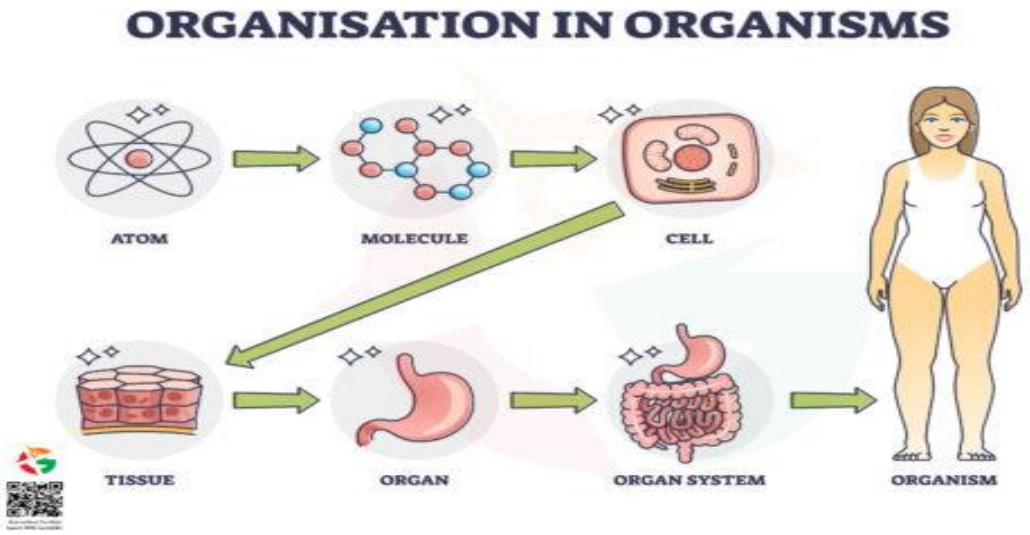
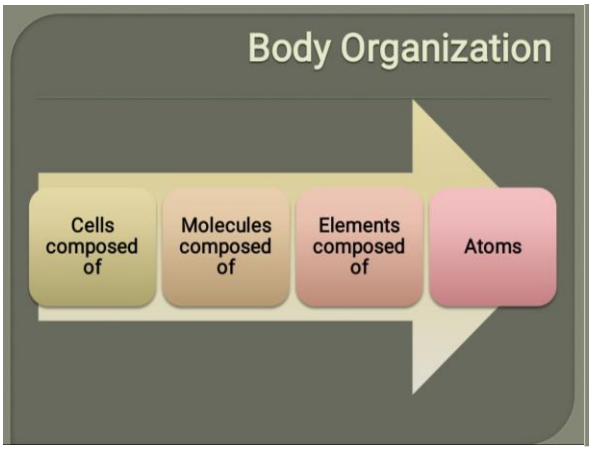
MEDICAL BIOCHEMISTRY STUDY GUIDE

1st Year MBBS - Module II

SECTION I: CELL BIOCHEMISTRY





1. Basic Elements of Biochemistry & The Human Genome Project

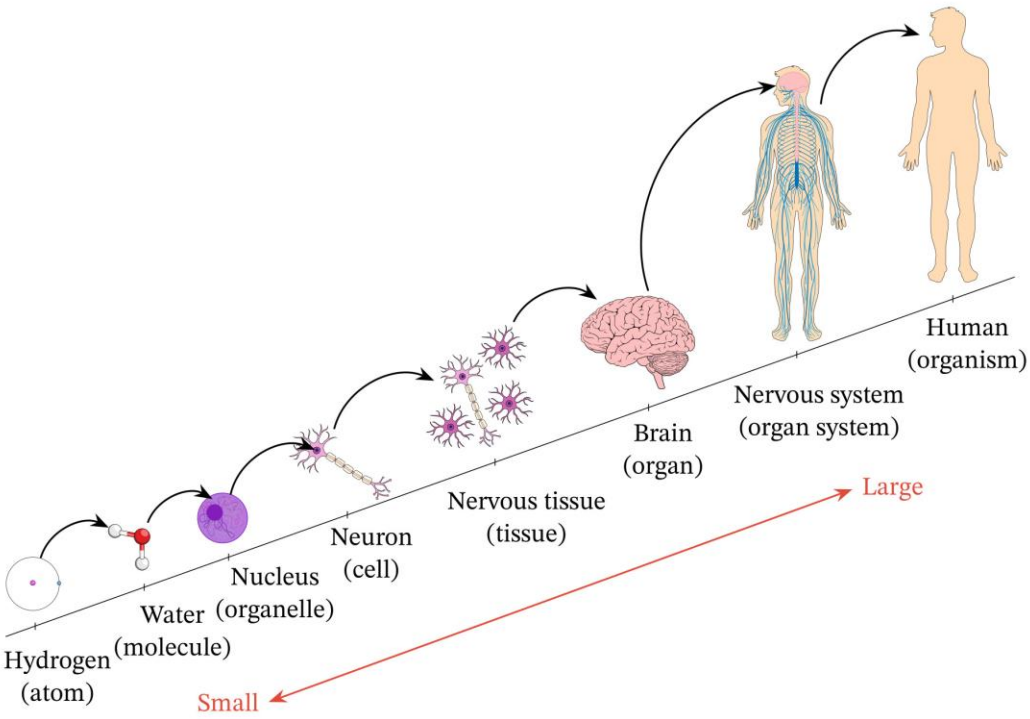
Key Concepts

Chemical Building Blocks:

