanolamine N-methyl transferase

Degradation

By monoamine oxidase and catechol O methyl transferase.

End products:

- Vanillyl mandelic acid
- Metanephrine

10. Describe the steps of catabolism of phenyl alanine and tyrosine. Add a note on inborn errors associated with them.

Pathway

Phenylalanine → Tyrosine → p-hydroxyphenylpyruvate → homogentisate → fumarate + acetoacetate.

Inborn errors

1. Phenylketonuria
2. Alkaptonuria
3. Albinism
4. Tyrosinemia

11. Metabolism of tryptophan

Pathways

1. Kynurenine pathway
2. Serotonin synthesis
3. Niacin synthesis

Products

1. Serotonin
2. Melatonin
3. Niacin

Disorder

Hartnup disease.

SHORT ANSWERS

12. Alkaptonuria

Deficiency of homogentisate oxidase.

Features

1. Black urine on standing
2. Ochronosis
3. Arthritis

13. Hartnup's disease

Defect in transport of neutral amino acids including tryptophan.

Features

1. Pellagra-like rash
2. Cerebellar ataxia
3. Aminoaciduria

14. Discuss the formation of melanin and add a note on albinism

Tyrosine converted to DOPA and melanin by tyrosinase.

Albinism

- Deficiency of tyrosinase
- Defective melanin synthesis
- Hypopigmentation

15. Biochemical defect, clinical features and diagnosis of phenylketonuria.

Defect

Phenylalanine hydroxylase deficiency.

Clinical features

1. Mental retardation
2. Convulsions
3. Hypopigmentation
4. Mousy odor

Diagnosis

1. Ferric chloride test
2. Guthrie test
3. Increased blood phenylalanine

16. Name the metabolic disorders associated with aromatic amino acids

1. Phenylketonuria
2. Alkaptonuria
3. Albinism
4. Tyrosinemia
5. Hartnup disease

17. Phenylketonuria

Inherited disorder due to phenylalanine hydroxylase deficiency.

Features

- Mental retardation
- Seizures
- Hypopigmentation
- Mousy odor

Tests

- Ferric chloride test
- Guthrie test

18. Albinism

Cause

Tyrosinase deficiency.

Features

1. Lack of melanin
2. White skin and hair
3. Photophobia

19. Enzyme defect and abnormal metabolites in phenylketonuria

Enzyme defect

Phenylalanine hydroxylase.

Abnormal metabolites

1. Phenylpyruvate
2. Phenylacetate
3. Phenyllactate

20. Specialised product of tryptophan

1. Serotonin
2. Melatonin
3. Niacin

21. What is phenylketonuria and name the enzymatic defect

Phenylketonuria is an inherited disorder due to deficiency of phenylalanine hydroxylase.

22. Name the biochemical test for phenylketonuria.

1. Ferric chloride test
2. Guthrie bacterial inhibition test
3. Tandem mass spectrometry

CITRIC ACID CYCLE, BIOLOGICAL OXIDATION AND ELECTRON TRANSPORT CHAIN

LONG ESSAYS

1. Describe the reactions of the Citric Acid Cycle. Explain the Amphibolic nature of this cycle. Add a note on its energetics.

Definition

Citric acid cycle is the final common pathway for oxidation of carbohydrates, fats and proteins.

Site

Mitochondria.

Steps

1. Acetyl CoA + oxaloacetate → citrate
2. Citrate → isocitrate
3. Isocitrate → α-ketoglutarate
4. α-ketoglutarate → succinyl CoA
5. Succinyl CoA → succinate
6. Succinate → fumarate
7. Fumarate → malate
8. Malate → oxaloacetate

Energetics

For one acetyl CoA:

- 3 NADH
- 1 FADH2
- 1 GTP

Total ATP yield ≈ 10 ATP.

Amphibolic nature

Catabolic role

Oxidation of acetyl CoA.

Anabolic role

Intermediates used for:

1. Amino acid synthesis
2. Heme synthesis
3. Gluconeogenesis
4. Fatty acid synthesis

2. Describe the mitochondrial electron transport chain. What is substrate level phosphorylation. Give two examples.

Electron transport chain

Series of electron carriers in inner mitochondrial membrane.

Components

1. Complex I – NADH dehydrogenase
2. Complex II – Succinate dehydrogenase
3. Coenzyme Q
4. Complex III – Cytochrome bc1
5. Cytochrome c
6. Complex IV – Cytochrome oxidase

ATP synthesis

Occurs by oxidative phosphorylation.

Inhibitors

- Rotenone
- Antimycin A
- Cyanide

Substrate level phosphorylation

Direct formation of ATP independent of ETC.

Examples

1. Succinyl CoA → Succinate
2. Phosphoenol pyruvate → Pyruvate

SHORT ESSAYS

5. Discuss the structural and functional organization of the electron transport chain. Add a note on its inhibitors

ETC is located in inner mitochondrial membrane.

Components

Complex I, II, III, IV and ATP synthase.

Function

Transfer electrons to oxygen with ATP production.

Inhibitors

Complex	Inhibitor
I	Rotenone
III	Antimycin A
IV	Cyanide, CO
ATP synthase	Oligomycin

6. Define oxidative phosphorylation. Explain the chemiosmotic theory

Oxidative phosphorylation

Formation of ATP coupled with oxidation of NADH and FADH2.

Chemiosmotic theory

Proposed by Peter Mitchell.

Electron transport pumps protons across inner mitochondrial membrane creating proton gradient. Return of protons through ATP synthase forms ATP.

7. Explain electron transport chain with a suitable diagram. Add a note on the inhibitors of ETC

REFER DIAGRAM SECTION

Inhibitors

1. Rotenone – Complex I
2. Antimycin A – Complex III
3. Cyanide – Complex IV
4. Oligomycin – ATP synthase

8. Enumerate the steps of TCA cycle. Add a note on malate shuttle.

Steps of TCA cycle

1. Citrate formation
2. Isomerization
3. Oxidative decarboxylation
4. Formation of succinyl CoA
5. Succinate formation
6. Fumarate formation
7. Malate formation
8. Oxaloacetate regeneration

Malate shuttle

Transfers cytosolic NADH into mitochondria through malate-aspartate system.

9. Draw a neat labeled diagram of electron transport chain. Add a note on chemiosmotic hypothesis.

REFER DIAGRAM SECTION

Chemiosmotic hypothesis

Proton gradient generated during electron transport drives ATP synthesis.

10. Diagrammatic representation of mitochondrial electron transport chain and location of ATP synthesis

REFER DIAGRAM SECTION

11. Chemiosmotic mechanism in ATP synthesis

Electron transport pumps protons into intermembrane space. Proton gradient drives ATP synthase leading to ATP formation.

12. Tricarboxylic acid cycle

REFER DIAGRAM SECTION

Functions

1. Oxidation of acetyl CoA
2. ATP production
3. Provides intermediates for biosynthesis

Site

Mitochondria.

SHORT ANSWERS

13. Inhibitors of oxidative phosphorylation

1. Oligomycin
2. Atractyloside
3. Dinitrophenol (uncoupler)

14. Uncouplers of oxidative phosphorylation

1. Dinitrophenol
2. Thermogenin
3. High dose salicylates

15. Describe the Malate Aspartate shuttle.

Transfers reducing equivalents of cytosolic NADH into mitochondria using malate and aspartate.

16. Chemiosmotic theory

ATP synthesis is driven by proton gradient generated during electron transport.

17. Amphibolic role of TCA cycle

Catabolic role

Oxidation of acetyl CoA.

Anabolic role

Provides intermediates for synthesis of:

1. Amino acids
2. Heme
3. Glucose
4. Fatty acids

18. Role of cytokine in ETC

Cytochromes transfer electrons in ETC through reversible oxidation reduction of iron.

19. What is anaplerosis.

Reactions that replenish TCA cycle intermediates are called anaplerotic reactions.

Example: Pyruvate → Oxaloacetate.

20. Name the inhibitors of electron transport chain and state at what level they act.

Inhibitor	Site
Rotenone	Complex I
Antimycin A	Complex III
Cyanide	Complex IV
CO	Complex IV

21. Inhibitors of ETC

1. Rotenone
2. Amytal
3. Antimycin A

4. Cyanide
5. Carbon monoxide

22. Sources of acetyl CoA.

1. Pyruvate
2. Fatty acids
3. Ketogenic amino acids
4. Ketone bodies

23. Anaplerotic reactions of citric acid cycle

1. Pyruvate → Oxaloacetate
2. Transamination reactions
3. Propionyl CoA → Succinyl CoA

24. Name the inhibitors of ETC and state at what level they act

Inhibitor	Site of action
Rotenone	Complex I
Antimycin A	Complex III
Cyanide	Complex IV

25. Diagrammatically represent the electron transport chain

NADH → Complex I → CoQ → Complex III → Cyt c → Complex IV → O2.

Succinate → Complex II → CoQ.

26. Anaplerotic role of TCA cycle

TCA cycle intermediates are replenished by anaplerotic reactions.

Example:
Pyruvate carboxylase forms oxaloacetate.

27. ATP synthesis

ATP synthesis occurs by oxidative phosphorylation through ATP synthase using proton gradient.

28. What is substrate level phosphorylation. Mention one example

Direct formation of ATP without ETC.

Example

Succinyl CoA → Succinate.

NUTRITION

FAT SOLUBLE VITAMINS (A,D,E,K)

LONG ESSAYS

1. Explain the active form, activation, biochemical functions, RDA and deficiency manifestations of vitamin D.

Active form

1,25-dihydroxy cholecalciferol (Calcitriol).

Activation

1. Skin: 7-dehydrocholesterol → Cholecalciferol
2. Liver: 25-hydroxylation
3. Kidney: 1α-hydroxylation to active form

Functions

1. Increases calcium absorption from intestine
2. Increases phosphate absorption
3. Bone mineralization
4. Maintains calcium homeostasis

RDA

400 IU/day approximately.

Deficiency manifestations

1. Rickets in children
2. Osteomalacia in adults
3. Hypocalcemic tetany

Sources

Fish liver oil, egg yolk, sunlight.

2. Discuss vitamin D under the following headings:

a. Source
b. Daily requirement
c. Metabolism
d. Biochemical functions
e. Deficiency manifestations

a. Sources

1. Sunlight
2. Fish liver oil
3. Egg yolk
4. Butter
5. Fortified milk

b. Daily requirement

Approximately 400 IU/day in adults.

c. Metabolism

1. 7-dehydrocholesterol in skin forms cholecalciferol by ultraviolet rays.
2. In liver, cholecalciferol is converted to 25-hydroxy cholecalciferol.
3. In kidney, it is converted to active form 1,25-dihydroxy cholecalciferol by 1α-hydroxylase.

d. Biochemical functions

1. Increases intestinal absorption of calcium.
2. Increases phosphate absorption.
3. Promotes bone mineralization.
4. Maintains plasma calcium and phosphate levels.
5. Helps in normal growth of bones and teeth.

e. Deficiency manifestations

In children – Rickets

- Bow legs
- Rachitic rosary
- Delayed dentition

In adults – Osteomalacia

- Bone pain
- Fragile bones
- Muscle weakness

Laboratory findings

- Decreased serum calcium
- Decreased phosphate
- Increased alkaline phosphatase

3. Explain in detail the active forms, biochemical functions, RDA and deficiency manifestations of Vitamin A with a note on Wald's Visual Cycle

Vitamin A

Vitamin A is a fat-soluble vitamin essential for vision, growth, epithelial integrity and immunity.

Active forms

1. Retinol – alcohol form; transport and storage form.
2. Retinal – aldehyde form; involved in vision.
3. Retinoic acid – acid form; involved in gene expression and growth.
4. Retinyl esters – storage form in liver.

Biochemical functions

1. Vision

- 11-cis retinal combines with opsin to form rhodopsin in rods.
- Essential for dim light vision.

2. Maintenance of epithelium

- Maintains integrity of epithelial tissues.
- Prevents keratinization.

3. Growth and differentiation

- Regulates gene expression.
- Required for skeletal growth.

4. Reproduction

- Essential for spermatogenesis and fetal development.

5. Immunity

- Enhances resistance to infections.

6. Antioxidant action

- Beta-carotene acts as antioxidant.

RDA

- Adult male: 1000 microgram retinol equivalents/day.
- Adult female: 800 microgram/day.
- Pregnancy/lactation: increased requirement.

Deficiency manifestations

Ocular manifestations

1. Night blindness.
2. Xerophthalmia.
3. Bitot spots.
4. Keratomalacia.
5. Complete blindness.

Skin changes

- Dry rough skin.
- Follicular hyperkeratosis.

Growth retardation

- Stunted growth in children.

Increased infections

- Recurrent respiratory and gastrointestinal infections.

Wald's Visual Cycle

1. Rhodopsin = opsin + 11-cis retinal.
2. Light converts 11-cis retinal to all-trans retinal.
3. Rhodopsin dissociates producing visual impulse.
4. All-trans retinal is reduced to retinol.
5. Retinol is transported to pigment epithelium.
6. Retinol reconverted to 11-cis retinal.
7. 11-cis retinal combines with opsin to regenerate rhodopsin.

4. Describe the synthesis, biochemical functions, daily requirements, sources and deficiency manifestation of vitamin D.

Vitamin D

Vitamin D is a fat-soluble vitamin functioning like a hormone.

Synthesis

1. 7-dehydrocholesterol in skin is converted to cholecalciferol by ultraviolet rays.
2. In liver:

- Cholecalciferol converted to 25-hydroxy cholecalciferol.

3. In kidney:

- Converted to active form 1,25-dihydroxy cholecalciferol (calcitriol) by 1-alpha hydroxylase.

Biochemical functions

1. Intestinal absorption

- Increases calcium and phosphorus absorption.

2. Bone mineralization

- Essential for normal bone formation.

3. Renal action

- Increases renal tubular reabsorption of calcium.

4. Plasma calcium regulation

- Maintains serum calcium and phosphorus.

Daily requirement

- Adults: 400 IU/day.
- Children and pregnancy: 400–800 IU/day.

Sources

Animal sources

- Fish liver oil.
- Egg yolk.
- Butter.
- Liver.

Endogenous source

- Skin synthesis by sunlight exposure.

Deficiency manifestations

In children – Rickets

- Bow legs.
- Rachitic rosary.
- Delayed dentition.
- Craniotabes.

In adults – Osteomalacia

- Bone pain.
- Fragile bones.
- Muscle weakness.

5. Describe the chemistry, biochemical functions, requirements and deficiency symptoms of vitamin A.

Chemistry

- Vitamin A is an isoprenoid alcohol.
- Exists as retinol, retinal and retinoic acid.
- Fat soluble and stored in liver.

Biochemical functions

1. Vision.
2. Maintenance of epithelial tissues.
3. Growth and differentiation.
4. Reproduction.
5. Immunity.
6. Antioxidant action of carotenoids.

Requirements

- Adult male: 1000 microgram/day.

- Adult female: 800 microgram/day.

Deficiency symptoms

1. Night blindness.
2. Xerophthalmia.
3. Bitot spots.
4. Keratomalacia.
5. Follicular hyperkeratosis.
6. Increased infections.
7. Growth retardation.

6. Describe the chemistry, biochemical functions, daily requirements, sources and deficiency manifestations of vitamin D

Chemistry

- Vitamin D is a sterol derivative.
- Vitamin D2 = Ergocalciferol.
- Vitamin D3 = Cholecalciferol.

Biochemical functions

1. Increases calcium absorption.
2. Increases phosphorus absorption.
3. Promotes bone mineralization.
4. Maintains calcium homeostasis.

Daily requirements

- 400 IU/day.

Sources

1. Fish liver oil.
2. Egg yolk.
3. Butter.
4. Liver.
5. Sunlight exposure.

Deficiency manifestations

Rickets in children

- Bow legs.
- Pigeon chest.
- Delayed closure of fontanelle.

Osteomalacia in adults

- Bone pain.
- Fractures.

7. Describe the sources, RDA, functions and deficiency disorders associated with vitamin D

Sources

1. Fish liver oil.
2. Egg yolk.
3. Butter.
4. Liver.
5. Sunlight.

RDA

- Adults: 400 IU/day.
- Children/pregnancy: 400–800 IU/day.

Functions

1. Calcium absorption.
2. Phosphorus absorption.
3. Bone mineralization.
4. Calcium homeostasis.

Deficiency disorders

Rickets

- Seen in children.
- Bone deformities.

Osteomalacia

- Seen in adults.
- Soft bones.

8. Describe the source, dietary requirements, biochemical functions and deficiency manifestations of vitamin A

Sources

Animal sources

- Liver.
- Egg yolk.
- Milk.
- Butter.

Vegetable sources

- Carrot.
- Mango.
- Papaya.
- Green leafy vegetables.

Dietary requirements

- Adult male: 1000 microgram/day.
- Adult female: 800 microgram/day.

Biochemical functions

1. Vision.
2. Epithelial integrity.
3. Growth.
4. Immunity.
5. Reproduction.

Deficiency manifestations

1. Night blindness.
2. Xerophthalmia.
3. Bitot spots.
4. Keratomalacia.
5. Dry skin.
6. Increased infections.

9. Describe the sources RDA, biochemical functions and deficiency manifestations of vitamin D

Sources

1. Fish liver oil.
2. Egg yolk.
3. Butter.
4. Liver.
5. Sunlight.

RDA

- 400 IU/day.

Biochemical functions

1. Enhances calcium absorption.
2. Bone mineralization.
3. Maintains calcium-phosphorus balance.

Deficiency manifestations

Rickets

- Bow legs.
- Delayed dentition.

Osteomalacia

- Bone pain.
- Fragility fractures.

SHORT ESSAYS

10. A five-year-old girl from a rural area was brought to a primary health care centre with a history of frequent falls and bumping into objects after sunset. Her mother gave a history of repeated respiratory infections. On examination, she was found to have Vitamin A deficiency.

a) List the signs/manifestations of Vitamin A deficiency

1. Night blindness.

2. Xerophthalmia.
3. Bitot spots.
4. Keratomalacia.
5. Dry skin.
6. Follicular hyperkeratosis.
7. Growth retardation.
8. Increased susceptibility to infections.

b) Mention the dietary sources of Vitamin A

Animal sources

- Liver.
- Egg yolk.
- Butter.
- Milk.

Vegetable sources

- Carrot.
- Papaya.
- Mango.
- Green leafy vegetables.

c) Explain the biochemical functions of Vitamin A

1. Visual cycle.
2. Maintenance of epithelial tissue.
3. Growth and differentiation.
4. Reproduction.
5. Immunity.
6. Antioxidant action.

11. Describe the dietary sources, daily requirement and deficiency symptoms of Vitamin D.

Dietary sources

1. Fish liver oil.
2. Egg yolk.
3. Butter.
4. Liver.
5. Sunlight.

Daily requirement

- 400 IU/day.

Deficiency symptoms

Rickets

- Bow legs.
- Delayed dentition.

Osteomalacia

- Bone pain.
- Muscle weakness.

12. What are the sources of vitamin A. Enumerate the biochemical role and deficiency manifestations of vitamin A.

Sources

Animal sources

- Liver.
- Butter.
- Egg yolk.

Vegetable sources

- Carrot.
- Mango.
- Papaya.
- Green leafy vegetables.

Biochemical role

1. Vision.
2. Epithelial maintenance.
3. Growth.
4. Immunity.
5. Reproduction.

Deficiency manifestations

1. Night blindness.

2. Xerophthalmia.
3. Bitot spots.
4. Keratomalacia.
5. Dry skin.

13. Sources, RDA and biochemical functions of vitamin D

Sources

1. Fish liver oil.
2. Egg yolk.
3. Butter.
4. Sunlight.

RDA

- 400 IU/day.

Biochemical functions

1. Calcium absorption.
2. Bone mineralization.
3. Calcium homeostasis.

SHORT ANSWERS

14. Biological role of Vitamin K

1. Required for gamma-carboxylation of glutamate residues.
2. Essential for synthesis of clotting factors II, VII, IX and X.
3. Needed for proteins C and S.
4. Important in bone proteins like osteocalcin.

15. Biochemical functions of vitamin A

1. Vision.
2. Maintenance of epithelium.
3. Growth and differentiation.
4. Immunity.
5. Reproduction.
6. Antioxidant action.

16. Describe the Wald's visual cycle

1. Rhodopsin contains opsin + 11-cis retinal.
2. Light converts 11-cis retinal to all-trans retinal.
3. Rhodopsin dissociates generating nerve impulse.
4. All-trans retinal converted to retinol.
5. Retinol transported to pigment epithelium.
6. Reconverted to 11-cis retinal.
7. Rhodopsin regenerated.

17. Functions of vitamin E

1. Antioxidant action.
2. Prevents lipid peroxidation.
3. Protects red blood cell membrane.
4. Maintains reproductive function.

18. Rickets

- Deficiency disease of vitamin D in children.
- Features:

1. Bow legs.
2. Rachitic rosary.
3. Delayed dentition.
4. Craniotabes.

19. Active forms of Vitamin A and the deficiency manifestation

Active forms

1. Retinol.
2. Retinal.
3. Retinoic acid.

Deficiency manifestations

1. Night blindness.
2. Xerophthalmia.
3. Keratomalacia.

4. Dry skin.

20. Vitamin K Cycle

1. Reduced vitamin K acts as coenzyme for gamma-carboxylation.
2. Oxidized to epoxide form.
3. Vitamin K epoxide reductase regenerates reduced vitamin K.
4. Warfarin inhibits this cycle.

21. Functions and deficiency manifestations of vitamin E

Functions

1. Antioxidant.
2. Protects cell membranes.
3. Prevents lipid peroxidation.

Deficiency manifestations

1. Hemolytic anemia.
2. Neuromuscular disorders.
3. Retinopathy.

22. Calcitriol

- Active form of vitamin D.
- Chemically 1,25-dihydroxy cholecalciferol.

Functions

1. Increases calcium absorption.
2. Increases phosphorus absorption.
3. Bone mineralization.

WATER SOLUBLE VITAMINS (B COMPLEX & C)

LONG ESSAYS

1. In detail about sources, RDA, coenzyme forms, and deficiency manifestations of folic acid

Sources

1. Green leafy vegetables.
2. Liver.
3. Yeast.
4. Pulses.

RDA

- Adults: 200 microgram/day.
- Pregnancy: 400 microgram/day.

Coenzyme form

- Tetrahydrofolate (THF).

Functions

1. One-carbon transfer reactions.
2. Purine synthesis.
3. Thymidylate synthesis.
4. Amino acid metabolism.

Deficiency manifestations

1. Megaloblastic anemia.
2. Glossitis.
3. Diarrhea.
4. Neural tube defects in fetus.

2. Describe the sources, RDA, functions and deficiency manifestations of ascorbic acid

Sources

1. Citrus fruits.
2. Amla.
3. Guava.
4. Tomato.
5. Green vegetables.

RDA

- 40–60 mg/day.

Functions

1. Collagen synthesis.
2. Antioxidant action.
3. Iron absorption.
4. Wound healing.
5. Hydroxylation reactions.

Deficiency manifestations

Scurvy

1. Bleeding gums.
2. Petechiae.
3. Delayed wound healing.
4. Bone changes.

3. Describe the chemistry, biochemical functions, requirements and deficiency symptoms of vitamin C

Chemistry

- Vitamin C is ascorbic acid.
- Water-soluble reducing agent.

Biochemical functions

1. Collagen synthesis.
2. Antioxidant action.
3. Iron absorption.
4. Wound healing.

Requirements

- 40–60 mg/day.

Deficiency symptoms

Scurvy

1. Bleeding gums.
2. Petechiae.
3. Anemia.
4. Delayed wound healing.

SHORT ESSAYS

4. A 22-year-old women presented with progressive neuropathy for over a few months. She developed numbness and tingling of his hands and feet. Symptoms progressed to difficulty in walking and loss of position sense. For the past 6 years she has stopped eating all nonvegetarian diet including dairy products. Her laboratory results are as follows. Hemoglobin: 10 g/dL, Hematocrit: 47%, Mean corpuscular volume [MCV]: 114fl

a) What is the probable micronutrient deficiency the woman is suffering from

- Vitamin B12 deficiency.

b) What is the RDA, sources, biochemical functions and lab diagnosis of this micronutrient

RDA

- 1–2 microgram/day.

Sources

1. Liver.
2. Meat.
3. Fish.
4. Egg.
5. Milk.

Biochemical functions

1. Conversion of methylmalonyl CoA to succinyl CoA.
2. Methionine synthase reaction.
3. DNA synthesis.

Laboratory diagnosis

1. Megaloblastic anemia.
2. Increased MCV.

3. Low serum vitamin B12.
4. Increased methylmalonic acid.
5. Hypersegmented neutrophils.

5. Deficiency of folate and vitamin B12 leads to megaloblastic anaemia, substantiate the statement

1. Folate and vitamin B12 are required for DNA synthesis.
2. Deficiency causes defective thymidylate synthesis.
3. Nuclear maturation is impaired.
4. Cell division decreases.
5. Large immature RBC precursors appear in marrow.
6. Peripheral blood shows macrocytic megaloblastic anemia.
7. Hypersegmented neutrophils are present.

6. Describe the source, biochemical functions, and deficiency manifestations of thiamine

Sources

1. Cereals.
2. Pulses.
3. Yeast.
4. Liver.

Biochemical functions

1. Coenzyme as thiamine pyrophosphate.
2. Oxidative decarboxylation.
3. Transketolase reaction.

Deficiency manifestations

Beriberi

- Dry beriberi.
- Wet beriberi.

Wernicke-Korsakoff syndrome

- Seen in alcoholics.

7. Enumerate the sources, daily requirement and deficiency manifestation of vitamin C

Sources

1. Citrus fruits.
2. Guava.
3. Amla.
4. Tomato.

Daily requirement

- 40–60 mg/day.

Deficiency manifestation

Scurvy

1. Bleeding gums.
2. Petechiae.
3. Delayed wound healing.
4. Bone pain.

8. Describe the coenzyme form, sources, biomedical role and deficiency manifestation of thiamine

Coenzyme form

- Thiamine pyrophosphate (TPP).

Sources

1. Whole cereals.
2. Pulses.
3. Liver.
4. Yeast.

Biomedical role

1. Oxidative decarboxylation.

2. Pentose phosphate pathway.
3. Carbohydrate metabolism.

Deficiency manifestation

1. Beriberi.
2. Wernicke encephalopathy.
3. Peripheral neuropathy.

9. Sources, biochemical functions and deficiency manifestations of niacin.

Sources

1. Meat.
2. Fish.
3. Groundnut.
4. Cereals.

Biochemical functions

1. Forms NAD and NADP.
2. Oxidation-reduction reactions.
3. Energy metabolism.

Deficiency manifestations

Pellagra

- Dermatitis.
- Diarrhea.
- Dementia.

10. Biochemical functions and deficiency manifestations of vitamin B12

Biochemical functions

1. Methionine synthase reaction.
2. Methylmalonyl CoA mutase reaction.
3. DNA synthesis.

Deficiency manifestations

1. Megaloblastic anemia.
2. Peripheral neuropathy.
3. Subacute combined degeneration.
4. Glossitis.

11. Discuss the co-enzyme role of thiamine and the deficiency disorder.

Coenzyme role

- Thiamine pyrophosphate acts in:

1. Pyruvate dehydrogenase.
2. Alpha-ketoglutarate dehydrogenase.
3. Branched chain ketoacid dehydrogenase.
4. Transketolase reaction.

Deficiency disorder

Beriberi

- Dry beriberi: neuropathy.
- Wet beriberi: cardiac failure.

Wernicke-Korsakoff syndrome

- Confusion.
- Ataxia.
- Ophthalmoplegia.

SHORT ANSWERS

12. Beri Beri

- Caused by thiamine deficiency.

Types

1. Dry beriberi – neuropathy.
2. Wet beriberi – cardiac manifestations.
3. Infantile beriberi.

13. Describe the signs and symptoms of Thiamine deficiency.

1. Peripheral neuropathy.
2. Muscle wasting.
3. Cardiac failure.
4. Edema.
5. Wernicke encephalopathy.

14. Biochemical basis of- "Anemia In pyridoxine deficiency"

- Pyridoxal phosphate is required for ALA synthase in heme synthesis.
- Deficiency decreases heme synthesis.
- Causes sideroblastic anemia.

15. FIGLU excretion Test

- Histidine metabolism requires folate.
- In folate deficiency FIGLU excretion increases after histidine load.
- Used to diagnose folate deficiency.

16. Scurvy

- Disease due to vitamin C deficiency.

Features

1. Bleeding gums.
2. Petechiae.
3. Delayed wound healing.
4. Bone changes.

17. Folate trap

- In vitamin B12 deficiency methyl THF cannot convert to THF.
- Folate trapped as methyl THF.
- Functional folate deficiency results.

18. Functions of pyridoxal phosphate

1. Transamination.
2. Decarboxylation.
3. Heme synthesis.
4. Neurotransmitter synthesis.
5. Glycogen phosphorylase reaction.

19. FIGLU excretion test

- Increased urinary FIGLU after histidine load indicates folate deficiency.

20. Functions and deficiency manifestations of thiamine

Functions

1. Oxidative decarboxylation.
2. Transketolase reaction.
3. Energy metabolism.

Deficiency manifestations

1. Beriberi.
2. Wernicke encephalopathy.

21. Folic acid antagonists

1. Methotrexate.
2. Trimethoprim.
3. Pyrimethamine.

22. Mention one function and one deficiency manifestation of vitamin B12

Function

- DNA synthesis.

Deficiency manifestation

- Megaloblastic anemia.

23. Name three B complex vitamins and its coenzyme form

1. Thiamine – Thiamine pyrophosphate.
2. Riboflavin – FMN/FAD.
3. Niacin – NAD/NADP.

24. Functions of vitamin B6

1. Transamination.
2. Decarboxylation.
3. Heme synthesis.
4. Neurotransmitter synthesis.

25. Biochemical role of thiamine pyrophosphate

1. Oxidative decarboxylation.
2. Transketolase reaction.
3. Carbohydrate metabolism.

26. Pellagra

- Niacin deficiency disease.

Features

1. Dermatitis.
2. Diarrhea.
3. Dementia.

27. Functions of thiamine pyrophosphate

1. Coenzyme in pyruvate dehydrogenase.
2. Alpha-ketoglutarate dehydrogenase.
3. Transketolase reaction.

28. Folate anatogonists

1. Methotrexate.
2. Trimethoprim.
3. Pyrimethamine.

29. Co-enzyme functions of biotin

1. Carboxylation reactions.
2. Pyruvate carboxylase.
3. Acetyl CoA carboxylase.
4. Propionyl CoA carboxylase.

30. Two co-enzyme roles of NADPH

1. Fatty acid synthesis.
2. Maintenance of reduced glutathione.

31. Biochemical functions of thiamine

1. Energy metabolism.
2. Oxidative decarboxylation.
3. Pentose phosphate pathway.

32. List two reactions where the folic acid is the co-enzyme

1. Thymidylate synthesis.
2. Purine synthesis.

33. Name the co-enzyme forms of niacin and write important functions for each one of them

Coenzyme forms

1. NAD.
2. NADP.

Functions

NAD

- Oxidation reactions in glycolysis and TCA cycle.

NADP

- Reductive biosynthesis.
- Pentose phosphate pathway.

MINERAL METABOLISM AND ABNORMALITIES

LONG ESSAYS

1. A ten-year-old girl presented to the out-patient department of the hospital from a nearby village with excessive tiredness, weakness, abdominal pain with frequent alternate episodes of constipation and

diarrhea. She gave a history of frequently playing with mud, walking barefoot on poor personal hygiene and sanitation. On examination, the physician found pallor of the conjunctiva, angular stomatitis and koilonychia to be present. Laboratory examination revealed low hemoglobin level & hypochromic microcytic RBC. Microscopic examination of fresh stool samples showed presence of hookworm eggs.

a) Name the nutrient whose deficiency presents with the above manifestations

- Iron deficiency.

b) Name any two dietary sources of that nutrient

1. Liver.
2. Green leafy vegetables.

c) Name any four proteins that contain this nutrient along with their functions

1. Hemoglobin – oxygen transport.
2. Myoglobin – oxygen storage.
3. Cytochromes – electron transport.
4. Catalase – breakdown of hydrogen peroxide.

d) Describe the dietary absorption and transport of the nutrient

Absorption

1. Iron absorbed mainly in duodenum.
2. Ferric iron reduced to ferrous form.
3. Ferrous iron absorbed by DMT1 transporter.
4. Heme iron absorbed efficiently.

Transport

1. Iron transported by transferrin.
2. Stored as ferritin and hemosiderin.
3. Transported to bone marrow for hemoglobin synthesis.

2. A patient aged 35 years complains of pain, cramps, tingling sensation in the hands and feet, recurrent carpopedal spasms. Her past history revealed history of thyroidectomy for goiter. Her blood investigation report is as follows: Serum Creatinine – 1.0 mg %, Serum Calcium – 4.1mg%, serum Phosphorous – 5.4 mg %, Albumin – 4.0 gm%, Alkaline phosphatase – 60 IU

a) What could be your probable diagnosis

- Hypoparathyroidism.

b) What is the Biochemical Basis for this disorder

1. Deficiency of parathyroid hormone after thyroidectomy.
2. Decreased calcium mobilization from bone.
3. Decreased renal calcium reabsorption.
4. Hyperphosphatemia.
5. Hypocalcemia causes tetany and carpopedal spasm.

c) Explain the regulation of plasma levels of Calcium

1. Parathyroid hormone increases calcium.
2. Calcitriol increases intestinal calcium absorption.
3. Calcitonin decreases plasma calcium.
4. Kidney and bone regulate calcium homeostasis.

d) Write the normal Reference ranges for Serum Calcium, Serum Phosphorus, serum Creatinine and serum Albumin.

1. Serum calcium: 9–11 mg/dL.
2. Serum phosphorus: 2.5–4.5 mg/dL.
3. Serum creatinine: 0.7–1.2 mg/dL.
4. Serum albumin: 3.5–5 g/dL.

3. Describe the absorption, transport and storage of iron in the body. Explain the regulation of iron homeostasis. Enumerate the biochemical functions of iron. Add a note on disorders associated iron metabolism.

Absorption

1. Occurs mainly in duodenum.
2. Ferric iron reduced to ferrous form.
3. Absorbed by DMT1 transporter.
4. Heme iron absorbed directly.

Transport

- Iron transported in plasma by transferrin.

Storage

1. Ferritin – soluble storage form.
2. Hemosiderin – insoluble storage form.
3. Stored in liver, spleen and bone marrow.

Regulation of iron homeostasis

1. Hepcidin is major regulator.
2. Hepcidin inhibits ferroportin.
3. Increased hepcidin decreases absorption.
4. Iron deficiency suppresses hepcidin.

Biochemical functions of iron

1. Hemoglobin synthesis.
2. Myoglobin function.
3. Electron transport chain.
4. Catalase and peroxidase activity.
5. Cellular respiration.

Disorders associated with iron metabolism

Iron deficiency anemia

- Microcytic hypochromic anemia.
- Koilonychia.
- Glossitis.

Hemochromatosis

- Iron overload disorder.
- Liver cirrhosis.
- Diabetes mellitus.
- Skin pigmentation.

4. 35-year-old female, housewife, presented to the medicine department with excessive weakness, breathlessness and palpitations since 3 months. History revealed that she had complaints of excessive menstrual bleeding. She had followed strict vegetarian diet. Investigations revealed her hemoglobin was 7 Gms/dl

• What is the probable diagnosis

• Describe the sources, RDA, functions, absorption, transport and deficiency of the mineral involved

• Describe the biochemical investigations and blood picture relevant to this case

Answer

Probable diagnosis

Iron deficiency anemia.

Sources of iron

Animal sources

- Liver
- Meat
- Egg yolk
- Fish

Vegetable sources

- Green leafy vegetables
- Pulses
- Cereals
- Dates
- Jaggery

Recommended dietary allowance (RDA)

Group	RDA
Adult male	17 mg/day
Adult female	21 mg/day
Pregnancy	35 mg/day

Functions of iron

1. Hemoglobin synthesis
2. Myoglobin formation
3. Electron transport chain
4. Cellular respiration
5. Component of catalase and peroxidase
6. Oxidative metabolism

Absorption of iron

- Occurs in duodenum and jejunum.
- Ferric iron reduced to ferrous form.
- Ferrous iron absorbed via DMT-1.
- Stored as ferritin in mucosal cells.
- Exported by ferroportin.
- Bound to transferrin in plasma.

Transport of iron

- Transported by transferrin.
- Delivered to bone marrow and tissues.

Deficiency manifestations

- Pallor
- Fatigue
- Weakness
- Dyspnea
- Koilonychia
- Angular stomatitis
- Glossitis

Biochemical investigations

Investigation	Finding
Hemoglobin	Decreased
Serum iron	Decreased
Serum ferritin	Decreased
Total iron binding capacity	Increased
Transferrin saturation	Decreased
Bone marrow iron	Reduced

Peripheral blood picture

- Microcytic hypochromic anemia
- Anisocytosis
- Poikilocytosis
- Pencil cells may be present

SHORT ESSAYS

6. Enumerate the causes, peripheral blood picture and laboratory findings in iron deficiency anemia.

Answer

Causes

1. Nutritional deficiency
2. Chronic blood loss
3. Hookworm infestation
4. Menorrhagia
5. Pregnancy and lactation
6. Malabsorption
7. Repeated pregnancies

Peripheral blood picture

- Microcytic hypochromic RBCs
- Anisocytosis
- Poikilocytosis
- Pencil cells
- Reduced hemoglobin

Laboratory findings

Investigation	Finding
Hemoglobin	Decreased
Serum iron	Decreased
Serum ferritin	Decreased
TIBC	Increased
Transferrin saturation	Decreased
Bone marrow iron	Decreased
Mean corpuscular volume	Decreased
Mean corpuscular hemoglobin	Decreased

7. Absorption, transport and storage of iron in the body.

Answer

Absorption

- Site: Duodenum and jejunum.
- Ferric iron reduced to ferrous form.
- Absorbed through DMT-1.
- Heme iron absorbed efficiently.
- Iron stored temporarily as ferritin.
- Exported by ferroportin.

Factors increasing absorption

- Vitamin C
- Gastric acid
- Heme iron

Factors decreasing absorption

- Phytates
- Oxalates
- Tannins

Transport

- Transported by transferrin.
- One transferrin binds two ferric ions.
- Transported to bone marrow and liver.

Storage

Ferritin

- Soluble storage form.
- Present in liver, spleen and bone marrow.

Hemosiderin

- Insoluble storage form.
- Seen in iron overload.

8. Many metalloenzymes contains Copper. Write down the reactions catalyzed by copper metalloenzymes.

Answer

Copper containing enzyme	Reaction catalyzed
Cytochrome oxidase	Electron transport and oxidative phosphorylation
Ceruloplasmin	Ferrous to ferric iron oxidation
Tyrosinase	Tyrosine to melanin synthesis
Lysyl oxidase	Cross linking of collagen and elastin
Superoxide dismutase	Conversion of superoxide radical to hydrogen peroxide
Dopamine β-	Dopamine to

Copper containing enzyme	Reaction catalyzed
hydroxylase	norepinephrine

9. Absorption, transport and storage of iron.

Answer

Absorption

- Occurs in duodenum and jejunum.
- Ferric iron converted to ferrous form.
- Ferrous iron absorbed by DMT-1.
- Heme iron absorbed efficiently.
- Stored as ferritin in mucosal cells.

Transport

- Transported by transferrin.
- Delivered to bone marrow and tissues.

Storage

- Ferritin – soluble storage form.
- Hemosiderin – insoluble storage form.
- Storage sites: liver, spleen, bone marrow.

10. What is the normal serum calcium level. How is it regulated.

Answer

Normal serum calcium level

- Total calcium: 9–11 mg/dL
- Ionized calcium: 4.5–5.5 mg/dL

Regulation

Parathyroid hormone

- Increases serum calcium.
- Increases bone resorption.
- Increases renal calcium reabsorption.
- Activates vitamin D.

Calcitriol

- Increases intestinal absorption of calcium.
- Increases renal calcium reabsorption.

Calcitonin

- Lowers serum calcium.
- Inhibits osteoclastic activity.

11. What is the normal reference range for serum calcium. How is it regulated.

Answer

Normal reference range

- Total calcium: 9–11 mg/dL
- Ionized calcium: 4.5–5.5 mg/dL

Regulation

Regulated by:

1. Parathyroid hormone
2. Calcitriol
3. Calcitonin

PTH

- Raises serum calcium.

Calcitriol

- Increases intestinal absorption.

Calcitonin

- Decreases serum calcium.

12. Mention the biochemical functions of calcium and describe the blood calcium homeostasis

Answer

Biochemical functions of calcium

1. Bone and teeth formation
2. Blood coagulation
3. Muscle contraction
4. Nerve impulse transmission
5. Second messenger action
6. Activation of enzymes
7. Hormone secretion
8. Prevention of tetany

Blood calcium homeostasis

Parathyroid hormone

- Raises serum calcium.
- Increases bone resorption.
- Increases renal calcium reabsorption.

Calcitriol

- Increases intestinal absorption of calcium.

Calcitonin

- Decreases bone resorption.
- Lowers calcium.

Normal serum calcium maintained at 9–11 mg/dL.

13. Enumerate two hormones which affect Calcium and phosphorus metabolism. Mention how these hormones regulate them in the body.

Answer

Hormones

1. Parathyroid hormone
2. Calcitriol

Parathyroid hormone

Actions

- Increases serum calcium.
- Decreases serum phosphate.

Mechanism

- Stimulates bone resorption.
- Increases renal calcium reabsorption.
- Decreases renal phosphate reabsorption.
- Activates vitamin D.

Calcitriol

Actions

- Increases serum calcium and phosphate.

Mechanism

- Increases intestinal absorption of calcium and phosphate.
- Increases renal calcium reabsorption.

14. Explain source, RDA, absorption, transport and storage of iron

Answer

Sources

- Liver
- Meat
- Egg yolk
- Green leafy vegetables
- Pulses

RDA

- Adult male: 17 mg/day
- Adult female: 21 mg/day

Absorption

- Occurs in duodenum.
- Ferric to ferrous conversion.
- Absorbed via DMT-1.
- Stored as ferritin.

Transport

- Transported by transferrin.

Storage

- Ferritin
- Hemosiderin
- Liver, spleen and bone marrow are major storage sites.

15. Serum calcium homeostasis

Answer

Serum calcium is maintained within narrow limits by:

1. Parathyroid hormone
2. Calcitriol
3. Calcitonin

PTH

- Raises calcium.
- Lowers phosphate.

Calcitriol

- Increases intestinal absorption.

Calcitonin

- Lowers calcium by inhibiting bone resorption.

Normal serum calcium: 9–11 mg/dL.

16. Explain briefly- absorption, transport and functions of copper

Answer

Absorption

- Copper absorbed in stomach and small intestine.
- Transported to liver bound to albumin.

Transport

- Main transport protein is ceruloplasmin.

Functions

1. Component of cytochrome oxidase
2. Iron metabolism through ceruloplasmin
3. Melanin synthesis
4. Collagen synthesis
5. Antioxidant function through superoxide dismutase

17. Mention the normal level serum calcium. Explain the hormonal regulation of serum calcium

Answer

Normal serum calcium

- Total calcium: 9–11 mg/dL

Hormonal regulation

Parathyroid hormone

- Raises serum calcium.
- Increases bone resorption.
- Increases renal calcium reabsorption.

Calcitriol

- Increases intestinal absorption.

Calcitonin

- Lowers serum calcium.

SHORT ANSWERS

18. Importance of Selenium in the human body.

Answer

1. Component of glutathione peroxidase.
2. Antioxidant action.
3. Prevents oxidative damage.
4. Important for thyroid hormone metabolism.
5. Enhances immunity.
6. Deficiency causes cardiomyopathy and muscle weakness.

19. Biochemical test for the investigation of iron deficiency anaemia

Answer

1. Hemoglobin estimation – decreased
2. Serum iron – decreased
3. Serum ferritin – decreased
4. Total iron binding capacity – increased
5. Transferrin saturation – decreased
6. Peripheral smear – microcytic hypochromic anemia

20. Biochemical functions of Copper and disorders associated with copper metabolism

Answer

Functions

1. Component of cytochrome oxidase
2. Iron metabolism through ceruloplasmin
3. Melanin synthesis
4. Collagen synthesis
5. Antioxidant function

Disorders

Wilson disease

- Copper accumulation due to defective ceruloplasmin.
- Liver and neurological manifestations.

Menkes disease

- Defective copper absorption.
- Growth retardation and kinky hair.

21. Hormonal regulation of calcium level

Answer

Parathyroid hormone

- Raises serum calcium.

Calcitriol

- Increases intestinal calcium absorption.

Calcitonin

- Lowers serum calcium.

22. Regulation of absorption of iron

Answer

1. Regulated mainly by hepcidin.
2. Hepcidin inhibits ferroportin.
3. Iron deficiency increases absorption.

4. Vitamin C and gastric acid increase absorption.
5. Phytates and tannins decrease absorption.
6. Mucosal block theory regulates iron entry.

23. Iron deficiency anemia

Answer

Iron deficiency anemia is a microcytic hypochromic anemia due to inadequate iron.

Causes

- Nutritional deficiency
- Chronic blood loss
- Hookworm infestation

Features

- Pallor
- Fatigue
- Koilonychia

Laboratory findings

- Low hemoglobin
- Low serum ferritin
- Increased TIBC

24. Function of calcium responsible for prevention of tetany

Answer

Ionized calcium stabilizes neuromuscular excitability.

Low serum calcium increases nerve and muscle excitability causing tetany.

Hence calcium prevents tetany.

25. Mucosal block theory

Answer

According to mucosal block theory:

- Iron absorbed into intestinal mucosal cells is stored as ferritin.
- When body iron stores are adequate, further absorption is prevented.
- Thus mucosal cells regulate iron absorption.

26. Biochemical role of Iron

Answer

1. Hemoglobin synthesis
2. Myoglobin formation
3. Electron transport chain
4. Component of catalase and peroxidase
5. Cellular respiration
6. Oxidative metabolism

27. Biochemical role of Copper

Answer

1. Component of cytochrome oxidase
2. Required for iron metabolism
3. Melanin synthesis
4. Collagen cross linking
5. Antioxidant function

28. Trace elements

Answer

Trace elements are minerals required in very small amounts.

Examples:

- Iron
- Copper
- Zinc
- Selenium

- Chromium
- Manganese
- Iodine

Functions:

- Enzyme activity
- Hormone synthesis
- Oxidation reduction reactions

29. Wilson's disease

Answer

Wilson disease is an inherited disorder of copper metabolism.

Cause

- Defect in ATP7B gene.
- Decreased ceruloplasmin.

Features

- Liver disease
- Neurological symptoms
- Kayser–Fleischer ring

Biochemical findings

- Increased tissue copper
- Increased urinary copper
- Low ceruloplasmin

30. State factors affecting calcium absorption

Answer

Factors increasing absorption

1. Vitamin D
2. Acidic pH
3. Lactose
4. Growth and pregnancy

Factors decreasing absorption

1. Phytates
2. Oxalates
3. Excess phosphate
4. Vitamin D deficiency
5. Steatorrhea

31. Explain the absorption of iron

Answer

- Iron absorbed mainly in duodenum.
- Ferric iron converted to ferrous form.
- Ferrous iron absorbed by DMT-1.
- Heme iron absorbed efficiently.
- Iron stored as ferritin.
- Exported through ferroportin.
- Bound to transferrin in plasma.

32. Absorption and transport of Iron

Answer

Absorption

- Occurs in duodenum.
- Ferrous iron absorbed by DMT-1.
- Heme iron absorbed efficiently.

Transport

- Transported by transferrin.
- Delivered to tissues and bone marrow.

33. Role of zinc

Answer

1. Component of many enzymes.
2. Required for growth and wound healing.
3. Important for immunity.
4. Required for insulin storage.
5. Essential for taste sensation.

34. Wilson's disease

Answer

Wilson disease is a disorder of copper accumulation.

Features

- Liver cirrhosis
- Neurological symptoms
- Kayser–Fleischer ring

Biochemical findings

- Low ceruloplasmin
- Increased urinary copper

35. Transport of iron

Answer

- Iron transported in plasma by transferrin.
- Transferrin is synthesized in liver.
- Carries ferric iron.
- Delivers iron to bone marrow and tissues.

36. Ceruloplasmin

Answer

- Ceruloplasmin is a copper containing α2-globulin.
- Synthesized in liver.
- Main transport protein for copper.
- Has ferroxidase activity.
- Converts ferrous iron to ferric form.

37. Name three factors regulating plasma calcium levels

Answer

1. Parathyroid hormone
2. Calcitriol
3. Calcitonin

38. Fluorosis

Answer

Fluorosis is due to excess fluoride intake.

Features

- Dental mottling
- Brown discoloration of teeth
- Skeletal deformities
- Calcification of ligaments

39. Menke's disease

Answer

Menkes disease is a disorder of copper absorption.

Features

- Growth retardation
- Mental retardation
- Kinky hair
- Hypopigmentation

Cause: Defect in copper transport.

40. Functions of magnesium.

Answer

1. Activator of many enzymes
2. Required for ATP dependent reactions
3. Neuromuscular function
4. Bone formation
5. Protein synthesis

41. Role of calcitonin in regulation of calcium homeostasis

Answer

- Secreted by thyroid C cells.
- Inhibits osteoclastic bone resorption.
- Lowers serum calcium.
- Promotes calcium deposition in bone.

42. Name any two trace elements and mention the biological functions of each of them

Answer

Iron

- Hemoglobin synthesis
- Electron transport

Zinc

- Enzyme activity
- Growth and wound healing

43. Mention the Copper containing enzymes

Answer

1. Cytochrome oxidase
2. Ceruloplasmin
3. Tyrosinase
4. Superoxide dismutase
5. Lysyl oxidase
6. Dopamine β-hydroxylase

ENERGY METABOLISM AND NUTRITION

SHORT ESSAYS

1. Define Basal Metabolic Rate (BMR), mention how it can be measured, what are the normal values. Describe the factors determining BMR

Answer

Definition

Basal Metabolic Rate is the energy expenditure of the body at complete physical and mental rest in post absorptive state and at comfortable environmental temperature.

Measurement of BMR

Measured by indirect calorimetry using oxygen consumption.