The human body and all living organisms is primarily built from a few key elements:

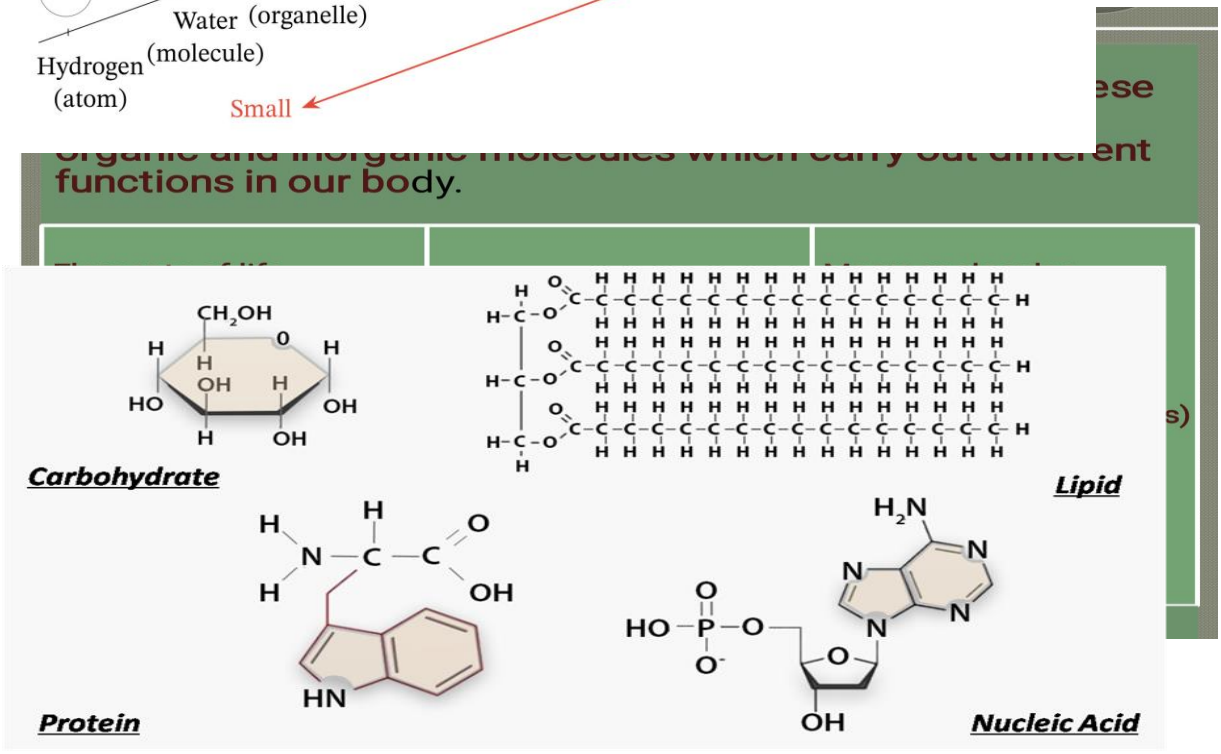
- **Carbon (C)**: Forms the backbone of organic molecules due to its ability to form stable covalent bonds with many elements, including itself.
- **Hydrogen (H)**: Present in almost all organic compounds; contributes to the formation of water and energy-rich molecules.
- **Oxygen (O)**: Critical for respiration, water formation, and many oxidation-reduction reactions.
- **Nitrogen (N)**: Essential for the construction of amino acids (the building blocks of proteins) and nucleic acids (DNA and RNA).
  Additional Elements:
- **Phosphorus (P)**: Integral to nucleotides (which form DNA and RNA) and energy molecules like ATP.
- **Sulfur (S)**: Found in some amino acids (e.g., cysteine and methionine) and contributes to protein structure through disulfide bonds.

Mnemonic: “CHON for Life” → Carbon, Hydrogen, Oxygen, Nitrogen

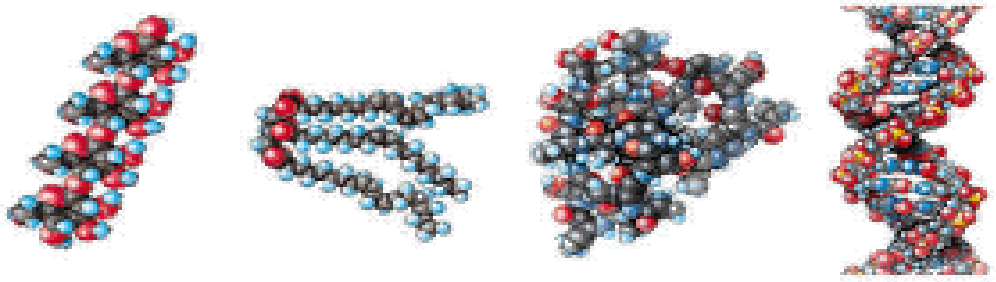


OR

Use “SPONCH” to remember the key elements:



Biological Macromolecules



Carbohydrate (starch) | Lipid (triacylglycerol) | Protein (enzyme) | Nucleic acid (DNA)

Carbon, Hydrogen, Oxygen, Nitrogen, Phosphorus, and Sulfur.