Conditions:

1. Complete rest
2. Post absorptive state
3. Normal temperature
4. Awake condition

Normal values

- Adult male: 38–40 kcal/m²/hour
- Adult female: 35–37 kcal/m²/hour

Factors affecting BMR

Increase BMR

1. Hyperthyroidism
2. Fever
3. Pregnancy
4. Growth
5. Cold climate
6. Emotional stress

Decrease BMR

1. Hypothyroidism
2. Starvation
3. Sleep
4. Old age

Other factors:

- Body surface area
- Sex
- Age
- Hormones

2. What is BMR. How is it measured. What is its normal value. What are the factors affecting BMR.

Answer

BMR

Basal Metabolic Rate is the minimum energy expenditure required for maintenance of vital functions at rest.

Measurement

Measured by indirect calorimetry using oxygen consumption.

Normal value

- Adult male: 38–40 kcal/m²/hour
- Adult female: 35–37 kcal/m²/hour

Factors affecting BMR

Increase

- Hyperthyroidism
- Fever
- Pregnancy
- Growth

Decrease

- Hypothyroidism
- Starvation
- Old age

3. Protein energy malnutrition.

Answer

Protein energy malnutrition is deficiency of both calories and proteins.

Types

1. Marasmus
2. Kwashiorkor

Causes

- Poverty
- Infections
- Improper feeding
- Malabsorption

Features

Marasmus

- Severe wasting
- Loss of subcutaneous fat
- No edema

Kwashiorkor

- Edema
- Fatty liver
- Growth retardation
- Hair changes

Biochemical changes

- Hypoproteinemia
- Negative nitrogen balance
- Low albumin

Prevention

- Balanced diet
- Breastfeeding
- Nutritional supplementation

4. Define nitrogen balance. Add a note on the clinical conditions altering nitrogen balance.

Answer

Definition

Nitrogen balance is the difference between nitrogen intake and nitrogen output.

Nitrogen balance = Nitrogen intake – Nitrogen loss

Types

Positive nitrogen balance

Nitrogen intake exceeds output.

Seen in:

- Growth
- Pregnancy
- Recovery from illness

Negative nitrogen balance

Nitrogen loss exceeds intake.

Seen in:

- Starvation
- Trauma
- Burns
- Infections
- Protein deficiency

Equilibrium

Input equals output.

Seen in healthy adults.

5. Glycemic index: definition and importance.

Answer

Definition

Glycemic index is the rise in blood glucose produced by a food compared to glucose.

Glucose is assigned glycemic index value of 100.

Importance

1. Useful in diabetic diet planning.
2. Low glycemic index foods prevent sudden glucose rise.
3. Helps control obesity.
4. Reduces cardiovascular risk.
5. Improves insulin sensitivity.

Examples of low glycemic index foods:

- Pulses
- Whole grains
- Vegetables

6. Causes, clinical features, biochemical manifestations and treatment of kwashiorkor.

Answer

Definition

Kwashiorkor is severe protein deficiency with relatively adequate calorie intake.

Causes

1. Protein deficient diet
2. Early weaning
3. Recurrent infections
4. Poverty

Clinical features

1. Edema
2. Moon face
3. Fatty liver
4. Hair discoloration
5. Growth retardation

6. Dermatosis
7. Muscle wasting

Biochemical manifestations

1. Hypoalbuminemia
2. Fatty liver
3. Negative nitrogen balance
4. Decreased plasma proteins

Treatment

1. High protein diet
2. Adequate calories
3. Vitamin and mineral supplementation
4. Treatment of infections
5. Gradual nutritional rehabilitation

SHORT ANSWERS

7. Define BMR. What are the various factors that influence BMR

Answer

Definition

Basal Metabolic Rate is the minimum energy expenditure required for maintenance of vital functions at rest.

Factors influencing BMR

1. Age
2. Sex
3. Body surface area
4. Thyroid hormones
5. Fever
6. Pregnancy
7. Starvation
8. Climate

8. Describe the Biochemical basis of: "Dietary fibre has Hypocholesterolemic effect "

Answer

Dietary fiber lowers blood cholesterol by:

1. Binding bile acids in intestine.
2. Increasing excretion of bile acids.
3. Cholesterol utilized for new bile acid synthesis.
4. Delays glucose absorption and reduces lipid synthesis.

Hence dietary fiber has hypocholesterolemic effect.

9. Dietary fiber

Answer

Dietary fiber is the indigestible portion of plant food.

Examples:

- Cellulose
- Hemicellulose
- Pectin
- Lignin

Functions:

1. Prevents constipation
2. Lowers cholesterol
3. Reduces risk of colon cancer
4. Helps diabetic control

10. Protein energy malnutrition

Answer

Protein energy malnutrition is deficiency of protein and calories.

Types:

1. Marasmus
2. Kwashiorkor

Features:

- Growth retardation
- Muscle wasting
- Edema in kwashiorkor

11. Kwashiorkor

Answer

Kwashiorkor is severe protein deficiency.

Features

- Edema
- Fatty liver
- Hair changes
- Growth retardation
- Dermatosis

Biochemical changes

- Hypoalbuminemia

12. Define dietary fibres. Give suitable examples and their biomedical importance.

Answer

Definition

Dietary fibers are indigestible plant polysaccharides.

Examples

- Cellulose
- Hemicellulose
- Pectin
- Lignin

Biomedical importance

1. Prevent constipation
2. Lower cholesterol
3. Reduce colon cancer risk
4. Helpful in diabetes mellitus
5. Promote bowel motility

13. Marasmus

Answer

Marasmus is severe calorie deficiency occurring in infants.

Features

- Severe wasting
- Loss of subcutaneous fat
- Old man appearance
- No edema

Biochemical changes

- Negative nitrogen balance
- Hypoglycemia

GENERAL QUESTIONS

SHORT ANSWERS

1. Write a note on why it is important for a physician to be committed to lifelong learning.

Answer

1. Medical knowledge changes rapidly.
2. Helps provide updated evidence based care.
3. Improves diagnostic and therapeutic skills.
4. Ensures patient safety.
5. Maintains professional competence.
6. Promotes ethical medical practice.

2. A primary health care physician regularly encounters patients suffering from different illnesses. Explain the role of physician as a communicator.

Answer

Role of physician as communicator

1. Establishes good doctor–patient relationship.
2. Obtains proper history.
3. Explains disease and treatment clearly.
4. Counsels patients and relatives.
5. Communicates with healthcare team.
6. Promotes health education and preventive care.
7. Maintains empathy and confidentiality.

3. Roles of a physician in health care

Answer

1. Clinician
2. Communicator
3. Leader
4. Lifelong learner
5. Professional
6. Health educator
7. Researcher
8. Community health provider

4. Briefly explain the Role of a Physician in Health care system.

Answer

1. Diagnosis and treatment of diseases.
2. Prevention and health promotion.
3. Rehabilitation services.
4. Patient counseling.
5. Coordination with healthcare team.
6. Emergency medical care.
7. Community health services.
8. Ethical and professional practice.

PAPER-II

MOLECULAR BIOLOGY

NUCLEOTIDES : CHEMISTRY AND METABOLISM

LONG ESSAYS

1. A 45-year-old male patient reported to orthopedics outpatient department on Monday morning with pain and swelling of first metatarsophalangeal joint of right foot. He had consumed alcoholic drinks heavily on Saturday night. On examination the first metatarsophalangeal joint of right foot was warm, swollen and tender.

• What is your diagnosis ?

• What are the causes of this disorder ?

• What are the investigations to confirm this disorder ?

• What are the biochemical basis of management of this condition?

Diagnosis

Acute gouty arthritis involving first metatarsophalangeal joint (Podagra).

Causes of Gout

1. Primary gout

Due to inherited metabolic defects causing hyperuricemia.

- Increased de novo synthesis of purines
- Partial deficiency of hypoxanthine guanine phosphoribosyl transferase
- Increased phosphoribosyl pyrophosphate synthetase activity

2. Secondary gout

Occurs secondary to other diseases.

Increased uric acid production

- Leukemia
- Polycythemia
- Psoriasis
- Chemotherapy
- Excess alcohol intake

Decreased uric acid excretion

- Renal failure
- Lactic acidosis
- Ketosis
- Diuretics
- Lead nephropathy

Biochemical Basis

- Purine catabolism produces uric acid.
- Humans lack uricase; hence uric acid is final product.
- Hyperuricemia leads to precipitation of monosodium urate crystals.
- Crystals induce inflammatory response in joints.
- Alcohol increases lactate production which decreases uric acid excretion.

Clinical Features

- Severe pain in great toe
- Swelling and redness
- Fever may occur
- Recurrent attacks
- Tophi formation
- Renal stones

Investigations

Laboratory investigations

- Serum uric acid increased (>7 mg/dL)
- Synovial fluid examination shows needle-shaped monosodium urate crystals
- Urinary uric acid estimation
- Blood urea and serum creatinine

Radiology

- X-ray shows punched-out erosions in chronic gout

Biochemical Basis of Management

1. Allopurinol

- Structural analogue of hypoxanthine
- Inhibits xanthine oxidase
- Decreases uric acid formation
- Xanthine and hypoxanthine are more soluble and excreted easily

2. Febuxostat

- Xanthine oxidase inhibitor

3. Uricosuric drugs

- Probenecid and sulfinpyrazone increase uric acid excretion

4. Colchicine

- Inhibits leukocyte migration and inflammation

5. Dietary management

- Avoid purine-rich diet
- Avoid alcohol
- Adequate hydration

2. Describe the salvage pathways for purine and pyrimidine. Explain the biochemical basis of - Lesch-Nyhan syndrome and Von Gierke disease.

Salvage Pathway of Purines

Definition

Salvage pathway is the reutilization of free purine bases for nucleotide synthesis.

Reactions

1. Formation of AMP

Adenine + PRPP → AMP
Enzyme: Adenine phosphoribosyl transferase

2. Formation of IMP

Hypoxanthine + PRPP → IMP
Enzyme: Hypoxanthine guanine phosphoribosyl transferase

3. Formation of GMP

Guanine + PRPP → GMP
Enzyme: Hypoxanthine guanine phosphoribosyl transferase

Importance

- Saves energy
- Important in brain and bone marrow
- Decreases uric acid formation

Salvage Pathway of Pyrimidines

- Pyrimidine bases combine with ribose phosphate.
- Uridine and cytidine are reutilized.
- Thymidine kinase converts thymidine to TMP.

Clinical Importance

Useful in rapidly dividing tissues.

Lesch-Nyhan Syndrome

Definition

X-linked recessive disorder due to complete deficiency of hypoxanthine guanine phosphoribosyl transferase.

Biochemical Basis

- Defect in purine salvage pathway
- PRPP accumulates
- Increased de novo purine synthesis
- Excess uric acid formation

Clinical Features

- Hyperuricemia
- Gout
- Mental retardation
- Self-mutilation
- Choreoathetosis
- Orange sand crystals in urine

Treatment

- Allopurinol
- Supportive care

Von Gierke Disease

Definition

Glycogen storage disease type I due to deficiency of glucose-6-phosphatase.

Biochemical Basis of Hyperuricemia

- Increased glucose-6-phosphate enters pentose phosphate pathway
- Increased ribose-5-phosphate and PRPP synthesis
- Increased purine synthesis
- Excess uric acid formation
- Lactic acidosis decreases uric acid excretion

Clinical Features

- Severe fasting hypoglycemia
- Hepatomegaly
- Hyperuricemia
- Hyperlipidemia
- Lactic acidosis

SHORT ESSAYS

3. Describe purine catabolism.

Definition

Purine catabolism is the degradation of purine nucleotides to uric acid.

Steps

Catabolism of AMP

AMP → Adenosine → Inosine → Hypoxanthine → Xanthine → Uric acid

Enzymes:

- 5′ nucleotidase
- Adenosine deaminase
- Purine nucleoside phosphorylase
- Xanthine oxidase

Catabolism of GMP

GMP → Guanosine → Guanine → Xanthine → Uric acid

Final Product

Uric acid is the end product in humans because uricase is absent.

Clinical Importance

- Hyperuricemia causes gout
- Xanthine oxidase inhibited by allopurinol
- Adenosine deaminase deficiency causes severe combined immunodeficiency

4. Discuss the salvage pathway of purine synthesis. Add a note on the synthetic nucleotide analogues and the clinical significance.

Salvage Pathway

Reactions

1. Adenine + PRPP → AMP
2. Hypoxanthine + PRPP → IMP
3. Guanine + PRPP → GMP

Enzymes

- Adenine phosphoribosyl transferase
- Hypoxanthine guanine phosphoribosyl transferase

Functions

- Conserves energy
- Decreases de novo synthesis
- Important in brain tissue

Synthetic Nucleotide Analogues

Purine analogues

- 6-Mercaptopurine
- Azathioprine
- 6-Thioguanine

Pyrimidine analogues

- 5-Fluorouracil
- Cytarabine

Clinical Significance

- Anticancer drugs
- Immunosuppressive agents
- Antiviral agents

5. Discuss the clinical features, Biochemical basis and diagnosis of Gout.

Definition

Gout is a disorder of purine metabolism characterized by hyperuricemia and urate crystal deposition.

Biochemical Basis

- Excess purine degradation produces hyperuricemia.
- Monosodium urate crystals deposit in joints.
- Alcohol and lactic acidosis decrease uric acid excretion.

Clinical Features

- Acute arthritis
- Podagra
- Tophi
- Renal stones
- Chronic deforming arthritis

Diagnosis

- Elevated serum uric acid
- Synovial fluid crystals
- Increased urinary uric acid
- X-ray changes

6. What is Gout. Give an account of the causes, biochemical base of clinical manifestations, investigations and management of Gout.

Definition

Gout is a metabolic disorder due to hyperuricemia resulting in deposition of urate crystals.

Causes

Primary gout

- Enzyme defects
- Increased PRPP synthetase activity

Secondary gout

- Leukemia
- Renal failure
- Alcoholism
- Diuretic therapy

Biochemical Basis of Clinical Manifestations

- Hyperuricemia causes urate crystal deposition.
- Crystals activate inflammatory mediators.
- Renal deposition causes nephropathy.

Investigations

- Serum uric acid
- Synovial fluid examination
- Urinary uric acid
- Renal function tests

Management

- Allopurinol
- Febuxostat
- Colchicine
- Probenecid

- Avoid alcohol and purine-rich food

7. Give the sources of carbon and nitrogen atoms of purine rings. How is the de novo synthesis regulated. Indicate the clinical uses of inhibitors of purine nucleotide synthesis.

Sources of Purine Ring Atoms

- N1 – Aspartate
- C2 and C8 – Formate
- N3 and N9 – Glutamine
- C4, C5 and N7 – Glycine
- C6 – Carbon dioxide

Regulation of De Novo Purine Synthesis

Key regulatory enzyme

Glutamine PRPP amidotransferase

Inhibitors

- AMP
- GMP
- IMP

Activator

- PRPP

Inhibitors of Purine Synthesis

- Methotrexate
- 6-Mercaptopurine
- Azathioprine
- Mycophenolate mofetil

Clinical Uses

- Cancer chemotherapy
- Immunosuppression
- Organ transplantation
- Autoimmune diseases

8. Enumerate the steps of purine catabolism. Add a note on gout.

Steps of Purine Catabolism

AMP degradation

AMP → Adenosine → Inosine → Hypoxanthine → Xanthine → Uric acid

GMP degradation

GMP → Guanosine → Guanine → Xanthine → Uric acid

Enzyme

Xanthine oxidase converts hypoxanthine and xanthine to uric acid.

Gout

Definition

Metabolic disorder characterized by hyperuricemia.

Features

- Acute arthritis
- Tophi
- Renal stones

Treatment

- Allopurinol
- Colchicine
- Low purine diet

9. What are the sources for purine ring. Enumerate the reactions in denovo synthesis of purine nucleotide. Add a note on its regulation.

Sources of Purine Ring

- Glycine
- Glutamine
- Aspartate
- Formate
- Carbon dioxide

Steps in De Novo Purine Synthesis

1. Ribose-5-phosphate → PRPP
2. PRPP → 5-phosphoribosylamine
3. Formation of glycinamide ribotide
4. Addition of formyl group
5. Addition of glutamine nitrogen
6. Cyclization reactions
7. Formation of inosine monophosphate

Regulation

Regulatory enzyme

Glutamine PRPP amidotransferase

Inhibited by

- AMP
- GMP
- IMP

Activated by

PRPP

Conclusion

IMP is the parent purine nucleotide for AMP and GMP synthesis.

10. How purine nucleotides are degraded. Add a note on abnormalities due to excessive purine catabolism.

Degradation of Purine Nucleotides

Purine nucleotides are degraded to uric acid.

AMP pathway

AMP → Adenosine → Inosine → Hypoxanthine → Xanthine → Uric acid

GMP pathway

GMP → Guanosine → Guanine → Xanthine → Uric acid

Abnormalities Due to Excessive Purine Catabolism

Hyperuricemia

Elevated uric acid level in blood.

Gout

- Acute arthritis
- Tophi
- Renal stones

Uric acid nephropathy

Urate crystal deposition in kidney.

Lesch-Nyhan syndrome

Defect in salvage pathway causing excess uric acid production.

11. Describe uric acid formation and mention the clinical significance of its estimation.

Uric Acid Formation

Uric acid is the end product of purine metabolism.

Formation pathway

Hypoxanthine → Xanthine → Uric acid

Enzyme

Xanthine oxidase

Clinical Significance of Uric Acid Estimation

Increased levels

- Gout
- Leukemia
- Renal failure
- Psoriasis

Decreased levels

- Xanthinuria
- Severe liver disease

Normal Values

- Male: 3–7 mg/dL
- Female: 2–6 mg/dL

12. Describe the salvage pathway of purine nucleotide synthesis with its significance Describe the disorder associated with it.

Salvage Pathway

Reactions

- Adenine + PRPP → AMP
- Hypoxanthine + PRPP → IMP
- Guanine + PRPP → GMP

Enzymes

- APRT
- HGPRT

Significance

- Conserves energy
- Reduces uric acid production
- Important in brain tissue

Disorder Associated

Lesch-Nyhan syndrome

Cause

Complete HGPRT deficiency.

Features

- Hyperuricemia
- Self mutilation
- Mental retardation
- Gout

Treatment

Allopurinol.

SHORT ANSWERS

13. Lesch-Nyhan syndrome

- X-linked recessive disorder.
- Due to deficiency of HGPRT.
- Causes defective purine salvage.
- Increased uric acid production.
- Features:
    - Hyperuricemia
    - Self-mutilation
    - Mental retardation
    - Choreoathetosis
- Treatment: Allopurinol.

14. Gout

- Disorder of purine metabolism with hyperuricemia.
- Deposition of monosodium urate crystals.
- Features:
    - Podagra
    - Tophi
    - Renal stones
- Diagnosis: Increased serum uric acid.
- Treatment: Allopurinol, colchicine.

15. Orotic aciduria

- Defect in pyrimidine synthesis.
- Deficiency of orotate phosphoribosyl transferase and orotidine decarboxylase.
- Features:
  - Megaloblastic anemia
  - Growth retardation
  - Orotic acid in urine
- Treatment: Uridine administration.

16. Salvage pathway of purine synthesis

- Reutilization of purine bases.
- Hypoxanthine + PRPP → IMP.
- Guanine + PRPP → GMP.
- Adenine + PRPP → AMP.
- Important enzymes: HGPRT and APRT.
- Conserves energy.

17. Outline the pathway of purine catabolism

AMP → Adenosine → Inosine → Hypoxanthine → Xanthine → Uric acid

GMP → Guanosine → Guanine → Xanthine → Uric acid

Enzyme: Xanthine oxidase.

18. Synthetic nucleotide and its uses.

Examples

- 5-Fluorouracil
- Methotrexate
- 6-Mercaptopurine
- Azathioprine

Uses

- Cancer chemotherapy
- Immunosuppression
- Antiviral therapy

19. Mention the origin of carbon and nitrogen atoms in purine ring.

- N1 – Aspartate
- C2 and C8 – Formate
- N3 and N9 – Glutamine
- C4, C5 and N7 – Glycine
- C6 – Carbon dioxide

20. Biochemical basis of allopurinol in treatment of gout

- Allopurinol is a hypoxanthine analogue.
- Inhibits xanthine oxidase.
- Decreases uric acid synthesis.
- Increases soluble hypoxanthine and xanthine excretion.
- Used in gout treatment.

21. Formation of uric acid

Hypoxanthine → Xanthine → Uric acid

Enzyme: Xanthine oxidase.

Uric acid is the end product of purine metabolism in humans.

22. Gout- clinical features and lab diagnosis.

Clinical features

- Podagra
- Painful swollen joints
- Tophi
- Renal stones

Laboratory diagnosis

- Increased serum uric acid
- Synovial fluid urate crystals
- Urinary uric acid estimation

23. Define gout. Mention the causes of primary gout

Definition

Gout is a metabolic disorder characterized by hyperuricemia and urate crystal deposition.

Causes of primary gout

- HGPRT deficiency
- Increased PRPP synthetase activity
- Increased de novo purine synthesis

24. Define nucleotide. Name two adenosine nucleotide derivatives

Definition

Nucleotide is a compound consisting of nitrogenous base, pentose sugar and phosphate.

Adenosine nucleotide derivatives

- ATP
- cAMP

DNA: STRUCTURE, ORGANIZATION AND REPLICATION

LONG ESSAYS

1. Define replication. Describe in detail the replicative process in prokaryotes with the help of diagrams.

Definition

Replication is the process by which DNA synthesizes an identical copy of itself.

Features of DNA Replication

- Semiconservative
- Bidirectional
- Semidiscontinuous
- Template directed

Steps in Replication

1. Initiation

- Begins at origin of replication.
- Helicase unwinds DNA.
- Single stranded binding proteins stabilize strands.
- Topoisomerase relieves supercoiling.

2. Primer formation

- Primase synthesizes RNA primer.

3. Elongation

- DNA polymerase III synthesizes new DNA in 5′→3′ direction.
- Leading strand synthesized continuously.
- Lagging strand synthesized discontinuously as Okazaki fragments.

4. Primer removal

- DNA polymerase I removes RNA primers.

5. Ligation

- DNA ligase joins Okazaki fragments.

6. Termination

- Replication terminates at termination sequences.

Enzymes Involved

- Helicase

- Primase
- DNA polymerase I
- DNA polymerase III
- Ligase
- Topoisomerase

REFER DIAGRAM SECTION

SHORT ESSAYS

2. Describe Watson & Crick model of DNA and substantiate the same with diagram.

REFER DIAGRAM SECTION

Watson and Crick Model

- DNA is a double helix.
- Two antiparallel polynucleotide chains.
- Sugar phosphate backbone outside.
- Bases inside.
- Adenine pairs with thymine by two hydrogen bonds.
- Guanine pairs with cytosine by three hydrogen bonds.
- One turn contains 10 base pairs.
- Pitch is 34 Å.
- Distance between bases is 3.4 Å.
- Diameter is 20 Å.

Significance

- Explains replication.
- Explains genetic information storage.

3. Describe the process of DNA replication in eukaryotes. Name two inhibitors of replication.

DNA Replication in Eukaryotes

- Occurs during S phase.
- Multiple origins of replication.
- Helicase unwinds DNA.
- Primase synthesizes primer.
- DNA polymerase α, δ and ε participate.
- Leading and lagging strand synthesis occur.
- Ligase joins Okazaki fragments.
- Telomerase maintains telomeres.

Inhibitors of replication

- Actinomycin D
- Mitomycin C

4. What are the principles of DNA replication. Add a note on inhibitors of replication.

Principles of DNA Replication

- Semiconservative
- Bidirectional
- Complementary base pairing
- Template directed synthesis
- Polymerization in 5′→3′ direction
- Semidiscontinuous synthesis

Inhibitors of replication

- Actinomycin D
- Mitomycin C
- Quinolones
- Acyclovir

5. Describe the various stages of replication and add a note on DNA repair mechanism

Stages of Replication

Initiation

Origin recognition and DNA unwinding.

Elongation

DNA synthesis by DNA polymerases.

Termination

Joining and completion of strands.

DNA Repair Mechanisms

1. Proofreading

By DNA polymerase.

2. Excision repair

Removal of damaged bases.

3. Mismatch repair

Corrects replication errors.

4. Recombinational repair

Repairs strand breaks.

Importance

Maintains genomic stability.

6. Structure of B-DNA. Add a note on different types of DNA.

Structure of B-DNA

- Right-handed double helix.
- 10 base pairs per turn.
- Diameter 20 Å.
- Pitch 34 Å.
- Antiparallel strands.

Types of DNA

A-DNA

- Right-handed
- Compact form

B-DNA

- Physiological form

Z-DNA

- Left-handed helix
- Zig-zag backbone

7. Structure of DNA

- Double helical structure.
- Antiparallel chains.
- Deoxyribose sugar and phosphate backbone.
- Purines and pyrimidines form base pairs.
- A=T and G≡C.
- Major and minor grooves present.

8. Explain DNA repair mechanisms

Types

Proofreading

By DNA polymerase.

Excision repair

Removal of damaged nucleotides.

Mismatch repair

Corrects mismatched bases.

Recombination repair

Repairs breaks.

Importance

Prevents mutations.

9. Describe process of DNA replication

- Initiation at origin.
- Helicase unwinds DNA.