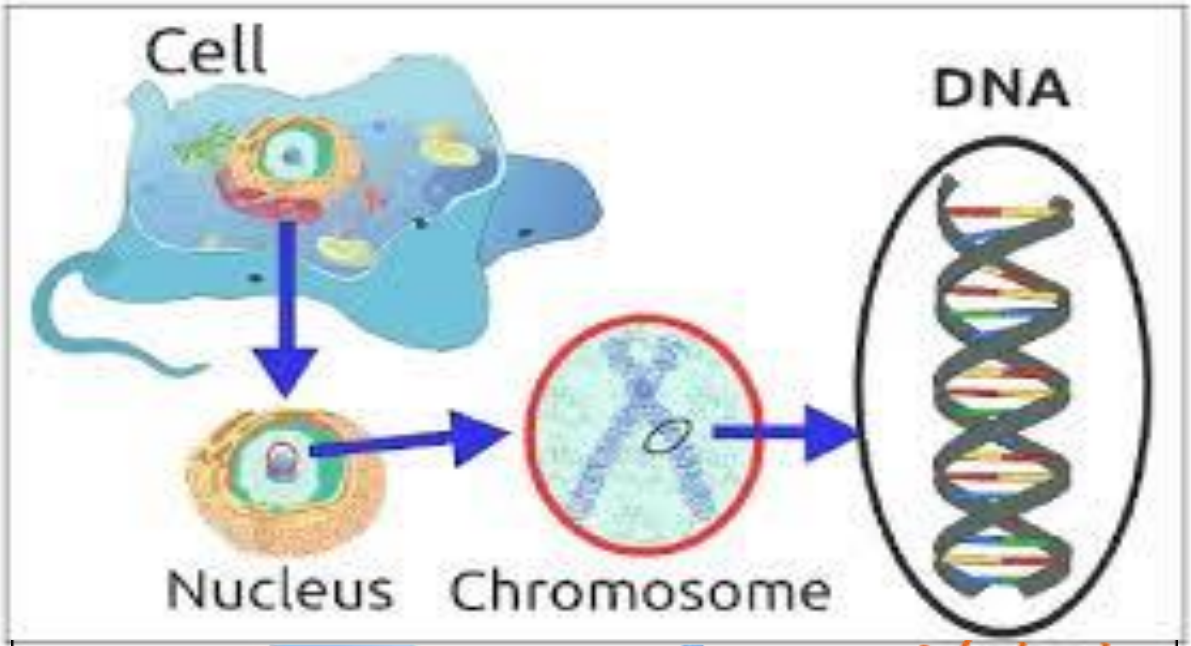
Formation of Biomolecules:

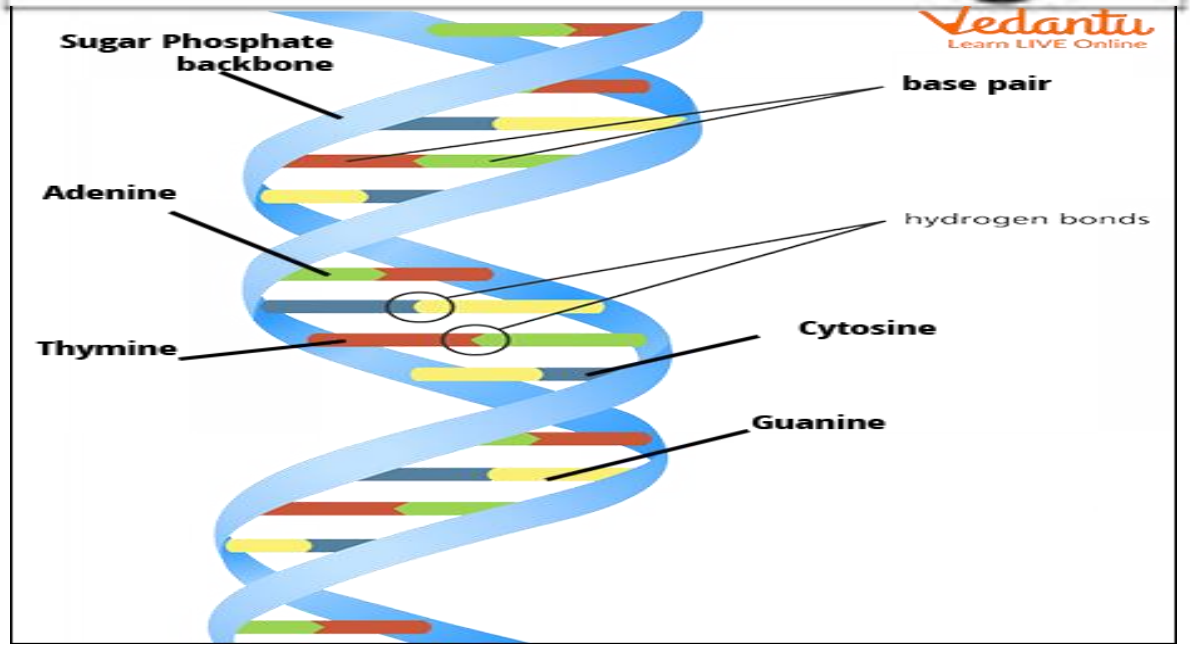
These elements combine to form the four major classes of biomolecules:

- **Carbohydrates**: Provide energy and structural support (e.g., glucose, starch, cellulose).
- **Proteins:** Serve as enzymes, structural components, and signaling molecules (e.g., hemoglobin, antibodies).
- **Lipids:** Function in energy storage, cell membrane structure, and signaling (e.g., triglycerides, phospholipids, steroids).
- **Nucleic Acids:** Carry genetic information and guide protein synthesis (e.g., DNA, RNA).

What is the Human Genome Project?

An international research effort (completed in 2003) that mapped and sequenced the entire human genome—approximately 3 billion base pairs of DNA.





Significance in Biochemistry and Medicine:

- **Understanding Genetic Blueprint:** The project provided a comprehensive map of all human genes, offering insights into how genetic variations contribute to health and disease.
- **Advancements in Gene Therapy & Personalized Medicine:** With the full sequence available, researchers can now pinpoint mutations that cause genetic disorders, paving the way for targeted therapies and individualized treatment plans.
- **Drug Development:** Knowledge of gene sequences allows for the development of drugs that can specifically target malfunctioning proteins or pathways.
- **Evolutionary Insights:** The HGP has enabled comparisons between the human genome and those of other organisms, enhancing our understanding of evolutionary biology and human ancestry.
- **Biochemical Research:** A complete genome sequence aids in studying the regulation of gene expression and the biochemical pathways that sustain life.

Mnemonic: Think of "Genome Map": The HGP provided a detailed map of our genome, just like having a complete road map for a vast and complex city.

? Self-Assessment

Fill in the Blanks:

1. The four most abundant elements in organic molecules are ___, ___, ___, and ___.
   (Answer: Carbon, Hydrogen, Oxygen, Nitrogen)
2. In addition to CHON, two other elements vital to biomolecules are ___ and ___.
   (Answer: Phosphorus and Sulfur)
3. The Human Genome Project aimed to sequence approximately ___ billion base pairs of human DNA. (Answer: 3)
4. One major impact of the HGP is its role in advancing ___ medicine, which tailors treatment to individual genetic profiles.
   (Answer: personalized)

Multiple Choice Question:

1). Which of the following is NOT one of the primary elements that form the backbone of biomolecules?

A) Carbon

B) Hydrogen

C) Oxygen

D) Iron

(Correct Answer: D) Iron – While iron is an important trace element, it is not one of the primary elements in organic molecules.)

2).What was one of the primary achievements of the Human Genome Project?

A) Discovering the structure of the cell membrane

B) Mapping and sequencing the entire human genome

C) Determining the metabolic rate of human cells

D) Classifying all biomolecules in the human body

(Correct Answer: B) Mapping and sequencing the entire human genome

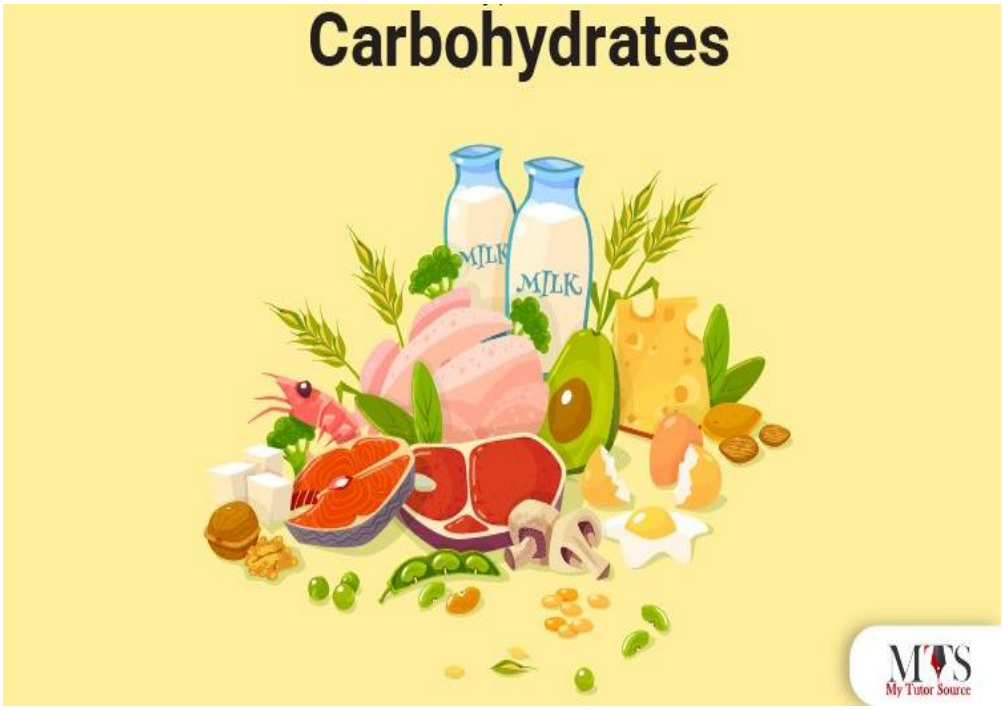
□ Fun Fact:

- □ Humans share 98.8% of their DNA with chimpanzees!
- Did you know? Humans share nearly 99% of their DNA with each other—yet even small differences can lead to significant variations in traits and disease susceptibilities!