- Primer synthesis.
- DNA polymerase synthesizes DNA.
- Leading and lagging strands formed.
- Primer removal.
- Ligation by DNA ligase.

SHORT ANSWERS

10. Write the differences between DNA and RNA.

DNA	RNA
Deoxyribose sugar	Ribose sugar
Thymine present	Uracil present
Double stranded	Usually single stranded
Genetic material	Protein synthesis
More stable	Less stable

11. Explain the Watson and Crick model of DNA.

- Double helix.
- Antiparallel strands.
- Complementary base pairing.
- A=T and G≡C.
- Right-handed helix.

12. DNA polymerases

Prokaryotic

- DNA polymerase I: primer removal.
- DNA polymerase II: repair.
- DNA polymerase III: replication.

Eukaryotic

- Polymerase α, δ, ε.

13. Base pairing rule

- Adenine pairs with thymine.
- Guanine pairs with cytosine.
- A=T by two hydrogen bonds.
- G≡C by three hydrogen bonds.
- Chargaff's rule.

14. DNA structure

- Double helix.
- Antiparallel strands.
- Sugar phosphate backbone.
- Complementary base pairing.

15. Mitochondrial DNA

- Circular double stranded DNA.
- Maternal inheritance.
- Lacks histones.
- Codes for oxidative phosphorylation proteins.

16. Discuss the base repair mechanism of DNA

- DNA glycosylase removes damaged base.
- AP endonuclease cuts strand.
- DNA polymerase fills gap.
- Ligase seals nick.

17. Define replication and mention four inhibitors of replication.

Definition

Replication is synthesis of identical DNA copies.

Inhibitors

- Actinomycin D
- Mitomycin C
- Acyclovir
- Quinolones

TRANSCRIPTION AND TRANSLATION

LONG ESSAYS

1. Describe protein biosynthesis in eukaryotes. Name two inhibitors of microbial protein synthesis.

Definition

Protein biosynthesis is the translation of genetic information into protein.

Steps of Translation

1. Activation of amino acids

Amino acids attach to tRNA by aminoacyl tRNA synthetase.

2. Initiation

- Small ribosomal subunit binds mRNA.
- Initiator tRNA binds AUG codon.
- Large subunit joins.

3. Elongation

- Amino acids added sequentially.
- Peptide bond formed by peptidyl transferase.
- Ribosome translocates.

4. Termination

- Stop codon recognized.
- Release factors release polypeptide.

Post translational modifications

- Phosphorylation
- Glycosylation
- Hydroxylation
- Proteolytic cleavage

Inhibitors of microbial protein synthesis

- Tetracycline
- Chloramphenicol

2. What is translation. Describe the steps of translation leading to protein synthesis in detail. Give a brief note on the inhibitors of protein synthesis.

Definition

Translation is synthesis of protein from mRNA template.

Steps

Activation

Formation of aminoacyl tRNA.

Initiation

Formation of initiation complex.

Elongation

- Codon recognition
- Peptide bond formation
- Translocation

Termination

Release of polypeptide chain.

Inhibitors of Protein Synthesis

Prokaryotic inhibitors

- Streptomycin
- Tetracycline
- Chloramphenicol
- Erythromycin

Eukaryotic inhibitors

- Cycloheximide
- Diphtheria toxin

3. Define translation and explain the steps involved in the process of Translation.

What is Post Translational modifications, give four examples.

Definition

Translation is the process by which proteins are synthesized using mRNA as template.

Steps

- Activation
- Initiation
- Elongation
- Termination

Post Translational Modifications

Changes occurring after protein synthesis.

Examples

- Hydroxylation of collagen
- Glycosylation
- Phosphorylation
- Proteolytic cleavage of insulin

4. Describe the process of eukaryotic translation. Add a note on post-translational modifications and inhibitors of translation.

Eukaryotic Translation

- Initiation at AUG codon.
- 40S and 60S ribosomal subunits participate.
- Methionine is initiator amino acid.
- Elongation and peptide bond formation occur.
- Termination at stop codons.

Post Translational Modifications

- Glycosylation
- Phosphorylation
- Acetylation
- Hydroxylation

Inhibitors

- Tetracycline
- Chloramphenicol
- Streptomycin
- Cycloheximide

5. Give a detailed account of the transcription process. How is it regulated. Name Inhibitors of transcription

Definition

Transcription is synthesis of RNA from DNA template.

Steps

Initiation

RNA polymerase binds promoter.

Elongation

RNA chain synthesized in 5′→3′ direction.

Termination

RNA polymerase detaches.

Regulation

- Operon mechanism
- Repressors and activators
- Hormonal regulation

Inhibitors

- Rifampicin
- Actinomycin D

6. Explain the steps of Transcription in Eukaryotes with a note on inhibitors of transcription.

Steps

Initiation

Formation of transcription initiation complex.

Elongation

RNA synthesis by RNA polymerase II.

Termination

Release of RNA transcript.

Post transcriptional modifications

- Capping
- Polyadenylation
- Splicing

Inhibitors

- Rifampicin
- Actinomycin D
- α-Amanitin

7. Definition steps and inhibitors of transaltion

Definition

Translation is synthesis of proteins using mRNA template.

Steps

- Activation
- Initiation
- Elongation
- Termination

Inhibitors

- Streptomycin
- Chloramphenicol
- Tetracycline
- Cycloheximide

8. Define translation. Describe the steps of Translation. Add a note on its inhibitors

Definition

Translation is synthesis of protein from mRNA.

Steps

- Amino acid activation
- Initiation
- Elongation
- Termination

Inhibitors

- Streptomycin
- Tetracycline
- Chloramphenicol
- Puromycin

9. Describe the process of transcription by providing the details on the following - Requisites, Promoters, Pre-initiation complex, Initiation, Elongation and termination, Inhibitors, Post-transcriptional modifications

Requisites

- DNA template
- RNA polymerase
- Ribonucleotides
- Transcription factors

Promoters

Specific DNA sequences for RNA polymerase binding.

Pre-initiation complex

Includes transcription factors and RNA polymerase.

Initiation

RNA synthesis starts.

Elongation

RNA chain elongates.

Termination

RNA transcript released.

Inhibitors

- Rifampicin
- Actinomycin D
- α-Amanitin

Post transcriptional modifications

- Capping
- Polyadenylation
- Splicing

10. Write the definition, steps and inhibitors of transcription

Definition

Transcription is synthesis of RNA from DNA.

Steps

- Initiation
- Elongation
- Termination

Inhibitors

- Rifampicin
- Actinomycin D
- α-Amanitin

11. Define transcription. Steps of transcription in prokaryotes. Post transcriptional modification. Inhibitors of transcription.

Definition

Transcription is synthesis of RNA using DNA template.

Steps in Prokaryotes

- Initiation by RNA polymerase.
- Elongation of RNA chain.
- Termination.

Post transcriptional modifications

- Minimal in prokaryotes.
- rRNA and tRNA processing occur.

Inhibitors

- Rifampicin
- Actinomycin D

12. Discuss the process of translation and add a note on post translational modifications

Translation

- Activation
- Initiation
- Elongation
- Termination

Post translational modifications

- Glycosylation
- Hydroxylation
- Phosphorylation
- Proteolytic cleavage

13. Define transcription and explain in detail the transcription in prokaryotes.

Add a note on post transcriptional modification

Definition

Transcription is synthesis of RNA from DNA template.

Prokaryotic transcription

Initiation

Sigma factor recognizes promoter.

Elongation

RNA polymerase synthesizes RNA.

Termination

Rho dependent and rho independent termination.

Post transcriptional modification

- tRNA processing
- rRNA cleavage

14. Describe the process of transcription. What are the posttranscriptional modifications? Mention two inhibitors of transcription

Process

- Initiation
- Elongation
- Termination

Post transcriptional modifications

- 5′ capping
- Poly A tail formation
- Splicing

Inhibitors

- Rifampicin
- Actinomycin D

15. What is transcription? Enumerate the steps in transcription and add a note on post transcriptional modifications

Definition

Transcription is synthesis of RNA from DNA.

Steps

- Initiation
- Elongation
- Termination

Post transcriptional modifications

- Capping
- Polyadenylation
- Splicing

16. Describe how protein is synthesized in body. Name any two inhibitors of protein biosynthesis. Add a note on post translational modifications

Protein synthesis

- Activation of amino acids
- Initiation
- Elongation
- Termination

Inhibitors

- Tetracycline
- Chloramphenicol

Post translational modifications

- Glycosylation
- Phosphorylation
- Hydroxylation

- Proteolytic cleavage

SHORT ESSAYS

17. Describe Post-translational modifications with suitable examples.

Definition

Changes occurring in proteins after translation.

Types with examples

- Glycosylation – Immunoglobulins
- Hydroxylation – Collagen
- Phosphorylation – Enzymes
- Proteolytic cleavage – Insulin
- Acetylation – Histones

Importance

Essential for functional activity of proteins.

18. Genetic code

Definition

Relationship between nucleotide sequence and amino acid sequence.

Features

- Triplet code
- Degenerate
- Non-overlapping
- Universal
- Commaless
- Unambiguous

19. Diagrammatically represent the structure of tRNA. Describe the functions of tRNA

REFER DIAGRAM SECTION

Functions

- Carrier of amino acids.
- Recognizes codons by anticodon.
- Participates in translation.

20. Post transcriptional modifications.

- 5′ capping
- Polyadenylation
- Splicing
- Formation of mature mRNA

Importance

Protects RNA and aids translation.

21. Describe post transcriptional modifications and its significance with examples

Modifications

- 5′ capping
- Poly A tail addition
- Splicing

Significance

- Stability of mRNA
- Protection from degradation
- Efficient translation

Example

Formation of mature mRNA from hnRNA.

22. Discuss the process of transcription in prokaryotes

Steps

Initiation

Sigma factor binds promoter.

Elongation

RNA polymerase synthesizes RNA.

Termination

Rho dependent or independent.

Enzyme

RNA polymerase.

23. Describe the structure and function of tRNA

Structure

- Clover leaf model.
- Acceptor arm.
- Anticodon loop.
- D loop.
- TψC loop.

Functions

- Amino acid transport.
- Codon recognition.
- Protein synthesis.

SHORT ANSWERS

24. Draw and label t – RNA

REFER DIAGRAM SECTION

25. Post translational modifications

- Glycosylation
- Phosphorylation
- Hydroxylation
- Proteolytic cleavage

26. Genetic code

- Triplet codons.
- Universal.
- Degenerate.
- Non-overlapping.
- Unambiguous.

27. What is code. Describe the salient features of genetic code

Definition

Genetic code is the relationship between codons and amino acids.

Features

- Triplet
- Degenerate
- Universal
- Non-overlapping
- Commaless
- Unambiguous

28. What are the different types of RNA. Add a note on function of tRNA.

Types of RNA

- mRNA
- tRNA
- rRNA

Functions of tRNA

- Carries amino acids.
- Recognizes codons.
- Participates in translation.

29. tRNA

- Transfer RNA.
- Clover leaf structure.
- Anticodon loop present.
- Carries amino acids to ribosome.

30. Contractile proteins

- Actin

- Myosin
- Troponin
- Tropomyosin

Functions

Responsible for muscle contraction.

31. Structure of tRNA and its function

Structure

- Clover leaf model.
- Anticodon arm.
- Acceptor arm.

Function

Transfers amino acids during protein synthesis.

32. Introns and exons.

Introns

Non-coding intervening sequences removed during splicing.

Exons

Coding sequences retained in mature mRNA.

33. Explain genetic code. What are salient features of genetic code.

Answer

Genetic Code

Genetic code is the relationship between the sequence of nucleotides in messenger ribonucleic acid and the sequence of amino acids in a protein.

A sequence of three nucleotides forms a codon which codes for one amino acid.

Example:

- AUG codes for methionine.

Salient features of genetic code

1. **Triplet code**
    - Three nucleotides form one codon.
2. **Degenerate**
    - More than one codon may code for same amino acid.
    - Example: Serine has six codons.
3. **Unambiguous**
    - One codon codes for only one amino acid.
4. **Universal**
    - Same genetic code operates in almost all organisms.
5. **Non-overlapping**
    - Adjacent codons do not overlap.
6. **Comma-less**
    - Codons are read continuously without punctuation.
7. **Start codon**
    - AUG is initiation codon.
8. **Stop codons**
    - UAA, UAG and UGA terminate protein synthesis.
9. **Colinear**
    - Sequence of codons corresponds to sequence of amino acids.
10. **Wobble phenomenon**

- Third base of codon shows flexible pairing.

34. Inhibitors of translation

Answer

Inhibitors of translation

These are substances that inhibit protein synthesis.

Inhibitor	Site/Action
Streptomycin	Inhibits initiation in prokaryotes
Tetracycline	Blocks attachment of aminoacyl transfer ribonucleic acid
Chloramphenicol	Inhibits peptidyl transferase
Erythromycin	Inhibits translocation
Puromycin	Causes premature chain termination
Cycloheximide	Inhibits eukaryotic protein synthesis
Diphtheria toxin	Inhibits elongation factor-2
Ricin	Inactivates 60S ribosomal subunit

Applications:

- Used as antibiotics.
- Useful in research studies.

35. Reverse transcriptase

Answer

Reverse transcriptase

Reverse transcriptase is a ribonucleic acid-dependent deoxyribonucleic acid polymerase enzyme that synthesizes deoxyribonucleic acid from ribonucleic acid template.

Source

- Retroviruses such as Human Immunodeficiency Virus.

Functions

1. Converts viral ribonucleic acid into complementary deoxyribonucleic acid.
2. Helps integration into host genome.

Applications

1. Complementary deoxyribonucleic acid synthesis.
2. Recombinant deoxyribonucleic acid technology.
3. Reverse transcription polymerase chain reaction.

36. Enumerate three post translational modifications of proteins with one example each

Answer

Post translational modification	Example
Phosphorylation	Glycogen phosphorylase
Hydroxylation	Hydroxyproline in collagen
Glycosylation	Immunoglobulins
Carboxylation	Prothrombin
Acetylation	Histones

37. Wobble hypothesis

Answer

Wobble hypothesis

Wobble hypothesis was proposed by Francis Crick.

It states that the third base of codon has flexible or “wobble” pairing with the first base of anticodon.

Significance

1. One transfer ribonucleic acid can recognize more than one codon.
2. Explains degeneracy of genetic code.
3. Fewer transfer ribonucleic acids are required.

Example

- Codons UCU, UCC and UCA may code for same amino acid serine due to wobble pairing.

INHERITANCE, MUTATION, CELL CYCLE AND CONTROL OF GENE EXPRESSION

LONG ESSAY

1. Mention the salient features of genetic code. Discuss in detail about the various types of mutation

Answer

Genetic Code – Definition

Genetic code is the relationship between the sequence of nucleotides in messenger ribonucleic acid and the sequence of amino acids in a protein.

Salient Features of Genetic Code

1. **Triplet code**
    - Three nucleotides form one codon.
    - Example: AUG codes for methionine.
2. **Degenerate code**
    - More than one codon codes for the same amino acid.
    - Example: UCU, UCC, UCA and UCG code for serine.
3. **Unambiguous**
    - One codon specifies only one amino acid.
4. **Universal**
    - Genetic code is almost same in all organisms.
5. **Non-overlapping**
    - One nucleotide is not shared by adjacent codons.
6. **Comma-less or continuous**
    - Codons are read continuously without punctuation.
7. **Start codon**
    - AUG is the initiation codon.
    - Codes for methionine.
8. **Stop codons**
    - UAA, UAG and UGA are termination codons.
9. **Colinearity**
    - Sequence of codons corresponds to sequence of amino acids.
10. **Wobble phenomenon**

- Third base of codon has flexibility in pairing

Mutation

Definition

Mutation is a heritable change in nucleotide sequence of deoxyribonucleic acid.

Types of Mutation

1. Point Mutation

Single base change in DNA.

a) Silent mutation

- Codon changes but amino acid remains same.
- Example: UCU → UCC (serine).

b) Missense mutation

- One amino acid replaced by another.
- Example: Sickle cell anemia.
- Glutamic acid replaced by valine.

c) Nonsense mutation

- Codon changed to stop codon.
- Leads to premature termination.

2. Frameshift Mutation

- Caused by insertion or deletion of nucleotides.
- Alters reading frame.
- Produces abnormal protein.

Example:

- Tay–Sachs disease.

3. Deletion Mutation

- Loss of segment of DNA.
- Example: Cri-du-chat syndrome.

4. Insertion Mutation

- Addition of nucleotide sequence into DNA.

5. Inversion

- Segment of chromosome becomes reversed.

6. Translocation

- Transfer of chromosomal segment to another chromosome.
- Example: Chronic myeloid leukemia.

7. Spontaneous Mutation

- Occurs naturally due to replication errors.

8. Induced Mutation

Caused by mutagens.

Physical mutagens

- X-rays
- Gamma rays
- Ultraviolet rays

Chemical mutagens

- Nitrous acid
- Alkylating agents

Biological mutagens

- Viruses

Effects of Mutation

1. Harmful mutation
2. Beneficial mutation
3. Lethal mutation
4. May produce genetic disorders
5. Important in evolution

SHORT ESSAYS

2. What is an operon. Draw the basic structure of Lac operon. Explain the regulation of Lac operon under following conditions,

a) presence of glucose only and
b) presence of lactose only

Answer

Operon – Definition

Operon is a cluster of structural genes regulated together with promoter and operator genes.

Structure of Lac Operon

Components:

1. Regulator gene (i gene)
2. Promoter gene (P)
3. Operator gene (O)
4. Structural genes:
    - lac Z
    - lac Y
    - lac A

Functions:

- lac Z → β-galactosidase
- lac Y → permease
- lac A → transacetylase

Diagram

REFER DIAGRAM SECTION

Regulation of Lac Operon

a) Presence of glucose only

- Lactose absent.
- Repressor protein binds operator gene.
- RNA polymerase cannot proceed.
- Structural genes not transcribed.
- Operon switched OFF.

b) Presence of lactose only

- Lactose acts as inducer.
- Converted to allolactose.
- Allolactose binds repressor protein.
- Repressor removed from operator.
- RNA polymerase transcribes structural genes.
- Enzymes for lactose metabolism produced.
- Operon switched ON.

SHORT ANSWERS

3. What is mutation. Describe point mutation and frameshift mutation

Answer

Mutation

Mutation is a heritable change in nucleotide sequence of DNA.

Point mutation

Single base substitution in DNA.

Types:

1. Silent mutation
2. Missense mutation
3. Nonsense mutation

Example:

- Sickle cell anemia.

Frameshift mutation

- Caused by insertion or deletion of nucleotides.
- Alters reading frame.
- Produces abnormal protein.

Example:

- Tay–Sachs disease.

4. Causes of mutations

Answer

Causes of Mutation

1. Spontaneous causes

- Replication errors
- Tautomeric shifts
- Depurination

2. Physical mutagens

- X-rays
- Gamma rays
- Ultraviolet rays

3. Chemical mutagens

- Nitrous acid
- Alkylating agents
- Base analogues

4. Biological agents

- Viruses
- Transposons

5. Define mutations

Answer

Mutation is a sudden, stable and heritable change in genetic material.

6. Define point mutations and types with one example

Answer

Point mutation

A mutation caused by change of a single nucleotide base.

Types

1. Silent mutation
2. Missense mutation
3. Nonsense mutation

Example

Sickle cell anemia due to substitution of valine for glutamic acid.

7. Lac operon

Answer

Lac operon is an inducible operon controlling lactose metabolism in Escherichia coli.

Components:

1. Regulator gene
2. Promoter
3. Operator
4. Structural genes – lac Z, lac Y, lac A

Functions:

- lac Z → β-galactosidase
- lac Y → permease
- lac A → transacetylase

Lactose induces transcription of these genes.

8. Effects of mutation

Answer

1. Production of abnormal proteins
2. Genetic diseases
3. Cancer formation
4. Lethal effects
5. Beneficial evolutionary changes

9. Point mutation

Answer

Point mutation is a mutation involving alteration of a single nucleotide base.

Types:

1. Silent mutation
2. Missense mutation
3. Nonsense mutation

Example:
Sickle cell anemia.

10. Apoptosis

Answer

Apoptosis is programmed cell death.

Features:

1. Cell shrinkage
2. Chromatin condensation
3. DNA fragmentation
4. Formation of apoptotic bodies
5. No inflammation

Importance:

- Embryogenesis
- Removal of damaged cells
- Prevention of cancer.

11. Frame shift mutation.

Answer

Frameshift mutation occurs due to insertion or deletion of nucleotides causing alteration of reading frame.

Effects:

1. Abnormal protein synthesis
2. Premature stop codon formation
3. Severe genetic disorders

Example:
Tay–Sachs disease.

RECOMBINANT DNA TECHNOLOGY AND GENE THERAPY

LONG ESSAY

1. Describe Recombinant DNA Technology and its applications in Medicine.

Answer

Recombinant DNA Technology

Definition

Recombinant DNA technology is the technique of combining DNA from different sources to produce recombinant DNA.

Steps in Recombinant DNA Technology

1. Isolation of DNA

- Desired gene isolated from donor cell.

2. Cutting DNA

- Restriction endonucleases cut DNA at specific sites.

3. Selection of vector

- Plasmids or bacteriophages used as vectors.

4. Formation of recombinant DNA

- DNA fragment inserted into vector using DNA ligase.

5. Transfer into host cell

- Recombinant vector introduced into bacteria.

6. Cloning and expression

- Host cells multiply and express desired protein.

7. Isolation and purification

- Product purified for medical use.

Applications in Medicine

1. Production of therapeutic proteins

- Human insulin
- Growth hormone
- Interferons
- Erythropoietin

2. Vaccine production

- Hepatitis B vaccine

3. Gene therapy

- Correction of defective genes.

4. Molecular diagnosis

- Detection of genetic diseases.
- PCR-based diagnosis.

5. Prenatal diagnosis

- Detection of inherited disorders.

6. Cancer diagnosis and treatment

- Tumor markers
- Monoclonal antibodies.

7. Production of monoclonal antibodies

- Used in diagnosis and therapy.

8. DNA fingerprinting

- Forensic identification.

Advantages

1. Large-scale production of proteins
2. Highly pure products
3. Better disease diagnosis
4. Improved therapy

SHORT ESSAYS

2. Describe recombinant DNA technology. What are the applications of the technique.

Answer

Recombinant DNA Technology

Recombinant DNA technology involves combining DNA from different sources to produce recombinant DNA molecules.

Steps

1. Isolation of desired DNA
2. Cutting by restriction enzymes
3. Insertion into vector
4. Ligation by DNA ligase
5. Transfer into host cell
6. Cloning and expression

Applications

1. Production of insulin
2. Hepatitis B vaccine
3. Gene therapy
4. Molecular diagnosis
5. DNA fingerprinting
6. Monoclonal antibodies
7. Prenatal diagnosis

3. Enumerate the applications of recombinant DNA technology. Add a note on vectors

Answer

Applications of Recombinant DNA Technology

1. Production of insulin
2. Production of growth hormone
3. Vaccine production
4. Gene therapy

5. DNA fingerprinting
6. Prenatal diagnosis
7. Cancer diagnosis
8. Production of monoclonal antibodies

Vectors

Vectors are DNA molecules used to carry foreign DNA into host cells.

Features of ideal vectors

1. Origin of replication
2. Selectable marker genes
3. Restriction sites
4. Small size

Types

1. Plasmids
2. Bacteriophages
3. Cosmids
4. Artificial chromosomes

4. Recombinant DNA technology and its applications.

Answer

Recombinant DNA Technology

Technique of combining DNA from different organisms.

Steps

1. DNA isolation
2. Cutting with restriction enzymes
3. Vector insertion
4. DNA ligation
5. Transfer into host
6. Cloning

Applications

1. Production of insulin
2. Vaccines
3. Gene therapy
4. Molecular diagnosis
5. DNA fingerprinting
6. Cancer therapy

5. Applications of recombinant DNA technology

Answer

1. Human insulin production
2. Growth hormone production
3. Hepatitis B vaccine
4. Gene therapy
5. DNA fingerprinting
6. Prenatal diagnosis
7. Cancer diagnosis
8. Monoclonal antibodies

SHORT ANSWERS

6. Restriction endonucleases – types, action and applications.

Answer

Restriction endonucleases

Enzymes that cleave DNA at specific sequences.

Types

1. Type I
2. Type II
3. Type III

Action

- Recognize palindromic sequences.
- Produce sticky or blunt ends.

Applications

1. Recombinant DNA technology

2. Gene cloning
3. DNA mapping
4. Molecular diagnosis

7. Name the applications of recombinant DNA technology

Answer

1. Insulin production
2. Vaccine production
3. Gene therapy
4. Prenatal diagnosis
5. DNA fingerprinting
6. Monoclonal antibodies
7. Cancer diagnosis

8. Gene therapy

Answer

Gene therapy is the introduction of normal genes into cells to treat genetic diseases.

Types

1. Somatic gene therapy
2. Germline gene therapy

Applications

- Severe combined immunodeficiency
- Hemophilia
- Cancer therapy

9. Give reason: "Plasmids are used commonly as vectors in recombinant DNA techniques"

Answer

Plasmids are commonly used as vectors because they:

1. Replicate independently
2. Have selectable marker genes
3. Are small and easy to manipulate
4. Possess restriction sites
5. Can carry foreign DNA efficiently

10. Restriction endonuclease

Answer

Restriction endonucleases are enzymes that cut DNA at specific nucleotide sequences.