Additional Tips & Tricks:

- Visual Learning: Create a chart or infographic that displays the periodic table highlighting CHON-PS. Also, include a simplified diagram of DNA's double helix and annotate it with the number of base pairs.
- Study Trick: Use flashcards for each element and its role in biomolecules. Similarly, create flashcards summarizing key milestones and outcomes of the Human Genome Project.

2.



Biomolecules & Their Role in Cellular Function

Key Concepts

✓Carbohydrates: Energy source → Glucose, Fructose, Glycogen

✓Proteins: Structural & functional molecules → Enzymes, Hemoglobin, Insulin

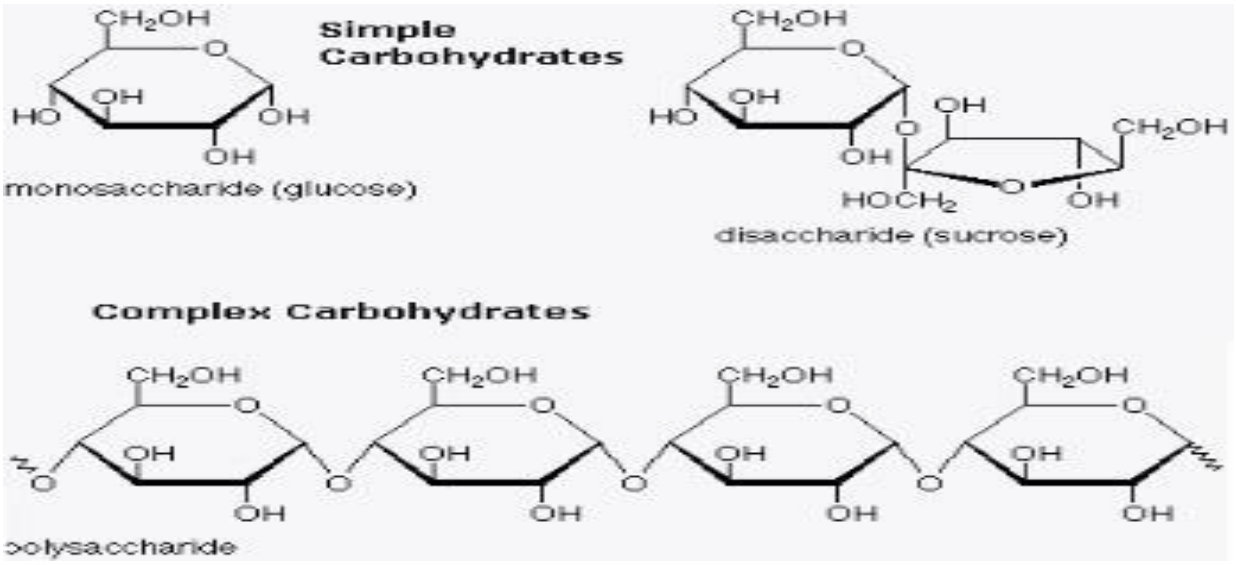
✓**Lipids: Cell membrane, energy storage → Cholesterol, Triglycerides, Phospholipids**

✓**Nucleic Acids: Genetic information → DNA, RNA**

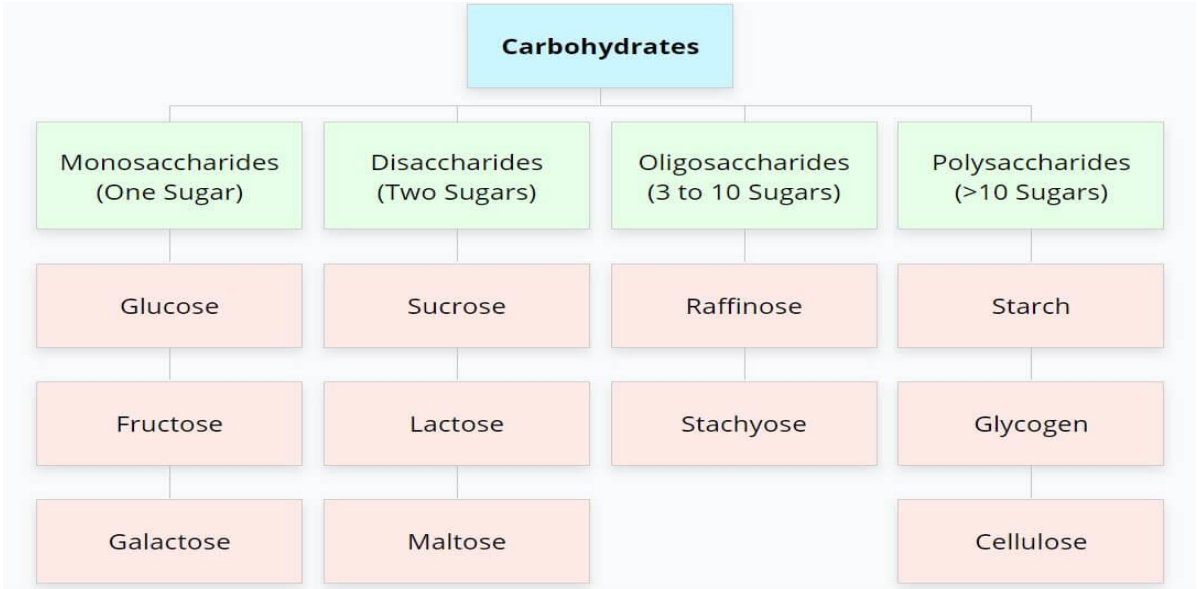
Cells are composed of four major classes of biomolecules. Each class has distinct structures and functions that contribute to the overall operation and maintenance of the cell.

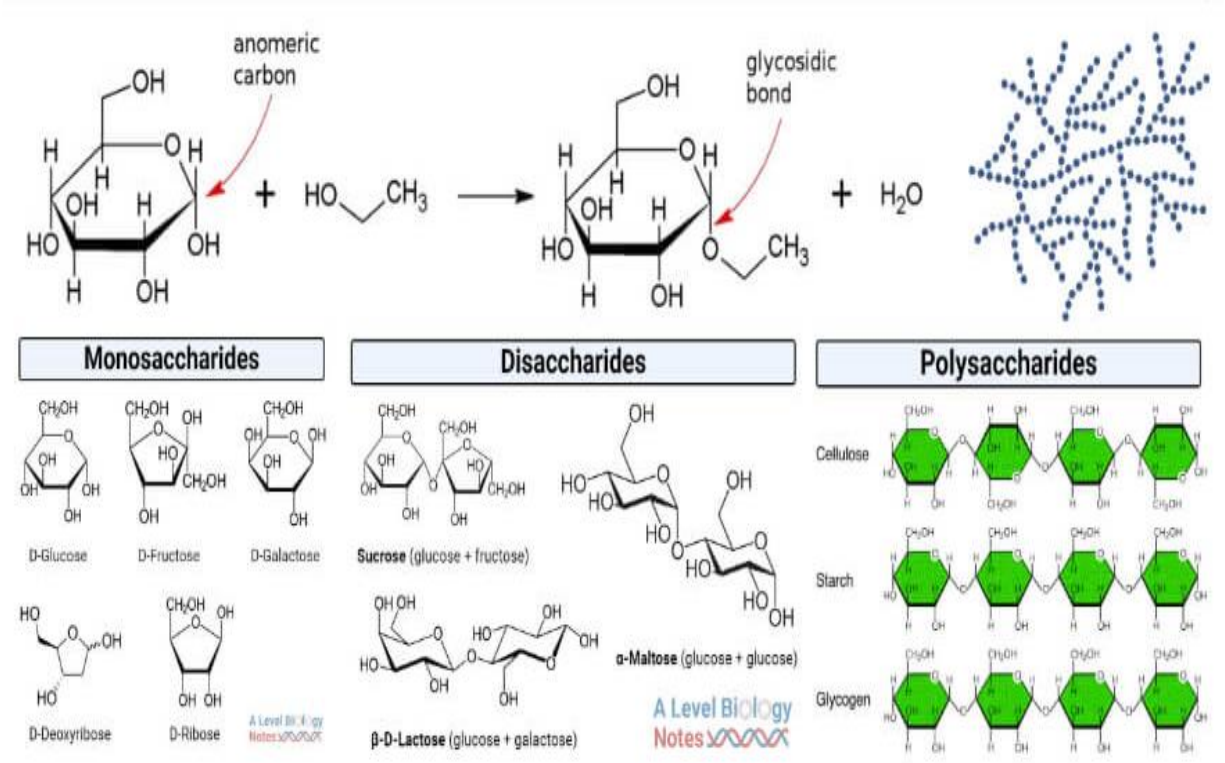
1. Carbohydrates

Structure:



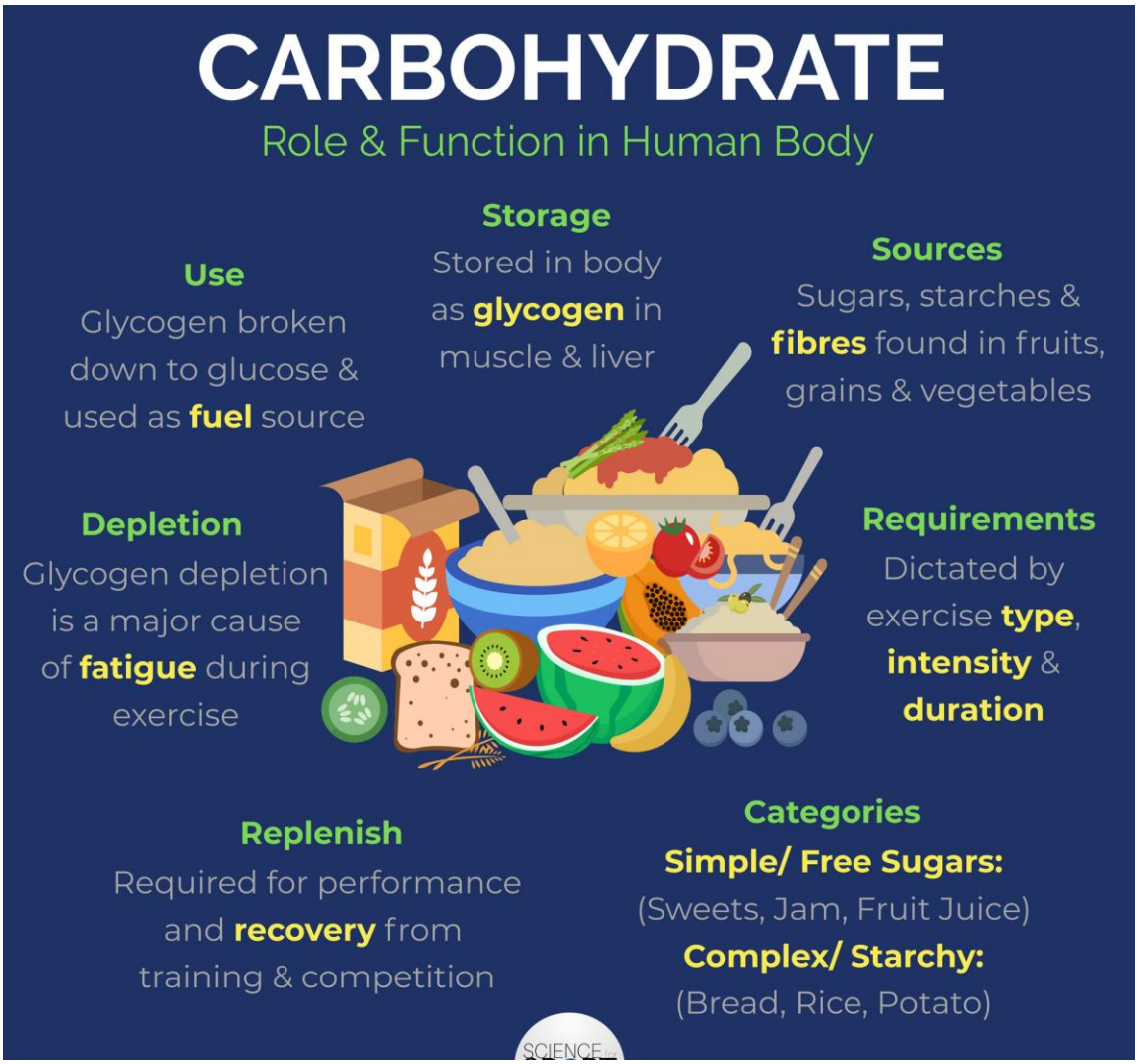
- **Monosaccharides**: Single sugar units such as glucose and fructose.
- **Disaccharides:** Two monosaccharides linked together (e.g., sucrose, lactose).
- **Polysaccharides:** Long chains of sugar units, including storage forms (glycogen in animals, starch in plants) and structural components (cellulose in plant cell walls, chitin in fungal cell walls).





Roles in Cellular Function:

- **Energy Source**: Glucose is the primary fuel for cellular respiration.
- **Energy Storage**: Glycogen stores energy in animal cells, while starch serves as energy storage in plants.
- **Structural Support**: Cellulose provides rigidity to plant cell walls, and chitin strengthens fungal cell walls.
- **Cell Recognition & Signaling:** Glycoproteins and glycolipids (carbohydrates attached to proteins or lipids) on the cell surface help in cell-to-cell recognition and communication.