Example:
Eco RI.

Applications:

1. Gene cloning
2. Recombinant DNA technology
3. DNA mapping

11. Restriction enzymes

Answer

Restriction enzymes are bacterial enzymes that cleave DNA at specific recognition sequences.

Types:

1. Exonucleases
2. Endonucleases

Uses:

1. Recombinant DNA technology
2. Molecular diagnosis
3. Gene mapping

12. List the restriction endonucleases and mention its uses

Answer

Examples of restriction endonucleases

1. Eco RI
2. Hind III
3. Bam HI
4. Hae III

Uses

1. Gene cloning
2. DNA fingerprinting
3. Recombinant DNA technology
4. Molecular diagnosis

MOLECULAR DIAGNOSTICS

SHORT ESSAYS

1. Explain the different steps in PCR. Add a note on its applications

Answer

Polymerase Chain Reaction (PCR)

Definition

PCR is a technique used for amplification of specific DNA sequences.

Requirements

1. Template DNA
2. Primers
3. Taq DNA polymerase
4. Deoxynucleotide triphosphates
5. Buffer solution

Steps in PCR

1. Denaturation

- Double stranded DNA heated to 94–95°C.
- DNA strands separate.

2. Annealing

- Temperature reduced to 50–65°C.
- Primers bind to template DNA.

3. Extension

- Temperature raised to 72°C.
- Taq polymerase synthesizes new DNA strands.

These steps repeated for 25–35 cycles.

Applications of PCR

1. Diagnosis of infectious diseases
2. Detection of genetic disorders
3. DNA fingerprinting
4. Prenatal diagnosis
5. Cancer diagnosis
6. Forensic medicine
7. Research purposes

2. Describe PCR and its applications. Add a note on its significance in diagnosis covid-19

Answer

PCR – Definition

PCR is an in vitro amplification of DNA using DNA polymerase.

Steps

1. Denaturation
2. Annealing
3. Extension

Applications

1. Diagnosis of infections
2. Genetic disease detection
3. DNA fingerprinting
4. Cancer diagnosis
5. Prenatal diagnosis

Significance in COVID-19 Diagnosis

- Reverse transcription PCR used.
- Viral RNA converted to complementary DNA.
- Amplifies SARS-CoV-2 genetic material.
- Highly sensitive and specific.
- Early diagnosis possible.

3. Steps and applications of polymerase chain reaction

Answer

Steps of PCR

1. Denaturation
2. Annealing
3. Extension

Applications

1. Infectious disease diagnosis
2. Genetic disorder diagnosis
3. Prenatal diagnosis
4. DNA fingerprinting
5. Cancer detection
6. Forensic medicine

SHORT ANSWERS

4. Southern blotting.

Answer

Southern blotting is a technique used for detection of specific DNA sequences.

Steps

1. DNA fragmentation
2. Gel electrophoresis
3. Transfer to membrane
4. Hybridization with labeled probe
5. Detection

Applications:

- Gene analysis
- Diagnosis of genetic disorders.

5. RFLP (Restriction Fragment Length Polymorphism)

Answer

RFLP is variation in length of DNA fragments produced by restriction enzymes.

Applications:

1. DNA fingerprinting
2. Paternity testing
3. Genetic disease diagnosis
4. Forensic identification

6. PCR (Polymerase Chain Reaction)

Answer

PCR is a method for amplification of specific DNA sequences.

Steps

1. Denaturation
2. Annealing
3. Extension

Uses:

1. Molecular diagnosis
2. DNA fingerprinting
3. Prenatal diagnosis

7. Applications of PCR (Polymerase Chain Reaction)

Answer

1. Diagnosis of infections
2. Detection of genetic disorders

3. DNA fingerprinting
4. Prenatal diagnosis
5. Cancer diagnosis
6. Forensic medicine

8. Western blot technique

Answer

Western blot is a technique used for detection of proteins.

Steps

1. Protein separation by electrophoresis
2. Transfer to membrane
3. Addition of antibodies
4. Detection of antigen-antibody reaction

Applications:

- HIV diagnosis
- Protein analysis

9. Name various blotting techniques and their significance

Answer

1. Southern blot – DNA detection
2. Northern blot – RNA detection
3. Western blot – Protein detection
4. Eastern blot – Post translational modifications

10. Uses of restriction fragment length polymorphism (RFLP)

Answer

1. DNA fingerprinting
2. Paternity testing
3. Forensic medicine
4. Genetic disease diagnosis
5. Linkage analysis

11. Mention two applications of polymerase chain reaction

Answer

1. Diagnosis of infectious diseases
2. DNA fingerprinting

12. DNA fingerprinting

Answer

DNA fingerprinting is identification of individuals based on unique DNA patterns.

Principle

Based on polymorphism in repetitive DNA sequences.

Applications

1. Forensic identification
2. Paternity testing
3. Criminal investigations

13. Mention the principles and application of polymerase chain reaction

Answer

Principle

PCR amplifies specific DNA sequences using repeated cycles of denaturation, annealing and extension.

Applications

1. Diagnosis of infections
2. Genetic disorder diagnosis
3. DNA fingerprinting
4. Prenatal diagnosis

CLINICAL AND APPLIED BIOCHEMISTRY

LIVER AND GASTRIC FUNCTION TESTS

LONG ESSAYS

1. A 53-year-old woman presents to emergency department with persistent right upper abdominal pain and vomiting. She gives a history of having intermittent, less severe episodes of abdominal discomfort, especially on eating fatty and heavy meals over the previous year. Over last 6 days her urine had become darker in colour and stools pale. An abdominal ultrasound scan revealed gall stones. She was found to have yellowish discolouration of sclera. Lab investigations revealed

Total Bilirubin- 9mg/dl, Direct Bilirubin- 6mg/dl, Alkaline Phosphatase- 510 U/L, AST- 80 U/L, ALT - 76 U/L

a) What is the type of jaundice
b) What are the other probable causes of this type of jaundice
c) Describe the formation and excretion of bilirubin in the body
d) What are the biochemical findings in different types of jaundice

Answer

a) Type of jaundice

Obstructive jaundice.

Evidence:

1. Elevated direct bilirubin
2. Markedly elevated alkaline phosphatase
3. Dark urine
4. Pale stools
5. Gall stones on ultrasound

b) Other probable causes of obstructive jaundice

1. Common bile duct stones
2. Carcinoma head of pancreas
3. Cholangiocarcinoma
4. Biliary stricture
5. Congenital biliary atresia
6. Compression by tumors

c) Formation and excretion of bilirubin

Formation of bilirubin

1. Senescent red blood cells destroyed in reticuloendothelial system.
2. Hemoglobin split into globin and heme.
3. Heme converted to biliverdin by heme oxygenase.
4. Biliverdin reduced to bilirubin by biliverdin reductase.
5. Bilirubin transported bound to albumin.

Hepatic uptake and conjugation

1. Bilirubin taken up by liver cells.
2. Conjugated with glucuronic acid by UDP-glucuronyl transferase.
3. Forms bilirubin diglucuronide.

Excretion

1. Conjugated bilirubin secreted into bile.
2. In intestine converted to urobilinogen.
3. Part oxidized to stercobilin in stool.
4. Small amount reabsorbed and excreted in urine as urobilin.

d) Biochemical findings in different types of jaundice

Findings	Hemolytic	Hepatocellular	Obstructive
Serum bilirubin	Unconjugated ↑	Mixed ↑	Conjugated ↑
Urine bilirubin	Absent	Present	Present
Urine urobilinogen	Increased	Increased	Absent
Stool colour	Dark	Normal/pale	Clay coloured
ALP	Normal	Mild increase	Marked increase
AST/ALT	Normal	Marked increase	Mild increase

Conclusion

This patient has obstructive jaundice due to gall stones causing biliary obstruction.

2. 42-year-old obese lady presented with intolerance to fatty foods and pain in right abdominal region. On examination, her eyes were yellowish; stools had clay-colored appearance. Her investigations revealed the following

Serum bilirubin-18 mg/dl, Direct bilirubin-17 mg/dl, AST-35 IU/L, ALT-40 IU/L, ALP-400 IU/L

•What is the probable diagnosis
•What is normal serum Bilirubin level
•Describe the catabolism of Heme
•What is the biochemical basis of clay colored stools
•What will be the probable urinary findings

Answer

Probable diagnosis

Obstructive jaundice.

Evidence:

1. Direct hyperbilirubinemia
2. Elevated alkaline phosphatase
3. Clay coloured stools
4. Fat intolerance

Normal serum bilirubin level

0.2–1.0 mg/dL.

Catabolism of heme

1. Senescent RBCs destroyed in reticuloendothelial system.
2. Hemoglobin split into globin and heme.
3. Heme converted to biliverdin by heme oxygenase.
4. Biliverdin reduced to bilirubin.
5. Bilirubin transported to liver bound to albumin.
6. Conjugated with glucuronic acid.
7. Excreted in bile.
8. Intestinal bacteria convert it to urobilinogen.
9. Stercobilin gives colour to stool.

Biochemical basis of clay coloured stools

Due to absence of stercobilin in stool because bile pigments do not reach intestine in obstructive jaundice.

Probable urinary findings

1. Bile pigments – positive
2. Bile salts – positive
3. Urine dark coloured
4. Urobilinogen absent

3. A 42-year-old obese lady presented with pain abdomen. She also complaints of passing clay coloured stool on examination there was yellowish discoloration of skin.

•What is the diagnosis.
•Describe the laboratory findings in hemolytic, hepatocellular and obstructive jaundice.
•Van den Bergh reaction.

Answer

Diagnosis

Obstructive jaundice.

Laboratory findings in jaundice

Findings	Hemolytic	Hepatocellular	Obstructive
Serum bilirubin	Unconjugated ↑	Mixed ↑	Conjugated ↑
Urine bilirubin	Absent	Present	Present
Urine urobilinogen	Increased	Increased	Absent
Stool colour	Dark	Pale	Clay coloured
ALP	Normal	Mild increase	Marked increase
AST/ALT	Mild increase	Marked increase	Mild increase

Van den Bergh reaction

It is a test used to detect bilirubin in serum.

Types

1. Direct positive reaction
    - Seen in conjugated hyperbilirubinemia.
2. Indirect positive reaction
    - Seen in unconjugated hyperbilirubinemia.
3. Biphasic reaction
    - Seen in hepatocellular jaundice.

4. A 70-year-old male presented to his family physician with yellow discolouration of sclera associated with epigastric pain and weight loss. Urine had become darker in color and his stools pale. A CT scan of the abdomen revealed a tumor in the pancreas. Investigations:

Total Bilirubin - 4.2mg/dl; Direct Bilirubin – 3.8mg/dl; ALP – 510U/L; AST – 80U/L; ALT -76U/L. Answer the following using the above data:
•What is the probable diagnosis
•Define and classify Jaundice
•Which enzyme is specific for this type of jaundice and why
•Explain the urinary findings
•Why urine is dark in color and stools pale
•Enumerate the causes of jaundice
•List the laboratory investigations used to differentiate between the types of jaundice.

Answer

Probable diagnosis

Obstructive jaundice due to carcinoma head of pancreas.

Definition of jaundice

Jaundice is yellow discoloration of skin, sclera and mucous membrane due to increased serum bilirubin.

Classification

1. Hemolytic jaundice
2. Hepatocellular jaundice
3. Obstructive jaundice

Enzyme specific for obstructive jaundice

Alkaline phosphatase.

Reason

ALP is markedly elevated due to cholestasis and increased synthesis by biliary canalicular cells.

Urinary findings

1. Bile pigments positive
2. Bile salts positive
3. Urobilinogen absent
4. Dark coloured urine

Reason for dark urine and pale stools

Dark urine

Excretion of conjugated bilirubin in urine.

Pale stools

Absence of stercobilin in intestine.

Causes of jaundice

Hemolytic

- Hemolytic anemia
- Malaria

Hepatocellular

- Viral hepatitis
- Cirrhosis

Obstructive

- Gall stones
- Pancreatic carcinoma
- Biliary obstruction

Laboratory investigations differentiating jaundice

1. Serum bilirubin
2. Direct and indirect bilirubin
3. AST
4. ALT
5. ALP
6. Urine bile pigments
7. Urine bile salts
8. Urine urobilinogen
9. Stool colour

5. Explain bilirubin formation and excretion in detail. Describe the biochemical changes in hepato-cellular and obstructive jaundice.

Answer

Bilirubin formation

1. RBC destruction in reticuloendothelial system.
2. Hemoglobin split into globin and heme.
3. Heme converted to biliverdin.
4. Biliverdin converted to bilirubin.
5. Bilirubin transported bound to albumin.

Hepatic conjugation

1. Uptake by hepatocytes.
2. Conjugation with glucuronic acid.
3. Enzyme: UDP-glucuronyl transferase.

Excretion

1. Conjugated bilirubin excreted in bile.
2. Intestinal bacteria convert to urobilinogen.
3. Stercobilin formed in stool.
4. Small amount excreted in urine.

Biochemical changes in hepatocellular jaundice

1. Mixed hyperbilirubinemia
2. AST and ALT markedly elevated
3. Mild increase in ALP
4. Urine bilirubin positive
5. Urine urobilinogen increased

Biochemical changes in obstructive jaundice

1. Conjugated hyperbilirubinemia
2. Marked elevation of ALP
3. Mild increase in AST and ALT
4. Bile pigments positive in urine
5. Urobilinogen absent
6. Clay coloured stools

SHORT ESSAYS

6. Discuss the biochemical alterations seen in blood and urine in different types of jaundice.

Answer

Findings	Hemolytic	Hepatocellular	Obstructive
Serum bilirubin	Unconjugated ↑	Mixed ↑	Conjugated ↑
AST/ALT	Normal	Markedly increased	Mild increase
ALP	Normal	Mild increase	Marked increase
Urine bilirubin	Absent	Present	Present
Urine urobilinogen	Increased	Increased	Absent
Stool colour	Dark	Pale	Clay coloured

7. A 57-year-old woman presented at clinic with intense jaundice, pruritus and hepatomegaly with abnormal liver function tests-Total bilirubin-12 mg/dl, Conjugated bilirubin- 10 mg/dl, unconjugated bilirubin- 2 mg/dl Serum ALP-826 U/L

a) What is the probable diagnosis
b) Discuss the causes and lab findings for the above condition

Answer

a) Probable diagnosis

Obstructive jaundice.

Evidence:

1. Conjugated hyperbilirubinemia
2. Very high ALP
3. Pruritus
4. Hepatomegaly

b) Causes

1. Gall stones
2. Carcinoma pancreas
3. Cholangiocarcinoma
4. Biliary strictures
5. Extrahepatic obstruction

Laboratory findings

1. Serum bilirubin increased mainly conjugated
2. ALP markedly elevated
3. Mild AST and ALT increase
4. Urine bile pigments positive
5. Bile salts positive
6. Urobilinogen absent
7. Clay coloured stools

8. A patient gave history of recurrent episodes of vomiting and fever. On examination he was icteric, dehydrated and his liver was palpable.

Following is the biochemical report of this patient:
S. total Bilirubin- 12 mg%, conjugated bilirubin – 5.5 mg %, unconjugated bilirubin – 6.5 mg %, S. Alkaline phosphatase – 278 IU/L, AST – 235 IU/L, ALT – 365 IU/ L, Bile salts – Negative, Bile Pigments – positive, Fecal stercobilinogen – positive.

a) What could be your probable Diagnosis
b) Explain how Bilirubin is formed and excreted from the body

Answer

a) Probable diagnosis

Hepatocellular jaundice.

Evidence:

1. Mixed hyperbilirubinemia
2. AST and ALT markedly elevated
3. Stercobilinogen present
4. Bile salts negative

b) Bilirubin formation and excretion

1. RBC destruction releases hemoglobin.
2. Heme converted to biliverdin.
3. Biliverdin reduced to bilirubin.
4. Bilirubin transported with albumin.
5. Liver conjugates bilirubin with glucuronic acid.
6. Conjugated bilirubin excreted into bile.
7. Intestinal bacteria convert it to urobilinogen.
8. Stercobilin gives colour to stool.
9. Small amount excreted in urine.

9. Enumerate liver function tests. Describe any two of them in detail

Answer

Liver function tests

1. Serum bilirubin
2. AST
3. ALT
4. Alkaline phosphatase
5. Serum proteins
6. Prothrombin time
7. Urine bile pigments
8. Bromsulphthalein excretion test

1. Serum bilirubin estimation

Normal value

0.2–1.0 mg/dL.

Significance

- Increased in jaundice.
- Helps differentiate types of jaundice.

2. Alkaline phosphatase

Normal value

30–120 IU/L.

Significance

- Markedly elevated in obstructive jaundice.
- Mildly elevated in hepatocellular disease.

SHORT ANSWERS

10. Van den Bergh test

Definition

Van den Bergh test is used for estimation and differentiation of bilirubin into direct

(conjugated) and indirect (unconjugated) bilirubin.

Principle

Bilirubin reacts with diazotized sulphanilic acid to form a purple coloured azobilirubin compound.

Types of reaction

1. **Direct positive reaction**
    - Immediate colour formation.
    - Due to conjugated bilirubin.
    - Seen in obstructive jaundice.
2. **Indirect positive reaction**
    - Colour appears only after adding alcohol.
    - Due to unconjugated bilirubin.
    - Seen in hemolytic jaundice.
3. **Biphasic reaction**
    - Immediate colour develops and intensifies after alcohol addition.
    - Seen in hepatocellular jaundice.

Clinical significance

- Helps in differential diagnosis of jaundice.
- Measures serum bilirubin fractions.

11. Discuss the biochemical alterations seen in blood and urine in hepatocellular jaundice

Blood findings

1. Serum bilirubin increased (mixed type).
2. Both conjugated and unconjugated bilirubin elevated.
3. Serum Alanine aminotransferase and Aspartate aminotransferase markedly increased.
4. Alkaline phosphatase moderately elevated.
5. Serum cholesterol normal or decreased.
6. Prothrombin time prolonged.
7. Serum albumin decreased in chronic liver disease.

Urine findings

1. Urine bilirubin present.
2. Urobilinogen increased.
3. Urine dark coloured.
4. Bile salts may be present.

Stool

- Clay coloured only in severe obstruction.
- Usually normal or pale.

12. Urinary picture of different types of Jaundice

Feature	Hemolytic jaundice	Hepatocellular jaundice	Obstructive jaundice
Urine bilirubin	Absent	Present	Present
Urine urobilinogen	Increased	Increased	Absent
Urine colour	Normal	Dark	Dark yellow
Bile salts	Absent	May be present	Present
Stool colour	Dark	Pale	Clay coloured

13. Differential diagnosis of jaundice by laboratory tests

Laboratory test	Hemolytic	Hepatocellular	Obstructive
Serum bilirubin	Unconjugated ↑	Mixed ↑	Conjugated ↑
Van den Bergh reaction	Indirect	Biphasic	Direct
Urine bilirubin	Absent	Present	Present
Urine urobilinogen	Increased	Increased	Absent
Serum Alanine aminotransferase/Aspartate aminotransferase	Mild increase	Marked increase	Mild increase
Alkaline phosphatase	Normal	Moderate increase	Marked increase
Serum cholesterol	Normal	Decreased	Increased
Stool colour	Dark	Pale	Clay coloured

14. Fatty liver

Definition

Fatty liver is excessive accumulation of triglycerides in liver cells.

Causes

1. Alcoholism.
2. Diabetes mellitus.
3. Obesity.
4. Protein malnutrition.
5. Starvation.
6. Toxins and drugs.

Biochemical basis

- Increased fatty acid mobilization.
- Decreased lipoprotein synthesis.
- Impaired beta oxidation.
- Increased triglyceride synthesis.

Morphology

- Liver enlarged, yellow and greasy.

Complications

- Cirrhosis.
- Liver failure.

15. Clinical significance of ALP

Normal value

- 40–125 IU/L.

Sources

- Liver.
- Bone.
- Placenta.
- Intestine.

Increased in

1. Obstructive jaundice.
2. Bone diseases:
    - Rickets.
    - Osteomalacia.
    - Paget disease.
3. Hyperparathyroidism.
4. Healing fractures.
5. Pregnancy.

Decreased in

- Hypophosphatasia.
- Severe malnutrition.

Clinical importance

- Marker of cholestasis.

- Marker of osteoblastic activity.

16. Liver function tests

Tests based on excretory function

1. Serum bilirubin.
2. Van den Bergh test.
3. Urine bile pigments.
4. Bromsulphthalein excretion test.

Tests based on hepatocellular integrity

1. Alanine aminotransferase.
2. Aspartate aminotransferase.
3. Lactate dehydrogenase.

Tests based on synthetic function

1. Serum proteins.
2. Albumin/globulin ratio.
3. Prothrombin time.

Tests based on cholestasis

1. Alkaline phosphatase.
2. Gamma glutamyl transferase.

Tests based on detoxification

1. Blood ammonia.

17. What is post hepatic jaundice and how it is diagnosed biochemically

Definition

Post hepatic jaundice is obstructive jaundice caused by obstruction to bile flow after conjugation in liver.

Causes

1. Gall stones.
2. Carcinoma head of pancreas.
3. Biliary stricture.

Biochemical diagnosis

1. Serum conjugated bilirubin markedly increased.
2. Direct Van den Bergh reaction positive.
3. Alkaline phosphatase markedly elevated.
4. Urine bilirubin present.
5. Urine urobilinogen absent.
6. Stool clay coloured.
7. Serum cholesterol increased.

KIDNEY FUNCTION TESTS

SHORT ESSAYS

1. What is clearance? Describe clearance tests with their significance.

Definition

Renal clearance is the volume of plasma completely cleared of a substance by kidneys per minute.

Formula

$C = UV/P$

Where:

- C = Clearance in mL/min
- U = Urine concentration
- V = Urine volume/minute
- P = Plasma concentration

Types of clearance tests

1. Inulin clearance

- Gold standard for Glomerular filtration rate.
- Inulin is freely filtered and neither reabsorbed nor secreted.
- Normal GFR: 125 mL/min.

2. Creatinine clearance

- Endogenous method for estimating GFR.
- Normal: 90–130 mL/min.

3. Urea clearance

- Measures renal function.
- Less accurate because urea is reabsorbed.

4. Para aminohippuric acid clearance

- Measures renal plasma flow.
- PAH is filtered and secreted.

Significance

1. Assessment of Glomerular filtration rate.
2. Diagnosis of renal failure.
3. Monitoring progression of kidney disease.
4. Dose adjustment of drugs.

2. Name the renal clearance tests. Give details of any one of them. What is its clinical significance

Renal clearance tests

1. Inulin clearance.
2. Creatinine clearance.
3. Urea clearance.
4. Para aminohippuric acid clearance.

Creatinine clearance test

Principle

Creatinine is filtered by glomeruli with minimal tubular reabsorption.

Formula

$C = UV/P$

Procedure

- 24 hour urine collection.
- Plasma creatinine estimation.
- Urine creatinine estimation.

Normal value

- 90–130 mL/min.

Clinical significance

1. Best routine test for GFR.
2. Decreased in renal failure.
3. Used for staging chronic kidney disease.
4. Helps in monitoring nephrotoxic drugs.

3. Classify renal function tests. Describe clearance tests in detail

Classification of renal function tests

1. Tests for glomerular function

- Inulin clearance.
- Creatinine clearance.
- Urea clearance.

2. Tests for tubular function

- Concentration test.
- Dilution test.
- Acidification test.

3. Routine tests

- Blood urea.
- Serum creatinine.
- Serum electrolytes.

Clearance tests

Definition

Clearance is volume of plasma cleared of a substance per minute.

Formula

C = UV/P

Inulin clearance

- Gold standard for GFR.
- Normal: 125 mL/min.

Creatinine clearance

- Endogenous marker.
- Normal: 90–130 mL/min.

Urea clearance

- Less accurate.
- Normal maximum clearance: 75 mL/min.

Para aminohippuric acid clearance

- Used for renal plasma flow.
- Normal renal plasma flow: about 600 mL/min.

Significance

- Assessment of kidney function.
- Diagnosis and prognosis of renal diseases.

4. Creatinine clearance and its clinical significance.

Definition

Creatinine clearance is the volume of plasma cleared of creatinine per minute.

Formula

C = UV/P

Normal value

- 90–130 mL/min.

Advantages

1. Endogenous substance.
2. Simple and practical.
3. Good estimate of GFR.

Clinical significance

1. Decreased in renal failure.
2. Detects early renal impairment.
3. Used to assess severity of kidney disease.
4. Useful in monitoring progression and treatment.

SHORT ANSWERS

5. Tubular function tests.

1. Concentration test.
2. Dilution test.
3. Water deprivation test.
4. Acidification test.
5. Phenolsulfonphthalein excretion test.

Significance

- Assess tubular reabsorption and secretion.

6. Discuss about the different types of proteinuria in detail.

Definition

Presence of excess proteins in urine.

Types

1. Functional proteinuria

- Temporary.
- Seen after exercise, fever and stress.

2. Glomerular proteinuria

- Due to increased glomerular permeability.
- Seen in nephrotic syndrome.

3. Tubular proteinuria

- Due to defective tubular reabsorption.
- Seen in tubular damage.

4. Overflow proteinuria

- Excess low molecular weight proteins in plasma.
- Example: Bence Jones proteins.

5. Post renal proteinuria

- Due to urinary tract infection.

Detection

- Heat and acetic acid test.
- Sulfosalicylic acid test.

7. Creatinine clearance

Definition

Volume of plasma cleared of creatinine per minute.

Formula

C = UV/P

Normal value

- 90–130 mL/min.

Importance

- Measures GFR.
- Detects renal impairment.

8. Creatinine clearance tests and its significance.

Test

- 24 hour urine creatinine and plasma creatinine estimation.

Significance

1. Reliable estimate of GFR.
2. Detects early renal failure.
3. Monitoring chronic kidney disease.

9. Creatinine clearance test

Principle

Creatinine filtered by glomeruli is excreted in urine.

Formula

C = UV/P

Normal value

- 90–130 mL/min.

Uses

- Estimation of GFR.

10. Define clearance and how it is estimated? Add a note on its diagnostic importance

Definition

Clearance is volume of plasma completely cleared of a substance per minute.

Estimation

C = UV/P

Diagnostic importance

1. Assess GFR.
2. Detect renal disease.
3. Evaluate renal plasma flow.
4. Monitor renal therapy.

11. Urea clearance test

Principle

Measures rate of urea excretion.

Formula

C = UV/P

Normal values

- Maximum clearance: 75 mL/min.
- Standard clearance: 54 mL/min.

Limitations

- Urea is reabsorbed; less accurate.

Significance

- Assessment of renal function.

PLASMA PROTEINS

SHORT ESSAYS

1. Electrophoresis

Definition

Electrophoresis is separation of charged particles under electric field.

Principle

At alkaline pH, serum proteins are negatively charged and migrate towards anode.

Fractions separated

1. Albumin.
2. Alpha 1 globulin.
3. Alpha 2 globulin.
4. Beta globulin.
5. Gamma globulin.

Procedure

- Sample applied on supporting medium.
- Electric current passed.
- Proteins separate according to charge and size.

Clinical significance

1. Multiple myeloma.
2. Nephrotic syndrome.
3. Liver cirrhosis.
4. Immunodeficiency disorders.

2. Plasma proteins and its functions

Plasma proteins

1. Albumin.
2. Globulins.
3. Fibrinogen.

Functions

1. Maintenance of colloidal osmotic pressure.
2. Transport of substances.
3. Buffer action.
4. Immunological functions.
5. Blood coagulation.
6. Nutritional role.
7. Viscosity maintenance.

Clinical importance

- Altered in liver disease, nephrotic syndrome and malnutrition.

SHORT ANSWERS

3. A/G ratio

Definition

Ratio of albumin to globulin in plasma.

Normal value

- 1.2 : 1 to 1.5 : 1.

Decreased in

1. Cirrhosis.
2. Nephrotic syndrome.
3. Multiple myeloma.

4. Serum electrophoresis and its clinical importance

Principle

Proteins separate in electric field based on charge.

Clinical importance

1. Multiple myeloma.
2. Nephrotic syndrome.
3. Liver cirrhosis.
4. Chronic infections.

5. Functions of albumin

1. Maintains oncotic pressure.
2. Transport protein.
3. Buffer action.
4. Nutritional function.
5. Drug binding.

6. Albumin

Features

- Synthesized in liver.
- Major plasma protein.
- Normal value: 3.5–5 g/dL.

Functions

1. Maintains colloidal osmotic pressure.
2. Transport function.
3. Buffer action.

Decreased in

- Liver disease.
- Nephrotic syndrome.
- Malnutrition.

7. List the functions of plasma proteins

1. Maintain osmotic pressure.
2. Transport substances.
3. Buffering action.
4. Blood coagulation.
5. Immunity.
6. Nutrition.

8. Explain why edema develops in hypoalbuminemia

Albumin maintains plasma colloidal osmotic pressure. In hypoalbuminemia, plasma oncotic pressure decreases causing fluid to move from blood vessels into interstitial spaces producing edema.

ACID-BASE BALANCE AND pH

LONG ESSAYS

1. A 35-year-old male patient was admitted with complaints of drowsiness and vision loss. Detailed history revealed he has consumed alcohol adulterated with

methanol on the previous day. His Arterial blood gas analysis report is as follows:

pH: 7.2, HCO_3^-: 16 mmol/L, pCO_2: 41 mmHg

a) What acid base imbalance, the patient probably has
b) What are the normal reference ranges for the given ABG parameters
c) What are buffers. List any TWO intracellular buffers and extracellular buffers.
d) Explain the role of kidneys in blood pH regulation

a) Acid base imbalance

High anion gap metabolic acidosis due to methanol poisoning.

b) Normal reference ranges

- pH: 7.35–7.45
- HCO_3^-: 22–26 mmol/L
- pCO_2: 35–45 mmHg

c) Buffers

Buffers are substances that resist changes in pH when acids or alkalis are added.

Intracellular buffers

1. Hemoglobin.
2. Phosphate buffer.

Extracellular buffers

1. Bicarbonate buffer.
2. Plasma proteins.

d) Role of kidneys in blood pH regulation

1. Reabsorption of bicarbonate.
2. Excretion of hydrogen ions.
3. Formation of ammonium ions.
4. Excretion of titratable acids.
5. Generation of new bicarbonate.

Mechanism

- Hydrogen ions are secreted by tubular cells.
- Filtered bicarbonate is reabsorbed.
- Phosphate and ammonia buffers help acid excretion.

2. An unconscious patient was rushed to the Emergency department of the hospital. History taken from the attendant revealed that patient was a known Diabetic, blood samples were collected and sent to clinical laboratory for analysis.

a) What could be probable diagnosis
b) Which relevant investigations would you suggest for this patient
c) Explain the role of Kidneys in maintenance of Acid base homeostasis
d) How is the compensation brought about in this patient

a) Probable diagnosis

Diabetic ketoacidosis causing high anion gap metabolic acidosis.

b) Relevant investigations

1. Blood glucose.
2. Urine ketone bodies.
3. Arterial blood gas analysis.
4. Serum electrolytes.
5. Serum bicarbonate.
6. Blood urea and creatinine.
7. Serum ketone bodies.

c) Role of kidneys in acid base homeostasis

1. Reabsorption of bicarbonate.
2. Hydrogen ion secretion.
3. Ammonia production.
4. Excretion of titratable acid.
5. Formation of new bicarbonate.

d) Compensation

- Hyperventilation (Kussmaul breathing) decreases pCO2.
- Renal compensation increases acid excretion.

3. A 68-year-old man, known diabetic for the past 20 years was brought to the emergency in a disoriented state. Relatives informed that he had fever for the last few days and skipped his regular doses of insulin. On examination he had rapid pulse and rapid deep breathing. Laboratory results as follows:

pH: 7.2, HCO3−: 12 meq/L, PCO2: 35mm of Hg, Na+: 135meq/L, K+: 4.9meq/L, Cl−: 101meq/L

a) What is the most likely acid base disorder in this patient
b) Calculate the anion gap and comments
c) Interpret the given laboratory parameters and give their reference interval
d) Enumerate the causes for this type of acid base imbalance
e) Describe the role of lungs and kidney in maintaining normal plasma pH

a) Acid base disorder

High anion gap metabolic acidosis due to diabetic ketoacidosis.

b) Anion gap

Formula:
Anion gap = Na+ – (Cl− + HCO3−)

Normal anion gap: 8–16 mEq/L.

Hence increased anion gap metabolic acidosis.

c) Interpretation and reference values

Parameter	Patient value	Normal value	Interpretation
pH	7.2	7.35–7.45	Acidosis
HCO3−	12 mEq/L	22–26 mEq/L	Decreased
PCO2	35 mmHg	35–45 mmHg	Compensatory low-normal
Na+	135 mEq/L	135–145 mEq/L	Normal
K+	4.9 mEq/L	3.5–5 mEq/L	High-normal
Cl−	101 mEq/L	98–106 mEq/L	Normal

d) Causes of high anion gap metabolic acidosis

1. Diabetic ketoacidosis.
2. Lactic acidosis.
3. Renal failure.
4. Methanol poisoning.
5. Ethylene glycol poisoning.
6. Salicylate poisoning.

e) Role of lungs and kidney in maintaining plasma pH

Lungs

- Eliminate carbon dioxide.
- Hyperventilation lowers carbonic acid.

Kidneys

1. Hydrogen ion secretion.

2. Bicarbonate reabsorption.
3. Ammonia formation.
4. Titratable acid excretion.

4. A 54-year-old man was admitted to emergency in a disoriented state. He had a feeble pulse, low blood pressure and sweetish odour of breath. Arterial blood gas analysis showed:

pH : 7.1, HCO3 : 11 mmol/L, pCO2 : 38 mmHg.

a) What is the most likely acid base disorder in this case
b) Interpret the ABG findings and give the normal reference interval
c) Give four causes for the above acid base disorder
d) Enumerate the major buffer systems in the body
e) Discuss the renal regulatory mechanisms of acid base balance

a) Acid base disorder

Metabolic acidosis.

b) Interpretation

- pH decreased → acidosis.
- HCO_3^- decreased → metabolic cause.
- pCO2 near normal.

Normal reference values

- pH: 7.35–7.45
- HCO_3^-: 22–26 mmol/L
- pCO2: 35–45 mmHg

c) Causes

1. Diabetic ketoacidosis.
2. Renal failure.
3. Severe diarrhea.
4. Lactic acidosis.

d) Major buffer systems

1. Bicarbonate buffer.
2. Phosphate buffer.
3. Protein buffer.
4. Hemoglobin buffer.

e) Renal regulation of acid base balance

1. Reabsorption of bicarbonate.
2. Hydrogen ion secretion.
3. Ammonia formation.
4. Titratable acid excretion.
5. Generation of bicarbonate.

5. A 20 years old young man was bought to casualty with road traffic accident. He sustained injury to chest wall. ABG analysis showed pH 7.25, pCO2 54 mm Hg, HCO3 is 23 mEq/L.

• Explain the mechanism of maintaining blood pH.
• What is the diagnosis
• What is the biochemical change in these disorders
• Define the other acid base balance disorders

Mechanism of maintaining blood pH

1. Buffer systems.
2. Respiratory regulation.
3. Renal regulation.

Diagnosis

Respiratory acidosis.

Biochemical changes

- pH decreased.
- pCO2 increased.
- HCO_3^- normal initially.

Other acid base disorders

1. Metabolic acidosis.
2. Metabolic alkalosis.
3. Respiratory alkalosis.

6. What is the normal pH of blood. Describe in detail about the respiratory and renal regulation of blood pH and add a note on metabolic acidosis.

Normal blood pH

- 7.35–7.45.

Respiratory regulation of blood pH

Mechanism

- Lungs regulate pCO2.
- Carbon dioxide combines with water to form carbonic acid.

In acidosis

- Hyperventilation removes carbon dioxide.

In alkalosis

- Hypoventilation retains carbon dioxide.

Renal regulation of blood pH

1. Reabsorption of bicarbonate.
2. Hydrogen ion secretion.
3. Ammonia formation.
4. Titratable acid excretion.

Metabolic acidosis

Definition

Decrease in blood pH due to primary decrease in bicarbonate.

Causes

1. Diabetic ketoacidosis.
2. Renal failure.
3. Diarrhea.
4. Lactic acidosis.

Features

- Low pH.
- Low bicarbonate.
- Compensatory hyperventilation.

7. Discuss in detail the mechanism by which kidney maintains the blood pH. What is meant by metabolic acidosis and how it is compensated

Renal maintenance of blood pH

1. Reabsorption of bicarbonate

- Occurs mainly in proximal tubule.
- Prevents bicarbonate loss.

2. Hydrogen ion secretion

- Via Na+/H+ exchanger.
- Distal tubular secretion.

3. Titratable acid excretion

- Phosphate buffer accepts hydrogen ions.

4. Ammonia mechanism

- Ammonia formed from glutamine.
- NH3 combines with H+ to form NH4+.

5. Generation of new bicarbonate

- Returned to plasma.

Metabolic acidosis

Definition

Primary decrease in bicarbonate causing fall in pH.

Compensation

1. Buffer action.
2. Hyperventilation.
3. Renal increase in hydrogen ion excretion.

SHORT ESSAYS

8. A 72-year-old beggar was brought to hospital in a state of coma. He had the following biochemical findings.

Blood Glucose- 560 mg/dl, Urine Sugar- >2%, Plasma Bicarbonate 15 mEq/L, Rothera's test with urine positive, Blood pH- 7.3, pCO2- 31 mm Hg

a) Diagnose the Acid-Base disorder. What are the other causes for this disorder?
b) Describe kidney role in regulation of acid-base balance.
c) Describe compensatory mechanism for above Acid-Base disorder.

a) Diagnosis

High anion gap metabolic acidosis due to diabetic ketoacidosis.

Other causes

1. Renal failure.
2. Lactic acidosis.
3. Methanol poisoning.
4. Ethylene glycol poisoning.

b) Kidney role in acid base balance

1. Reabsorption of bicarbonate.
2. Hydrogen ion secretion.
3. Titratable acid excretion.
4. Ammonia production.

c) Compensation

1. Buffer systems.
2. Hyperventilation causing decreased pCO2.
3. Renal acid excretion.

9. Renal regulation of pH.

1. Reabsorption of bicarbonate.
2. Hydrogen ion secretion.
3. Excretion of titratable acids.
4. Ammonia formation.
5. Formation of new bicarbonate.

Significance

Maintains blood pH within normal range.

10. What is the normal pH of blood. Describe the renal regulation of Acid Base homeostasis.

Normal blood pH

- 7.35–7.45.

Renal regulation

1. Reabsorption of bicarbonate.
2. Hydrogen ion secretion.
3. Ammonia formation.
4. Titratable acid excretion.
5. Generation of bicarbonate.

Importance

- Maintains acid base balance.

11. What are the various renal mechanisms involved in regulation of blood pH

1. Reabsorption of bicarbonate.
2. Hydrogen ion secretion.
3. Sodium hydrogen exchange.
4. Phosphate buffer mechanism.
5. Ammonium ion excretion.
6. Formation of new bicarbonate.

12. Renal regulation of acid base balance

Mechanisms

1. Reabsorption of bicarbonate.
2. Hydrogen ion excretion.
3. Phosphate buffer action.
4. Ammonia mechanism.
5. Formation of bicarbonate.

13. What is the role of buffers in regulating blood pH

Buffers

Substances that resist change in pH.

Major blood buffers

1. Bicarbonate buffer.
2. Phosphate buffer.
3. Protein buffer.
4. Hemoglobin buffer.

Role

- Immediate defense against pH changes.

14. What are the causes. biochemical findings and compensatory mechanisms in metabolic acidosis

Causes

1. Diabetic ketoacidosis.
2. Renal failure.
3. Diarrhea.
4. Lactic acidosis.

Biochemical findings

- Decreased pH.
- Decreased bicarbonate.
- Compensatory decreased pCO2.

Compensation

1. Buffer systems.
2. Hyperventilation.
3. Renal acid excretion.

15. Metabolic acidosis

Definition

Decrease in blood pH due to primary fall in bicarbonate.

Causes

1. Ketoacidosis.
2. Renal failure.
3. Diarrhea.
4. Lactic acidosis.

Features

- Low pH.
- Low bicarbonate.
- Hyperventilation.

Compensation

- Respiratory hyperventilation.

16. Explain renal regulation of maintaining blood pH

1. Bicarbonate reabsorption.
2. Hydrogen ion secretion.
3. Phosphate buffer mechanism.
4. Ammonium ion formation.
5. Formation of new bicarbonate.

17. Define metabolic alkalosis. What are the characteristic features and causes of metabolic alkalosis. Mention the compensatory mechanisms.

Definition

Increase in blood pH due to primary increase in bicarbonate.

Features

- Increased pH.
- Increased bicarbonate.
- Hypoventilation.

Causes

1. Vomiting.
2. Excess alkali intake.
3. Diuretic therapy.
4. Hyperaldosteronism.

Compensation

1. Hypoventilation.
2. Renal bicarbonate excretion.

18. Define metabolic acidosis. What are the characteristic features and causes of metabolic acidosis. Mention the compensatory mechanisms.

Definition

Decrease in blood pH due to primary decrease in bicarbonate.

Characteristic features

1. Low pH.
2. Low bicarbonate.
3. Hyperventilation.
4. Kussmaul respiration.

Causes

1. Diabetic ketoacidosis.
2. Renal failure.
3. Severe diarrhea.
4. Lactic acidosis.

Compensation

1. Buffer systems.
2. Hyperventilation.
3. Increased renal acid excretion.

19. Role of kidney in regulation of plasma pH

1. Reabsorption of bicarbonate.
2. Hydrogen ion secretion.
3. Excretion of acids.
4. Ammonium ion excretion.
5. Generation of bicarbonate.

20. Plasma buffers

Major plasma buffers

1. Bicarbonate buffer.
2. Protein buffer.
3. Phosphate buffer.

Importance

- Maintain plasma pH.

21. Explain briefly on blood buffers and add a note on renal mechanism of maintaining acid base balance

Blood buffers

1. Bicarbonate buffer.
2. Phosphate buffer.
3. Protein buffer.
4. Hemoglobin buffer.

Renal mechanism

1. Reabsorption of bicarbonate.

2. Hydrogen ion secretion.
3. Ammonium ion formation.
4. Titratable acid excretion.

SHORT ANSWERS

22. Biochemistry basis of- Paradoxical aciduria in metabolic alkalosis

In metabolic alkalosis with volume depletion, kidneys conserve sodium by exchanging sodium with hydrogen ions leading to acidic urine despite systemic alkalosis. This is called paradoxical aciduria.

23. Give reason- High anion gap metabolic acidosis in renal failure

In renal failure, excretion of acids such as sulfate, phosphate and organic acids decreases leading to accumulation of unmeasured anions causing high anion gap metabolic acidosis.

24. Anion gap

Definition

Difference between measured cations and measured anions.

Formula

Anion gap = $N_a^+ - (Cl^- + HCO_3^-)$

Normal value

- 8–16 mEq/L.

Significance

Used in evaluation of metabolic acidosis.

25. Respiratory Regulation of Blood pH

Mechanism

Lungs regulate blood pH by altering carbon dioxide elimination.

- Hyperventilation decreases pCO2.
- Hypoventilation increases pCO2.

26. What is the role of kidney in the regulation of pH

1. Reabsorbs bicarbonate.
2. Secretes hydrogen ions.
3. Excretes titratable acids.
4. Forms ammonium ions.
5. Generates new bicarbonate.

27. Metabolic acidosis

Definition

Primary decrease in bicarbonate causing decreased blood pH.

Features

- Low pH.
- Low bicarbonate.
- Hyperventilation.

28. Define anion gap and mention its normal range

Definition

Difference between measured plasma cations and anions.

Formula

Na+ − (Cl− + HCO3−)

Normal range

- 8–16 mEq/L.

29. Respiratory acidosis

Definition

Decrease in blood pH due to carbon dioxide retention.

Causes

1. Chronic obstructive pulmonary disease.
2. Chest injury.
3. Respiratory depression.

Findings

- Increased pCO2.
- Decreased pH.

30. What is respiratory acidosis and mention one example

Definition

Decrease in blood pH due to increased pCO2.

Example

Chronic obstructive pulmonary disease.

31. Plasma pH

Normal plasma pH

- 7.35–7.45.

Importance

Necessary for normal enzyme and metabolic activity.

32. Difference between metabolic acidosis and respiratory acidosis

Feature	Metabolic acidosis	Respiratory acidosis
Primary defect	Decreased bicarbonate	Increased pCO2
pH	Decreased	Decreased
Cause	Ketoacidosis, diarrhea	Lung diseases
Compensation	Hyperventilation	Renal bicarbonate retention

33. Explain the role of kidney in acid base regulation

1. Reabsorption of bicarbonate.
2. Hydrogen ion secretion.
3. Excretion of titratable acids.
4. Ammonium ion excretion.
5. Generation of bicarbonate.

Importance

Maintains blood pH within normal range.

WATER BALANCE, ELECTROLYTE BALANCE AND BODY FLUIDS

SHORT ANSWERS

1. A 55-year-old man was admitted with altered sensorium in emergency department. His lab report was as follows. Serum sodium: 115 mmol/L, serum potassium 4.3 mmol/L, plasma glucose: 83 mg/dL

a) From the given lab report, what is the probable electrolyte imbalance seen in this patient.

b) List any THREE causes of the imbalance.

c) How is the said serum electrolyte level maintained in the body.

Answer

a) Probable electrolyte imbalance

The patient is having **Hyponatremia** because serum sodium is 115 mmol/L (normal: 135–145 mmol/L).

b) Causes of hyponatremia (any three)

1. Excessive vomiting and diarrhea
2. Syndrome of inappropriate antidiuretic hormone secretion (SIADH)
3. Renal failure
4. Congestive cardiac failure
5. Diuretic therapy
6. Adrenal insufficiency

c) Maintenance of serum sodium level in the body

Serum sodium is maintained by:

1. **Renin–Angiotensin–Aldosterone system (RAAS)** – Aldosterone increases sodium reabsorption in renal tubules.
2. **Antidiuretic hormone (ADH)** – Regulates water balance and plasma osmolality.
3. **Kidneys** – Control sodium excretion and reabsorption.
4. **Atrial natriuretic peptide (ANP)** – Promotes sodium excretion.
5. **Thirst mechanism** – Helps maintain osmotic balance.

2. What is Hypokalaemia. Name any one cause.

Answer

Hypokalaemia is defined as decrease in serum potassium level below 3.5 mmol/L.

Causes:

1. Vomiting
2. Diarrhea
3. Diuretic therapy
4. Hyperaldosteronism

3. Give reason: "Low salt diet is recommended in patients with hypertension"

Answer

Excess sodium intake causes water retention leading to increased extracellular fluid volume and increased blood pressure. Restriction of dietary salt decreases plasma volume and helps reduce hypertension.

4. Explain the Biochemical basis of : "Hyperkalemia is a life threatening situation"

Answer

Potassium is the major intracellular cation essential for maintaining resting membrane potential.

In hyperkalemia:

1. Resting membrane potential becomes less negative.
2. Cardiac muscle excitability is altered.
3. Severe cardiac arrhythmias occur.
4. Ventricular fibrillation and cardiac arrest may develop.

Hence hyperkalemia is life threatening.

5. Hyperkalemia

Answer

Hyperkalemia means serum potassium level above 5.5 mmol/L.

Causes

1. Renal failure
2. Metabolic acidosis
3. Addison disease
4. Excess potassium administration

Clinical features

1. Muscle weakness
2. Cardiac arrhythmias
3. ECG changes – tall T waves
4. Cardiac arrest

6. Normal values of serum electrolytes – Sodium, potassium, bicarbonates and chloride

Answer

Electrolyte	Normal value
Sodium	135–145 mmol/L
Potassium	3.5–5.0 mmol/L
Bicarbonate	22–28 mmol/L
Chloride	95–105 mmol/L

7. Distribution of total body water

Answer

Total body water constitutes about 60% of body weight in adults.

Distribution

1. **Intracellular fluid (ICF)** – 2/3 of total body water (40% body weight)
2. **Extracellular fluid (ECF)** – 1/3 of total body water (20% body weight)
    - Interstitial fluid – 15%
    - Plasma – 5%

8. Mention the normal sodium level and clinical manifestation of hyponatremia

Answer

Normal sodium level

135–145 mmol/L.

Clinical manifestations of hyponatremia

1. Nausea and vomiting
2. Muscle cramps
3. Headache
4. Confusion
5. Convulsions
6. Coma

9. What is the normal serum level range of sodium and potassium

Answer

1. Sodium: 135–145 mmol/L
2. Potassium: 3.5–5.0 mmol/L

FREE RADICALS AND ANTIOXIDANTS

SHORT ESSAYS

1. Explain how free radicals scavenged in the body.

Answer

Definition

Free radicals are highly reactive molecules containing unpaired electrons.

Mechanism of scavenging of free radicals

The body possesses antioxidant defense systems to neutralize free radicals.

1. Enzymatic antioxidants

a) Superoxide dismutase (SOD)

Converts superoxide radical to hydrogen peroxide.

$2O2^- + 2H^+ \rightarrow H2O2 + O2$

b) Catalase

Converts hydrogen peroxide to water and oxygen.

$2H2O2 \rightarrow 2H2O + O2$

c) Glutathione peroxidase

Reduces hydrogen peroxide and lipid peroxides using reduced glutathione.

$H2O2 + 2GSH \rightarrow 2H2O + GSSG$

2. Non-enzymatic antioxidants

1. Vitamin E – prevents lipid peroxidation.
2. Vitamin C – scavenges aqueous free radicals.
3. Beta carotene – quenches singlet oxygen.
4. Glutathione – detoxifies peroxides.
5. Uric acid and bilirubin – act as antioxidants.

3. Metal binding proteins

1. Ceruloplasmin
2. Transferrin
3. Ferritin

These bind iron and copper and prevent free radical formation.

Functions of antioxidant system

1. Prevents lipid peroxidation
2. Protects cell membranes
3. Prevents DNA damage
4. Delays aging and degenerative diseases

2. Antioxidants definition and classification

Answer

Definition

Antioxidants are substances that prevent or retard oxidation caused by free radicals.

Classification

I. Enzymatic antioxidants

1. Superoxide dismutase
2. Catalase
3. Glutathione peroxidase

II. Non-enzymatic antioxidants

a) Preventive antioxidants

1. Transferrin
2. Ceruloplasmin
3. Ferritin

b) Chain-breaking antioxidants

1. Vitamin E
2. Vitamin C
3. Beta carotene
4. Reduced glutathione

Functions

1. Scavenge free radicals
2. Prevent oxidative stress
3. Protect membranes and DNA

4. Prevent aging, cancer and atherosclerosis

SHORT ANSWERS

3. Define free radical and give any Two examples of free radicals. Name any two preventive and two chain-breaking antioxidants.

Answer

Definition

Free radicals are molecules containing one or more unpaired electrons.

Examples

1. Superoxide radical (O2−)
2. Hydroxyl radical (OH•)

Preventive antioxidants

1. Transferrin
2. Ceruloplasmin

Chain-breaking antioxidants

1. Vitamin E
2. Vitamin C

4. Anti oxidant enzymes and vitamins.

Answer

Antioxidant enzymes

1. Superoxide dismutase
2. Catalase
3. Glutathione peroxidase

Antioxidant vitamins

1. Vitamin E
2. Vitamin C
3. Beta carotene (Vitamin A precursor)

5. Name the types of antioxidants and discuss their role in scavenging of free radicals.

Answer

Types of antioxidants

1. Enzymatic antioxidants
2. Non-enzymatic antioxidants

Role

1. SOD converts superoxide radical to hydrogen peroxide.
2. Catalase converts hydrogen peroxide to water.
3. Glutathione peroxidase destroys lipid peroxides.
4. Vitamin E prevents membrane lipid peroxidation.
5. Vitamin C scavenges aqueous radicals.

6. Chain breaking and Preventive antioxidants

Answer

Preventive antioxidants

Prevent formation of free radicals.
Examples:

1. Transferrin
2. Ferritin
3. Ceruloplasmin

Chain-breaking antioxidants

Interrupt propagation of free radical chain reactions.
Examples:

1. Vitamin E
2. Vitamin C
3. Beta carotene

7. Name two antioxidants

Answer

1. Vitamin E
2. Vitamin C

8. Reactive oxygen species

Answer

Reactive oxygen species are oxygen-derived highly reactive compounds.

Examples:

1. Superoxide radical
2. Hydroxyl radical
3. Hydrogen peroxide
4. Singlet oxygen

They cause oxidative damage to lipids, proteins and DNA.

9. Free radicals

Answer

Free radicals are molecules with unpaired electrons.

Examples:

1. Superoxide radical
2. Hydroxyl radical
3. Nitric oxide

Effects:

1. Lipid peroxidation
2. Cell injury
3. DNA damage

10. Antioxidants

Answer

Antioxidants are substances that inhibit oxidation and neutralize free radicals.

Examples:

1. Vitamin E
2. Vitamin C
3. Glutathione
4. Catalase

11. Effects of free radicals

Answer

1. Lipid peroxidation
2. Protein denaturation
3. DNA damage
4. Cell membrane injury
5. Aging
6. Cancer and atherosclerosis

12. Vitamins with antioxidant function

Answer

1. Vitamin E
2. Vitamin C
3. Beta carotene

DETOXIFICATION AND BIOTRANSFORMATION OF XENOBIOTICS

SHORT ESSAYS

1. What is meant by detoxification? Name types of Phase one reactions. Explain Phase two reactions of detoxification, giving any Four examples.

Answer

Definition

Detoxification is the biochemical conversion of toxic substances or xenobiotics into less toxic, water-soluble compounds for excretion.

Phase I reactions

1. Oxidation
2. Reduction
3. Hydrolysis

These reactions introduce or expose functional groups.

Phase II reactions (Conjugation reactions)

Involve conjugation with endogenous compounds making substances water soluble.

Types and examples

1. Glucuronide conjugation

- Conjugating agent: UDP-glucuronic acid
- Example: Bilirubin → bilirubin diglucuronide

2. Sulfate conjugation

- Conjugating agent: PAPS
- Example: Phenol sulfate formation

3. Glycine conjugation

- Example: Benzoic acid → Hippuric acid

4. Glutathione conjugation

- Example: Detoxification of electrophilic compounds

5. Acetylation

- Example: Sulfonamides

6. Methylation

- Example: Catecholamines

Significance

1. Increases water solubility
2. Facilitates excretion
3. Decreases toxicity

2. Phase I detoxification reaction

Answer

Definition

Phase I reactions are functionalization reactions introducing reactive groups into xenobiotics.

Types

1. Oxidation
2. Reduction
3. Hydrolysis

Oxidation

Most common reaction catalyzed by cytochrome P450.
Examples:

- Hydroxylation
- Dealkylation

Reduction

Occurs in anaerobic conditions.
Example:

- Nitro compounds reduced to amines.

Hydrolysis

Catalyzed by esterases and amidases.
Example:

- Hydrolysis of aspirin.

Significance

1. Increases polarity
2. Prepares compounds for Phase II reactions

3. Define Detoxification. Mention four reactions of Phase 2 detoxification.

Answer

Definition

Detoxification is conversion of toxic compounds into non-toxic water-soluble substances.

Phase II reactions

1. Glucuronide conjugation
2. Sulfate conjugation
3. Glycine conjugation
4. Glutathione conjugation
5. Acetylation
6. Methylation

4. Detoxification by conjugation

Answer

Conjugation reactions combine toxic substances with endogenous compounds.

Types

1. Glucuronidation
2. Sulfation
3. Glycine conjugation
4. Glutathione conjugation
5. Acetylation
6. Methylation

Importance

1. Increases water solubility
2. Promotes excretion
3. Reduces toxicity

SHORT ANSWERS

5. Cytochrome P450

Answer

Cytochrome P450 is a heme-containing monooxygenase enzyme system present mainly in liver microsomes.

Functions

1. Catalyzes Phase I oxidation reactions
2. Detoxification of drugs and xenobiotics
3. Steroid metabolism

Properties

1. Requires NADPH and oxygen
2. Present in smooth endoplasmic reticulum

6. Role of Glucuronic acid in Detoxification

Answer

Glucuronic acid conjugates with toxic substances making them water soluble.

Examples:

1. Bilirubin conjugation
2. Steroid hormones
3. Drugs like chloramphenicol

Conjugation product is excreted in urine or bile.

7. Detoxification by conjugation

Answer

Detoxification by conjugation is a Phase II reaction where xenobiotics combine with endogenous compounds.

Examples:

1. Benzoic acid + glycine → Hippuric acid
2. Bilirubin + glucuronic acid → Bilirubin diglucuronide

8. Conjugation phase of Detoxification

Answer

Phase II detoxification reactions involve conjugation with endogenous molecules.

Types:

1. Glucuronidation
2. Sulfation
3. Acetylation
4. Methylation
5. Glutathione conjugation

9. Give two examples for Phase II detoxification reaction.

Answer

1. Benzoic acid → Hippuric acid
2. Bilirubin → Bilirubin diglucuronide

10. Explain detoxification. Explain different phases of detoxification.

Answer

Definition

Detoxification is conversion of toxic substances into less toxic excretable compounds.

Phases

Phase I

1. Oxidation
2. Reduction
3. Hydrolysis

Phase II

1. Glucuronidation
2. Sulfation
3. Acetylation
4. Glycine conjugation

Importance

Facilitates elimination of drugs and toxins.

11. Phase-I reactions of detoxification

Answer

1. Oxidation
2. Reduction
3. Hydrolysis

These reactions are catalyzed mainly by cytochrome P450 enzyme system.

12. Mention two examples for detoxification by reduction

Answer

1. Chloramphenicol reduction
2. Nitro compounds reduced to amines

13. One example each of detoxification by oxidation and conjugation

Answer

1. Oxidation – Phenobarbital hydroxylation
2. Conjugation – Benzoic acid to hippuric acid

14. How benzoic acid and sulphonylamide are detoxified in human body

Answer

1. Benzoic acid is detoxified by conjugation with glycine forming hippuric acid.
2. Sulphonylamide is detoxified by acetylation.

GENERAL METABOLISM

HEME AND HEMOGLOBIN

LONG ESSAYS

1. A 45-year-old known alcoholic for 15 years was admitted to emergency with hematemesis in an unconscious state. On examination, he was jaundiced and with massive ascites. His serum bilirubin was 11 mg/dL.

a) What is the probable diagnosis

b) Discuss the clinical features with pathophysiology

c) What types of hyperbilirubinemia is probable in this case

d) Name the biochemical investigations to arrive at a diagnosis

Answer

a) Probable diagnosis

Decompensated liver cirrhosis with portal hypertension presenting as ruptured esophageal varices.

b) Clinical features with pathophysiology

1. Jaundice

Due to impaired conjugation and excretion of bilirubin by damaged hepatocytes.

2. Ascites

Portal hypertension and hypoalbuminemia cause fluid accumulation in peritoneal cavity.

3. Hematemesis

Portal hypertension leads to esophageal varices which rupture causing bleeding.

4. Hepatic encephalopathy

Accumulation of ammonia and toxic metabolites causes altered sensorium and unconsciousness.

5. Edema

Reduced albumin synthesis lowers plasma oncotic pressure.

6. Coagulopathy

Reduced synthesis of clotting factors causes bleeding tendency.

c) Type of hyperbilirubinemia

Mixed hyperbilirubinemia with predominance of conjugated hyperbilirubinemia.

d) Biochemical investigations

1. Serum bilirubin – total and direct
2. Liver function tests
    - AST
    - ALT
    - ALP
    - GGT
3. Serum albumin
4. Prothrombin time
5. Blood ammonia
6. Urine bile pigments and bile salts
7. Ultrasonography liver
8. Viral markers

2. Describe the formation and excretion of bilirubin. Explain the significance of serum bilirubin and urobilinogen in the diagnosis of various types of jaundice

Answer

Formation of bilirubin

1. Senescent RBCs are destroyed in reticuloendothelial system.
2. Hemoglobin splits into globin and heme.
3. Heme oxygenase converts heme to biliverdin.
4. Biliverdin reductase converts biliverdin to bilirubin.
5. Unconjugated bilirubin binds albumin and transported to liver.

Conjugation in liver

1. Bilirubin conjugated with glucuronic acid by UDP-glucuronyl transferase.
2. Forms bilirubin diglucuronide.
3. Conjugated bilirubin excreted in bile.

Fate in intestine

1. Intestinal bacteria convert bilirubin to urobilinogen.
2. Part excreted in feces as stercobilin.
3. Small amount reabsorbed and excreted in urine.

Diagnostic significance in jaundice

Feature	Hemolytic	Hepatocellular	Obstructive
Serum bilirubin	Unconjugated ↑	Mixed ↑	Conjugated ↑
Urine bilirubin	Absent	Present	Present
Urine urobilinogen	Increased	Increased	Absent
Stool color	Dark	Normal	Clay colored

3. Describe heme synthesis and its regulation in detail.

Answer

Heme synthesis

Occurs in liver and bone marrow. Partly mitochondrial and partly cytosolic.

Steps

1. Formation of δ-ALA

Glycine + Succinyl CoA → δ-ALA
Enzyme: ALA synthase
Cofactor: Pyridoxal phosphate
Rate limiting step.

2. Formation of porphobilinogen

Two molecules of δ-ALA condense.
Enzyme: ALA dehydratase.

3. Formation of hydroxymethylbilane

Four porphobilinogen molecules condense.

4. Formation of uroporphyrinogen III

5. Formation of coproporphyrinogen III

6. Formation of protoporphyrin IX

Occurs in mitochondria.

7. Formation of heme

Ferrous iron inserted by ferrochelatase.

Regulation

1. ALA synthase is rate limiting enzyme.

2. Heme inhibits ALA synthase by feedback repression.

3. Drugs like barbiturates induce ALA synthase.

4. Glucose suppresses ALA synthase.

Disorders

Defects lead to porphyrias.

SHORT ESSAYS

4. A-two-year-old was brought to the pediatrics with complaints of increased tiredness and duration of sleep for past 6 months. On examination the child was anemic with frontal bossing and dental malocclusion. His Hb electrophoresis was as follows: HbA: 93.6% and HbA2: 6.4%.

a) What is the probable diagnosis

b) What are the types, clinical features and treatment of this disorder

Answer

a) Probable diagnosis

Beta thalassemia.

b) Types

1. Thalassemia major
2. Thalassemia minor
3. Thalassemia intermedia

Clinical features

1. Severe anemia
2. Frontal bossing
3. Maxillary hypertrophy
4. Hepatosplenomegaly
5. Growth retardation
6. Skeletal deformities

Treatment

1. Repeated blood transfusion
2. Iron chelation therapy
3. Folic acid supplementation
4. Splenectomy in selected cases
5. Bone marrow transplantation

5. Discuss the biochemical alterations seen in blood and urine in different types of jaundice.

Answer

Parameter	Hemolytic jaundice	Hepatocellular jaundice	Obstructive jaundice
Serum bilirubin	Unconjugated ↑	Mixed ↑	Conjugated ↑
Urine bilirubin	Absent	Present	Present
Urine urobilinogen	Increased	Increased	Absent
Stool color	Dark	Pale	Clay colored
Serum ALP	Normal	Mild ↑	Marked ↑

Parameter	Hemolytic jaundice	Hepatocellular jaundice	Obstructive jaundice
Serum AST/ALT	Mild ↑	Marked ↑	Mild ↑

6. Mention the types of Porphyrias with their enzyme defects

Answer

Porphyria	Enzyme defect
Acute intermittent porphyria	Porphobilinogen deaminase deficiency
Congenital erythropoietic porphyria	Uroporphyrinogen III synthase deficiency
Porphyria cutanea tarda	Uroporphyrinogen decarboxylase deficiency
Hereditary coproporphyria	Coproporphyrinogen oxidase deficiency
Variegate porphyria	Protoporphyrinogen oxidase deficiency

7. Outline the pathway of heme synthesis. Mention its regulation.

Answer

Pathway

1. Glycine + succinyl CoA → δ-ALA
2. δ-ALA → Porphobilinogen
3. Porphobilinogen → Uroporphyrinogen III
4. Uroporphyrinogen III → Coproporphyrinogen III
5. Coproporphyrinogen III → Protoporphyrin IX
6. Protoporphyrin IX + Fe2+ → Heme

Regulation

1. ALA synthase is rate limiting enzyme.
2. Heme inhibits ALA synthase.
3. Drugs induce enzyme activity.

8. Describe how heme is degraded into bile pigments. Add a note on different types of Jaundice

Answer

Degradation of heme

1. Heme converted to biliverdin by heme oxygenase.
2. Biliverdin converted to bilirubin by biliverdin reductase.
3. Bilirubin transported to liver bound to albumin.
4. Conjugated with glucuronic acid.
5. Excreted into bile.
6. Converted to urobilinogen in intestine.

Types of jaundice

1. Hemolytic jaundice

Excess RBC destruction.

2. Hepatocellular jaundice

Due to liver cell damage.

3. Obstructive jaundice

Due to bile duct obstruction.

9. How is heme synthesized. Add a note on its regulation

Answer

Heme is synthesized from glycine and succinyl CoA.

Important steps

1. Formation of δ-ALA by ALA synthase
2. Formation of porphobilinogen
3. Formation of protoporphyrin IX
4. Insertion of iron by ferrochelatase

Regulation

1. ALA synthase is rate limiting.
2. Heme inhibits ALA synthase.
3. Drugs induce enzyme synthesis.

10. What is thalassemia. Discuss the clinical features, molecular basis and laboratory diagnosis of thalassemia

Answer

Definition

Thalassemia is an inherited disorder characterized by decreased synthesis of globin chains.

Molecular basis

Mutations in globin genes lead to reduced globin synthesis.

Clinical features

1. Severe anemia
2. Frontal bossing
3. Hepatosplenomegaly
4. Growth retardation
5. Bone deformities

Laboratory diagnosis

1. Peripheral smear – microcytic hypochromic anemia
2. Hb electrophoresis
3. Increased HbA2 and HbF
4. Serum ferritin
5. Genetic studies

11. Discuss the catabolism of heme.

Answer

1. Senescent RBCs destroyed in spleen.
2. Heme converted to biliverdin by heme oxygenase.
3. Biliverdin converted to bilirubin.
4. Bilirubin transported to liver bound to albumin.
5. Conjugated bilirubin excreted in bile.
6. Intestinal bacteria convert bilirubin to urobilinogen.
7. Stercobilin gives color to feces.

12. Describe the causes and laboratory finding in obstructive jaundice

Answer

Causes

1. Gall stones
2. Carcinoma head of pancreas
3. Bile duct obstruction

Laboratory findings

1. Increased conjugated bilirubin
2. Increased ALP and GGT
3. Urine bile pigments positive
4. Urobilinogen absent in urine
5. Clay colored stool

13. Define porphyria. Classify porphyria and enumerate their salient features. Add a note on acute intermittent porphyria.

Answer

Definition

Porphyrias are inherited disorders due to defects in heme biosynthesis enzymes.

Classification

1. Hepatic porphyrias
2. Erythropoietic porphyrias

Salient features

1. Photosensitivity
2. Abdominal pain
3. Neurological manifestations
4. Increased porphyrins in urine

Acute intermittent porphyria

Enzyme defect

Porphobilinogen deaminase deficiency.

Features

1. Severe abdominal pain
2. Neurological symptoms
3. Psychiatric manifestations
4. No photosensitivity

Urine

Port wine colored urine due to porphobilin.

14. Molecular basis, clinical features and diagnosis of sickle cell anaemia

Answer

Molecular basis

Point mutation in β-globin gene.
Glutamic acid replaced by valine at 6th position.
HbS formed.

Clinical features

1. Hemolytic anemia
2. Painful crises
3. Splenomegaly
4. Jaundice

Diagnosis

1. Peripheral smear – sickle cells
2. Sickling test
3. Hb electrophoresis

15. Catabolism of heme

Answer

1. Heme → Biliverdin by heme oxygenase
2. Biliverdin → Bilirubin by biliverdin reductase
3. Bilirubin conjugated in liver
4. Excreted through bile
5. Converted to stercobilin and urobilinogen

16. Porphyrias

Answer

Porphyrias are disorders of heme biosynthesis due to enzyme deficiencies.

Features

1. Photosensitivity
2. Abdominal pain
3. Neurological manifestations

Examples

1. Acute intermittent porphyria
2. Porphyria cutanea tarda

17. Explain the degradation of heme

Answer

1. RBC destruction in RES
2. Heme converted to biliverdin
3. Biliverdin converted to bilirubin
4. Bilirubin conjugated in liver
5. Excreted in bile
6. Formation of stercobilin and urobilinogen

18. Outline the degradation of heme. Add a note on fate of conjugated bilirubin in intestine

Answer

Heme degradation

1. Heme → Biliverdin
2. Biliverdin → Bilirubin
3. Bilirubin conjugated in liver

Fate of conjugated bilirubin

1. Converted to urobilinogen by intestinal bacteria
2. Part reabsorbed – enterohepatic circulation
3. Oxidized to stercobilin in feces
4. Small amount excreted as urobilin in urine

19. Porphyrias presenting with photo sensitivity

Answer

1. Congenital erythropoietic porphyria
2. Porphyria cutanea tarda
3. Variegate porphyria

Features:

1. Photosensitivity
2. Skin blistering
3. Increased porphyrins

SHORT ANSWERS

20. Methemoglobinemias.

Answer

Methemoglobinemia is presence of excess methemoglobin in blood.

Causes

1. Nitrite poisoning
2. Congenital NADH methemoglobin reductase deficiency

Features

1. Cyanosis
2. Chocolate brown blood

21. Biochemistry basis of- Hyperbaric oxygen therapy in CO poisoning

Answer

Carbon monoxide binds hemoglobin with very high affinity forming carboxyhemoglobin.

Hyperbaric oxygen increases dissolved oxygen and displaces carbon monoxide from hemoglobin, restoring oxygen transport.

22. Give reason- “Iron overload in Thalassemia”

Answer

Repeated blood transfusions and increased intestinal iron absorption cause iron overload in thalassemia.

23. Give biochemical basis of : a) “ Anaemia in lead poisoning”

b) “ Sickling of RBC in Sickle cell Anaemia"

Answer

a) Anaemia in lead poisoning

Lead inhibits ALA dehydratase and ferrochelatase enzymes causing defective heme synthesis.

b) Sickling of RBC in sickle cell anemia

HbS polymerizes at low oxygen tension causing sickling of RBCs.

24. Regulation of heme synthesis

Answer

1. ALA synthase is rate limiting enzyme.
2. Heme inhibits ALA synthase.
3. Drugs induce enzyme synthesis.
4. Glucose suppresses ALA synthase.

25. Detoxification of bilirubin

Answer

Bilirubin is conjugated with glucuronic acid in liver by UDP-glucuronyl transferase forming water-soluble bilirubin diglucuronide.

26. Vandenberg test

Answer

Van den Bergh reaction is used for estimation of bilirubin.

Principle

Bilirubin reacts with diazotized sulfanilic acid forming purple azobilirubin.

Types

1. Direct reaction – conjugated bilirubin
2. Indirect reaction – unconjugated bilirubin

27. Acute intermittent porphyria

Answer

Enzyme defect

Porphobilinogen deaminase deficiency.

Features

1. Abdominal pain
2. Neurological symptoms
3. Psychiatric disturbances
4. Port wine colored urine

28. Molecular basis and diagnosis of sickle cell anemia

Answer

Molecular basis

Mutation in β-globin gene causes substitution of valine for glutamic acid.

Diagnosis

1. Sickling test
2. Hb electrophoresis
3. Peripheral smear

29. List two clinical conditions of abnormal haemoglobin

Answer

1. Sickle cell anemia
2. Methemoglobinemia

30. Biochemical basis of thalassemia

Answer

Defective synthesis of globin chains due to mutations in globin genes causing imbalance in globin chain production and hemolysis.

31. Significance of 2,3-BPG

Answer

2,3-Bisphosphoglycerate decreases affinity of hemoglobin for oxygen and facilitates oxygen release to tissues.

32. Chloride shift

Answer

Exchange of bicarbonate and chloride ions across RBC membrane is called chloride shift.

It helps transport carbon dioxide from tissues to lungs.

33. Vanden Berg reaction

Answer

Reaction between bilirubin and diazotized sulfanilic acid forming azobilirubin.

Used for estimation of bilirubin.

34. Unconjugated hyperbilirubinemias

Answer

Conditions with elevated unconjugated bilirubin.

Examples:

1. Hemolytic jaundice
2. Crigler-Najjar syndrome
3. Gilbert syndrome

35. Abnormal haemoglobins

Answer

Abnormal hemoglobins are structurally abnormal hemoglobin molecules due to genetic mutations.

Examples:

1. HbS
2. HbC
3. HbM

36. Obstructive jaundice

Answer

Obstructive jaundice occurs due to blockage of bile flow.

Features

1. Increased conjugated bilirubin
2. Clay colored stools
3. Dark urine
4. Increased ALP

37. Blood and urinary findings in various types of jaundice

Answer

Type	Serum bilirubin	Urine bilirubin	Urobilinogen
Hemolytic	Unconjugated ↑	Absent	Increased
Hepatic	Mixed ↑	Present	Increased
Obstructive	Conjugated ↑	Present	Absent

38. Congenital erythropoietic porphyrias

Answer

Enzyme defect

Uroporphyrinogen III synthase deficiency.

Features

1. Photosensitivity
2. Red colored urine
3. Hemolytic anemia

39. Define thalassemia and mention the different types of thalassemia

Answer

Definition

Thalassemia is inherited disorder with decreased synthesis of globin chains.

Types

1. Alpha thalassemia
2. Beta thalassemia
3. Thalassemia major
4. Thalassemia minor

40. Causes and clinical features of acute intermittent porphyria

Answer

Cause

Deficiency of porphobilinogen deaminase.

Clinical features

1. Severe abdominal pain
2. Neurological manifestations
3. Psychiatric symptoms
4. Port wine colored urine

ADVANCED BIOCHEMISTRY

MECHANISM OF ACTION OF HORMONES & IMMUNOCHEMISTRY

LONG ESSAYS

1. A 53-year-old woman came to OPD with history of weight gain, constipation, weakness and cold intolerance. On examination she had neck swelling. The following thyroid function tests were done, with the reports as given below:

TSH-54.6 mU/L (0.20-5.0), Free T4 (fT4)-5.7 pmol/L (12-25 pmol/L)

a) Write the probable diagnosis

b) Explain the laboratory assessment of the endocrine gland in detail

c) Give a brief account of the disorders related to the gland

a) Probable Diagnosis

Primary hypothyroidism.

b) Laboratory Assessment of Thyroid Gland

Thyroid Hormones Measured

1. Total T3
2. Total T4
3. Free T3
4. Free T4
5. Thyroid stimulating hormone (TSH)

Thyroid Function Tests

Serum TSH

- Most sensitive test.
- Increased in primary hypothyroidism.
- Decreased in hyperthyroidism.

Free T4

- Decreased in hypothyroidism.
- Increased in hyperthyroidism.

Free T3

- Useful in hyperthyroidism.

Thyroid Autoantibodies

- Anti thyroid peroxidase antibody
- Anti thyroglobulin antibody
- Increased in autoimmune thyroid disease.

Radioactive Iodine Uptake Test

- Increased in Graves disease.
- Decreased in thyroiditis.

Ultrasound

- Detects nodules and enlargement.

Fine Needle Aspiration Cytology

- Useful for thyroid nodules.

c) Disorders Related to Thyroid Gland

Hypothyroidism

- Causes: Iodine deficiency, Hashimoto thyroiditis.
- Features: Weight gain, cold intolerance, constipation.

Hyperthyroidism

- Graves disease common cause.
- Features: Weight loss, heat intolerance, tachycardia.

Goiter

- Enlargement of thyroid gland.

Cretinism

- Congenital hypothyroidism in children.

Myxedema

- Severe adult hypothyroidism.

2. Structure, type and functions of immunoglobulin

Structure of Immunoglobulin

- Y shaped glycoprotein.
- Composed of:
  - Two heavy chains
  - Two light chains
- Chains connected by disulfide bonds.

Regions

- Variable region binds antigen.
- Constant region determines class.

Fragments

- Fab fragment binds antigen.
- Fc fragment mediates biological functions.

Types of Immunoglobulins

1. IgG
2. IgA
3. IgM
4. IgD
5. IgE

Functions

IgG

- Most abundant.

- Crosses placenta.
- Opsonization.

IgA

- Secretory antibody.
- Present in saliva, tears and milk.

IgM

- First antibody produced.
- Strong complement activator.

IgD

- Antigen receptor on B cells.

IgE

- Allergy and anaphylaxis.
- Protection against parasites.

SHORT ESSAYS

3. Name different types of Immunoglobulins. Write their functions.

Types and Functions

IgG

- Most abundant immunoglobulin.
- Crosses placenta.
- Neutralization and opsonization.

IgA

- Secretory antibody.
- Protects mucosal surfaces.

IgM

- First antibody in primary response.
- Activates complement.

IgD

- B cell receptor.

IgE

- Mediates allergic reactions.
- Anti parasitic role.

4. A 23-year-old man attended endocrinology department with complaints of loss of weight in spite of good appetite and intolerance to heat. His eyes appearing bigger in the past few weeks. His physician suggested thyroid profile.

a) What is the probable diagnosis

b) What biochemical changes are expected in this thyroid profile in primary and secondary conditions

a) Probable Diagnosis

Graves disease (Hyperthyroidism).

b) Biochemical Changes

Primary Hyperthyroidism

- Increased T3 and T4
- Decreased TSH

Secondary Hyperthyroidism

- Increased T3 and T4
- Increased TSH

Primary Hypothyroidism

- Decreased T3 and T4
- Increased TSH

Secondary Hypothyroidism

- Decreased T3 and T4
- Decreased TSH

5. Explain the different types of immunoglobulins Add a brief note on Multiple myeloma

Multiple Myeloma

- Malignant proliferation of plasma cells.
- Monoclonal immunoglobulin produced.

Laboratory Findings

- M protein spike in serum electrophoresis.
- Bence Jones proteins in urine.
- Increased ESR.

Clinical Features

- Bone pain
- Anemia
- Renal failure

6. Thyroid function tests and their significance

Thyroid Function Tests

1. TSH
2. Total and free T3
3. Total and free T4
4. Thyroid antibodies
5. Radioiodine uptake test

Significance

- Diagnose hypo and hyperthyroidism.
- Monitor treatment.
- Detect autoimmune thyroid disease.

7. Differentiate between active and passive immunity

Feature	Active immunity	Passive immunity
Source	Produced by body	Ready made antibodies
Onset	Slow	Immediate
Duration	Long lasting	Short lasting
Memory	Present	Absent
Example	Vaccination	Antisera

8. Enumerate the immunoglobulin and classify their functions. Describe the structure of immunoglobulins.

Immunoglobulins

- IgG
- IgA
- IgM
- IgD
- IgE

Structure

- Two heavy chains and two light chains.
- Variable and constant regions.
- Fab and Fc fragments.

Functions

- Neutralization
- Complement activation
- Opsonization
- Allergy mediation
- Mucosal protection

9. Discuss the structure and functions of antibodies. Add a note on monoclonal antibodies

Structure

- Y shaped glycoprotein.
- Two heavy and two light chains.
- Fab binds antigen.
- Fc mediates biological actions.

Functions

- Neutralization
- Agglutination
- Complement activation
- Opsonization

Monoclonal Antibodies

- Produced by hybridoma technology.
- Specific against single epitope.

Uses

- Cancer therapy
- Diagnosis
- Autoimmune diseases

10. Primary and secondary immune response

Primary Immune Response

- Occurs after first exposure.
- Lag period present.
- IgM predominates.
- Lower antibody titer.

Secondary Immune Response

- Occurs after second exposure.
- Rapid response.
- IgG predominates.
- Higher antibody titer due to memory cells.

11. Describe the structure and functions of Immunoglobulins

Structure

- Two heavy and two light chains.
- Variable region for antigen binding.
- Constant region determines class.

Functions

- Neutralization
- Complement fixation
- Opsonization
- Allergy mediation

12. What are different types and functions of immunoglobulins

Types

- IgG
- IgA
- IgM
- IgD
- IgE

Functions

- Humoral immunity
- Complement activation
- Placental transfer
- Mucosal protection
- Allergy mediation

SHORT ANSWERS

13. Role of ADH in water balance.

- ADH increases water reabsorption in collecting ducts.
- Acts through aquaporin channels.
- Concentrates urine.
- Maintains plasma osmolality.

14. Bence Jones proteins.

- Free monoclonal light chains in urine.
- Seen in multiple myeloma.
- Precipitate at 40–60°C and dissolve on boiling.

15. Enumerate different immunoglobulins. Describe the structure of immunoglobulin

Immunoglobulins

- IgG
- IgA
- IgM
- IgD
- IgE

Structure

- Two heavy chains and two light chains.
- Fab and Fc portions.
- Disulfide bonds connect chains.

16. Immunoglobulin E and its significance

- Mediates type I hypersensitivity.
- Binds mast cells and basophils.
- Increased in allergic disorders and parasitic infections.

17. Ig G

- Most abundant immunoglobulin.
- Crosses placenta.
- Opsonization and neutralization.
- Activates complement.

18. Passive immunity

- Transfer of preformed antibodies.
- Immediate protection.
- Short duration.
- Example: Maternal antibodies.

19. Role of cytokines in immunity

- Mediate communication between immune cells.
- Regulate inflammation.
- Stimulate growth and differentiation of immune cells.
- Examples: Interleukins and interferons.

20. Functions of immunoglobulin

- Neutralization
- Opsonization
- Complement activation
- Agglutination
- Allergy mediation

21. Structure of immunoglobulin

- Y shaped glycoprotein.
- Two heavy and two light chains.
- Variable and constant regions.
- Fab and Fc fragments.

22. Two clinical conditions of hypergammaglobulinaemia

1. Multiple myeloma
2. Chronic infections

23. Explain the structure of IgG molecule and indicate its functions

Structure

- Monomeric immunoglobulin.
- Two gamma heavy chains and two light chains.
- Has Fab and Fc regions.

Functions

- Placental transfer
- Opsonization
- Complement activation
- Neutralization

BIOCHEMISTRY OF CANCER

SHORT ESSAYS

1. Protooncogenes are normal cellular genes which are activated to oncogenes. Explain the mechanisms by which

protooncogenes are converted to oncogenes with relevant examples.

Protooncogenes

Normal genes regulating cell growth and differentiation.

Mechanisms of Activation

1. Point Mutation

- Produces abnormal protein.
- Example: RAS gene.

2. Gene Amplification

- Multiple copies of gene formed.
- Example: HER2/neu in breast cancer.

3. Chromosomal Translocation

- Gene moved near active promoter.
- Example: c-myc in Burkitt lymphoma.

4. Insertional Mutagenesis

- Viral insertion activates oncogene.

Effects

- Uncontrolled cell proliferation.
- Malignant transformation.

2. What are Oncogenes. Name four tumour markers with their clinical relevance

Oncogenes

Mutated or overexpressed genes causing malignant transformation.

Tumour Markers

Tumour Marker	Clinical Relevance
AFP	Hepatocellular carcinoma
PSA	Prostate carcinoma
CEA	Colon carcinoma
CA-125	Ovarian carcinoma

SHORT ANSWERS

3. Oncogenes

Genes promoting cancer development.

Examples

- RAS
- MYC
- HER2

4. What are tumour markers. Give examples.

Tumour markers are substances produced by tumors and used in diagnosis or monitoring.

Examples

- AFP
- PSA
- CEA
- CA-125

5. Name the tumor markers for (a) prostate carcinoma (b) Colon cancer (c) carcinoid syndrome (d) hepatoma

a) Prostate carcinoma – PSA b) Colon cancer – CEA c) Carcinoid syndrome – 5-HIAA d) Hepatoma – AFP

6. Biological effect of radiation on tissues

- DNA damage
- Cell death
- Mutation

- Carcinogenesis
- Bone marrow suppression

7. Explain the Biochemical basis of: Folate antagonists are used as anti cancer drugs

- Folate required for nucleotide synthesis.
- Folate antagonists inhibit DNA synthesis.
- Rapidly dividing cancer cells affected.
- Example: Methotrexate.

8. Tumour markers

Substances elevated in cancers.

Uses

- Diagnosis
- Monitoring therapy
- Detect recurrence

Examples

- AFP
- PSA
- CEA

9. Role of oxidative stress in pathogenesis of cancer

- Free radicals cause DNA damage.
- Mutation of oncogenes and tumor suppressor genes.
- Promotes carcinogenesis.

10. Name two tumour markers with Clinical condition associated

1. AFP – Hepatocellular carcinoma
2. PSA – Prostate carcinoma

11. Alpha fetoprotein

- Fetal plasma protein.
- Elevated in hepatocellular carcinoma and yolk sac tumor.
- Used as tumor marker.

12. Clinical applications of tumor markers

- Diagnosis of cancer
- Monitoring treatment
- Detect recurrence
- Assess prognosis

13. Hormones as tumor markers

- Calcitonin – Medullary thyroid carcinoma
- hCG – Choriocarcinoma
- Catecholamines – Pheochromocytoma

14. One mechanism of activation of proto-oncogenes to oncogenes

Point mutation causing abnormal protein formation. Example: RAS gene mutation.

15. Name four tumour markers and its significance

Marker	Significance
AFP	Hepatoma
PSA	Prostate cancer
CEA	Colon cancer
CA-125	Ovarian cancer

16. Name any two tumour markers and conditions in which they are elevated

1. AFP – Hepatocellular carcinoma
2. CEA – Colon carcinoma

17. Cell cycle

Phases

1. G1 phase
2. S phase
3. G2 phase
4. M phase

- DNA synthesis occurs in S phase.
- Cell division occurs in M phase.

18. Define tumour markers and mention four examples

Tumor markers are biochemical substances elevated in malignancy.

Examples

- AFP
- PSA
- CEA
- CA-125

EXTRACELLULAR MATRIX & TISSUE PROTEINS IN HEALTH & DISEASES

SHORT ESSAYS

1. Explain how collagen structure is modified after it is synthesized. Add a note on any ONE clinical condition that affects post translational modifications of collagen.

Post Translational Modifications of Collagen

1. Hydroxylation

- Proline and lysine hydroxylated.
- Requires vitamin C.

2. Glycosylation

- Hydroxylysine residues glycosylated.

3. Triple Helix Formation

- Three chains form procollagen.

4. Secretion

- Procollagen secreted outside cell.

5. Cleavage

- Propeptides removed forming tropocollagen.

6. Cross Linking

- Lysyl oxidase forms covalent cross links.
- Requires copper.

Clinical Condition – Scurvy

Cause

- Vitamin C deficiency.

Biochemical Defect

- Defective hydroxylation of proline and lysine.

Features

- Bleeding gums
- Poor wound healing
- Fragile blood vessels

2. Explain the salient features of structural organization of collagen. Mention the major disorders associated with collagen structure and function

Structural Organization

- Triple helical protein.
- Glycine every third residue.
- Rich in proline and hydroxyproline.
- Forms fibrils and fibers.

Types

- Type I – Bone
- Type II – Cartilage
- Type III – Blood vessels
- Type IV – Basement membrane

Disorders

- Scurvy
- Ehlers Danlos syndrome
- Osteogenesis imperfecta
- Alport syndrome

SHORT ANSWERS

3. Collagen

Most abundant protein in body.

Features

- Triple helical structure.
- Rich in glycine and hydroxyproline.

Functions

- Tensile strength.
- Structural support.

4. Structure and two functions of Collagen

Structure

- Triple helix.
- Three polypeptide chains.

Functions

1. Provides tensile strength.
2. Structural support to connective tissue.

5. Elastin

- Elastic connective tissue protein.
- Rich in glycine and alanine.
- Provides elasticity to tissues.
- Present in lungs and blood vessels.

CLINICAL LABORATORY PRACTICE: LABORATORY INSTRUMENTATION, TECHNIQUES AND QUALITY CONTROL

SHORT ESSAYS

1. Principles and applications of ELISA

ELISA

Enzyme linked immunosorbent assay used for antigen or antibody detection.

Principle

- Antigen antibody reaction detected using enzyme labeled antibody.
- Color change produced by substrate.
- Color intensity proportional to amount of antigen or antibody.

Types

1. Direct ELISA
2. Indirect ELISA
3. Sandwich ELISA
4. Competitive ELISA

Applications

- HIV diagnosis
- Hepatitis diagnosis
- Hormone assays
- Tumor markers

2. Principle and applications of Beer-Lamberts law. Add a note on colorimetry

Beer Lambert Law

Absorbance is directly proportional to concentration and path length.

$A = \varepsilon cl$

Applications

- Estimation of glucose
- Urea estimation
- Hemoglobin estimation

Colorimetry

Principle

- Colored solution absorbs light of complementary wavelength.

Components

- Light source
- Filter
- Cuvette
- Detector

Uses

- Biochemical estimations in laboratory.

3. Principles and applications of electrophoresis

Principle

Charged particles migrate in electric field.

Factors Affecting Migration

- Charge
- Size
- pH

Types

- Paper electrophoresis
- Agarose gel electrophoresis
- Polyacrylamide gel electrophoresis

Applications

- Serum protein separation
- Hemoglobin electrophoresis
- DNA analysis

SHORT ANSWERS

4. Name Four variables leading to pre-analytical errors in clinical laboratory.

1. Improper sample collection
2. Hemolysis of sample
3. Delay in transport
4. Improper storage temperature

5. Application of ELISA test

Answer

ELISA (Enzyme Linked Immunosorbent Assay) is an immunological test used for detection of antigens or antibodies.

Applications of ELISA test

1. Diagnosis of infectious diseases:
    - Human Immunodeficiency Virus infection
    - Hepatitis B infection
    - Dengue infection
2. Detection of hormones:
    - Human Chorionic Gonadotropin in pregnancy
    - Insulin
    - Thyroid hormones
3. Detection of tumor markers:
    - Alpha fetoprotein

    - Prostate specific antigen
4. Detection of allergens and antibodies in autoimmune diseases.
5. Screening of blood donors for transmissible infections.
6. Detection of drugs and toxins in biological samples.

Advantages

- Highly sensitive and specific
- Rapid and economical
- Can test large number of samples simultaneously

6. Micro arrays

Answer

Microarray is a molecular biology technique in which thousands of DNA probes are fixed on a solid surface to study gene expression simultaneously.

Principle

Complementary DNA from the sample hybridizes with specific DNA probes present on the microarray chip.

Types

1. DNA microarray
2. Protein microarray
3. Tissue microarray

Applications

1. Analysis of gene expression
2. Detection of genetic mutations
3. Diagnosis of cancers
4. Pharmacogenomics
5. Detection of infectious agents
6. Research in molecular biology

Advantages

- Rapid analysis of thousands of genes
- Useful in personalized medicine

7. What is the role of buffers in regulating blood pH

Answer

Buffers are substances that resist sudden changes in pH by accepting or donating hydrogen ions.

Role of buffers in regulation of blood pH

Normal blood pH is maintained between 7.35 and 7.45.

Important buffer systems

1. Bicarbonate buffer system
    - Most important extracellular buffer
    - Consists of carbonic acid and sodium bicarbonate
2. Phosphate buffer system
    - Important intracellular and renal tubular buffer
3. Protein buffer system
    - Plasma proteins and hemoglobin act as buffers
4. Hemoglobin buffer system
    - Hemoglobin binds hydrogen ions formed during carbon dioxide transport

Importance

- Prevents acidosis and alkalosis
- Maintains enzyme activity and normal metabolism
- Essential for proper cellular function

8. Chromatography

Answer

Chromatography is a technique used for separation of substances based on differential distribution between stationary phase and mobile phase.

Principle

Different substances move at different rates depending on their adsorption, partition or affinity to stationary and mobile phases.

Types

1. Paper chromatography
2. Thin layer chromatography
3. Column chromatography
4. Gas chromatography
5. Ion exchange chromatography
6. Affinity chromatography
7. High performance liquid chromatography

Applications

1. Separation of amino acids and sugars
2. Detection of drugs and toxins
3. Hormone analysis
4. Purification of proteins and enzymes
5. Diagnosis of metabolic disorders

Advantages

- Sensitive and accurate
- Requires small sample volume

9. Radioimmunoassay

Answer

Radioimmunoassay is a highly sensitive technique used for estimation of substances by using radiolabeled antigen and specific antibodies.

Principle

Labeled antigen competes with unlabeled antigen in the sample for binding sites on a specific antibody.
The radioactivity measured is inversely proportional to concentration of substance in the sample.

Steps

1. Mixing of antigen with antibody
2. Addition of radiolabeled antigen
3. Separation of bound and free antigen
4. Measurement of radioactivity

Applications

1. Hormone estimation
2. Detection of drugs
3. Viral antigen detection
4. Tumor marker estimation

Advantages

- Highly sensitive and specific
- Detects very small quantities

Disadvantages

- Radiation hazard
- Expensive procedure

10. Principles of electrophoresis

Answer

Electrophoresis is a technique used for separation of charged particles under the influence of an electric field.

Principle

Charged particles migrate towards opposite electrode depending on their charge, size and shape.

- Positively charged particles move towards cathode.
- Negatively charged particles move towards anode.

Factors affecting electrophoresis

1. Net charge of molecule
2. Molecular size and shape
3. Strength of electric field
4. pH of buffer
5. Nature of supporting medium

Types

1. Paper electrophoresis
2. Agarose gel electrophoresis
3. Polyacrylamide gel electrophoresis
4. Capillary electrophoresis

Applications

1. Separation of serum proteins
2. Hemoglobin analysis
3. Deoxyribonucleic Acid analysis
4. Diagnosis of multiple myeloma and hemoglobinopathies

11. Principles of ELISA and two clinical applications in clinical diagnosis

Answer

ELISA (Enzyme Linked Immunosorbent Assay) is an immunological technique used for detection of antigen or antibody.

Principle of ELISA

- Antigen or antibody is adsorbed on a solid surface.
- Specific enzyme linked antibody binds with antigen-antibody complex.
- Addition of substrate produces color reaction.
- Intensity of color is proportional to amount of antigen or antibody present.

Types

1. Direct ELISA
2. Indirect ELISA
3. Sandwich ELISA
4. Competitive ELISA

Two clinical applications in diagnosis

1. Diagnosis of Human Immunodeficiency Virus infection.
2. Detection of Hepatitis B surface antigen.

Advantages

- Highly sensitive and specific
- Rapid and suitable for mass screening

12. Principle of chromatography

Answer

Chromatography is a method used for separation of substances based on differential distribution between stationary phase and mobile phase.

Principle

Different substances distribute differently between stationary phase and mobile phase. Hence each component moves at different speed leading to separation.

Components

1. Stationary phase
2. Mobile phase

Mechanisms

1. Adsorption
2. Partition
3. Ion exchange
4. Affinity

Applications

1. Separation of amino acids
2. Drug analysis
3. Hormone estimation
4. Protein purification

13. Principle of colorimetry

Answer

Colorimetry is a technique used for estimation of concentration of colored substances.

Principle

It is based on Beer-Lambert law.

$$A = \varepsilon cl$$

Absorbance is directly proportional to concentration of colored solution and path length.

Components of colorimeter

1. Light source
2. Filter
3. Cuvette
4. Photocell
5. Galvanometer

Applications

1. Estimation of blood glucose
2. Urea estimation
3. Cholesterol estimation
4. Hemoglobin estimation

Advantages

- Simple and economical
- Accurate quantitative analysis

14. Principles of radioimmunoassay

Answer

Radioimmunoassay is a sensitive immunological technique using radiolabeled antigen and antibody reaction.

Principle

Radiolabeled antigen and unlabeled antigen compete for limited antibody binding sites. The amount of radioactivity of bound fraction is inversely proportional to concentration of antigen in sample.

Requirements

1. Specific antibody
2. Radiolabeled antigen
3. Standard antigen
4. Gamma counter

Applications

1. Hormone estimation
2. Drug monitoring
3. Viral antigen detection
4. Tumor marker estimation

Advantages

- Very high sensitivity
- Specific and accurate

Disadvantages

- Radiation exposure
- Expensive equipment required

15. ELISA

Answer

ELISA (Enzyme Linked Immunosorbent Assay) is a sensitive immunological test for detecting antigen or antibody.

Principle

Specific antigen-antibody reaction is detected by enzyme linked antibody producing color change after substrate addition.

Types

1. Direct ELISA
2. Indirect ELISA
3. Sandwich ELISA
4. Competitive ELISA

Applications

1. Diagnosis of Human Immunodeficiency Virus infection
2. Detection of Hepatitis B surface antigen
3. Hormone assays
4. Detection of tumor markers

Advantages

- Highly sensitive
- Rapid and economical
- Suitable for screening large number of samples

APPLICATION OF ISOTOPES IN MEDICINE

SHORT ANSWERS

1. Applications of Radioactive Isotopes

Answer

Radioactive isotopes are widely used in diagnosis, treatment and research.

Applications

1. Diagnostic uses
    - Thyroid scan using Iodine-131
    - Bone scan using Technetium-99m
    - Positron emission tomography scan
2. Therapeutic uses
    - Iodine-131 for hyperthyroidism and thyroid cancer
    - Cobalt-60 in radiotherapy for cancer
3. Laboratory uses
    - Radioimmunoassay
    - Metabolic studies using tracer techniques
4. Sterilization
    - Sterilization of medical equipment using gamma radiation

2. Name four applications of radioactivity in diagnosis and management of diseases.

Answer

1. Thyroid scan and treatment using Iodine-131.
2. Cancer radiotherapy using Cobalt-60.
3. Bone scan using Technetium-99m.
4. Radioimmunoassay for hormone estimation.

3. Applications of radioisotopes in medicine

Answer

Diagnostic applications

1. Thyroid imaging
2. Renal scan

3. Bone scan
4. Positron emission tomography scan

Therapeutic applications

1. Treatment of hyperthyroidism
2. Cancer radiotherapy

Laboratory applications

1. Radioimmunoassay
2. Tracer studies in metabolism

Sterilization

Gamma radiation is used for sterilization of surgical instruments.

GENERAL QUESTIONS

SHORT ANSWERS

1. What is the role of a physician in the health care system.

Answer

A physician plays an important role in promotion, prevention and restoration of health.

Roles of a physician

1. Diagnose and treat diseases.
2. Provide preventive health care and immunization.
3. Educate patients regarding healthy lifestyle.
4. Participate in national health programs.
5. Maintain ethical and professional standards.
6. Communicate effectively with patients and health care team.
7. Promote community health and rehabilitation.

2. Lifelong learning is essential for a physician.

Answer

Lifelong learning refers to continuous acquisition of knowledge and skills throughout professional life.

Importance for a physician

1. Medical knowledge changes rapidly.
2. Helps in updating diagnostic and therapeutic skills.
3. Improves patient care and safety.
4. Promotes evidence based practice.
5. Helps maintain professional competence.
6. Encourages research and innovation.
7. Essential for ethical medical practice.

3. How is lifelong learning relevant to the professional growth of doctors

Answer

Lifelong learning is essential for continuous professional development of doctors.

Relevance to professional growth

1. Updates knowledge regarding recent advances in medicine.
2. Improves clinical and communication skills.
3. Enhances diagnostic accuracy and treatment outcome.
4. Promotes evidence based medical practice.
5. Helps in adapting to newer technologies.
6. Encourages participation in research and academic activities.

7. Improves confidence, professionalism and ethical standards.

4. Doctors should have a commitment for lifelong learning which is important for their professional growth – substantiate the statement.

Answer

Lifelong learning is the continuous process of acquiring medical knowledge, clinical skills and professional values throughout a doctor's career.

Need for lifelong learning

1. Rapid advancement in medical science.
2. Introduction of new diagnostic methods and therapies.
3. Changing disease patterns and emerging infections.
4. Need for evidence based practice.

Importance for professional growth

1. Maintains professional competence.
2. Improves quality of patient care.
3. Enhances clinical decision making.
4. Promotes ethical and responsible practice.
5. Develops communication and leadership skills.
6. Encourages research and innovation.
7. Helps doctors adapt to modern technology.

Methods of lifelong learning

1. Continuing medical education programs.
2. Workshops and conferences.
3. Reading journals and textbooks.
4. Online learning and research activities.