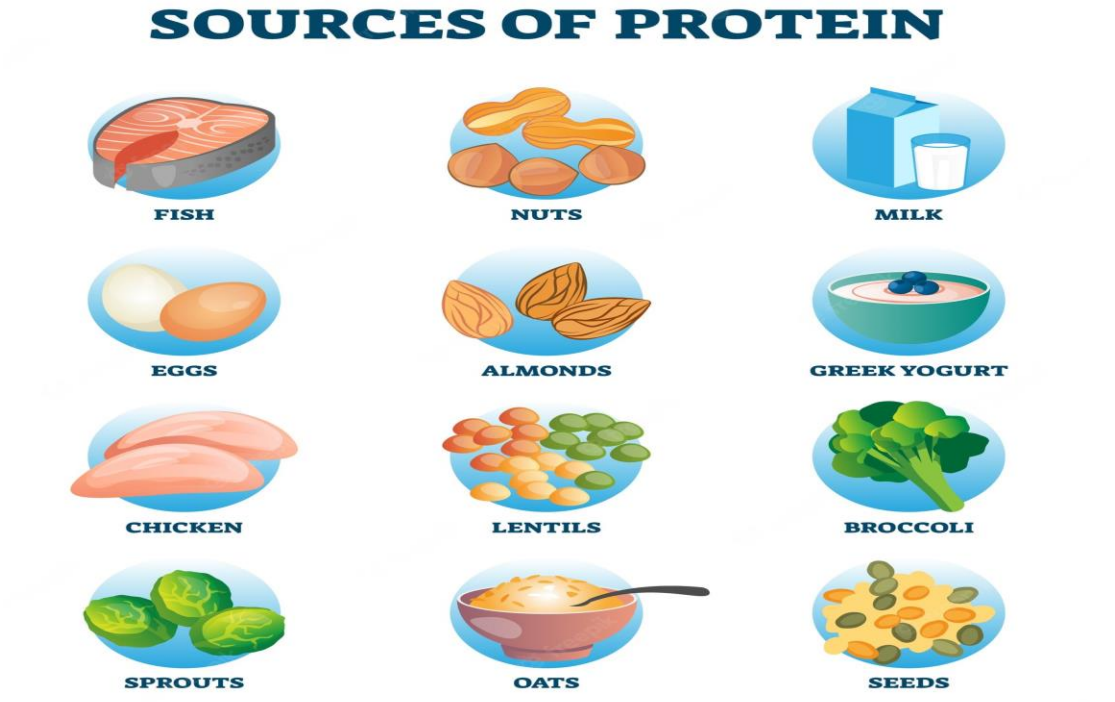


Mnemonic:

"M-D-P: Monosaccharides, Disaccharides, Polysaccharides" – Helps you recall the three types of carbohydrates.

2. Proteins


Protein


SOURCES OF PROTEIN
FISH
NUTS
MILK
EGGS
ALMONDS
GREEK YOGURT
CHICKEN
LENTILS
BROCCOLI
SPROUTS
OATS
SEEDS

Structure:

- **Amino Acids**: Proteins are polymers of 20 different amino acids.

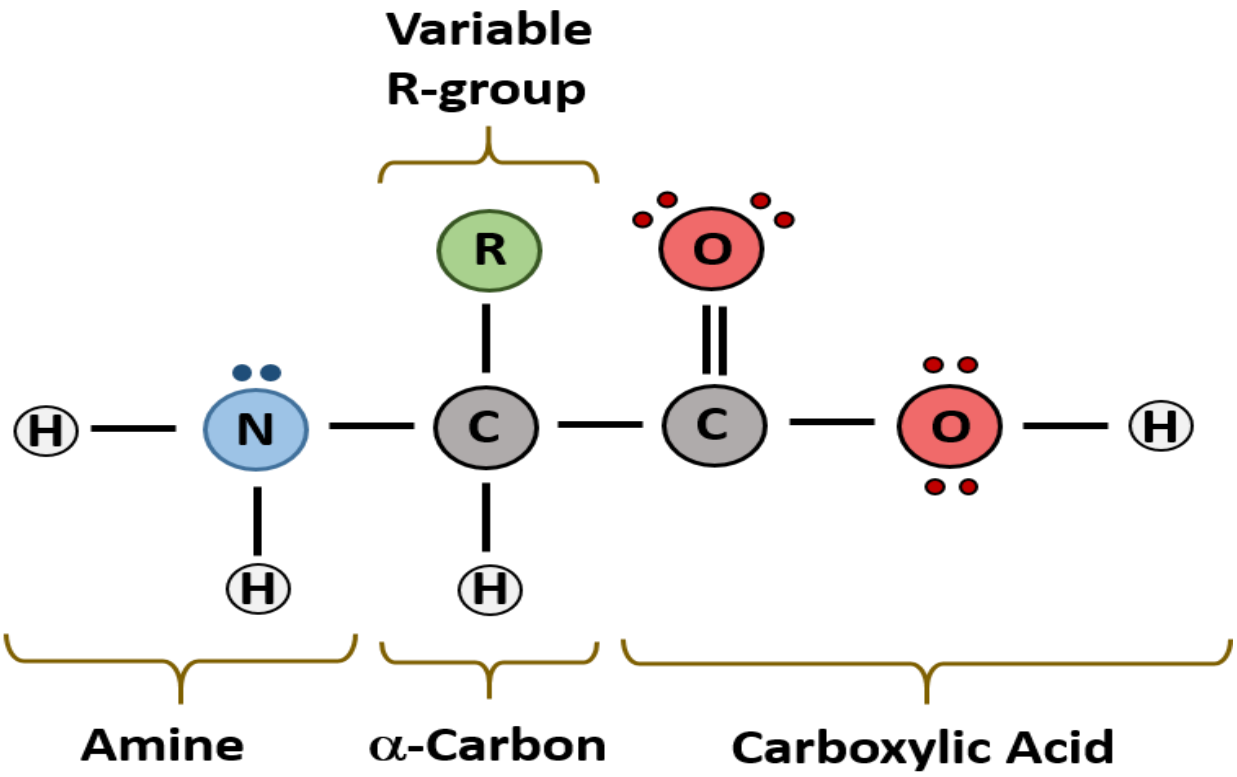
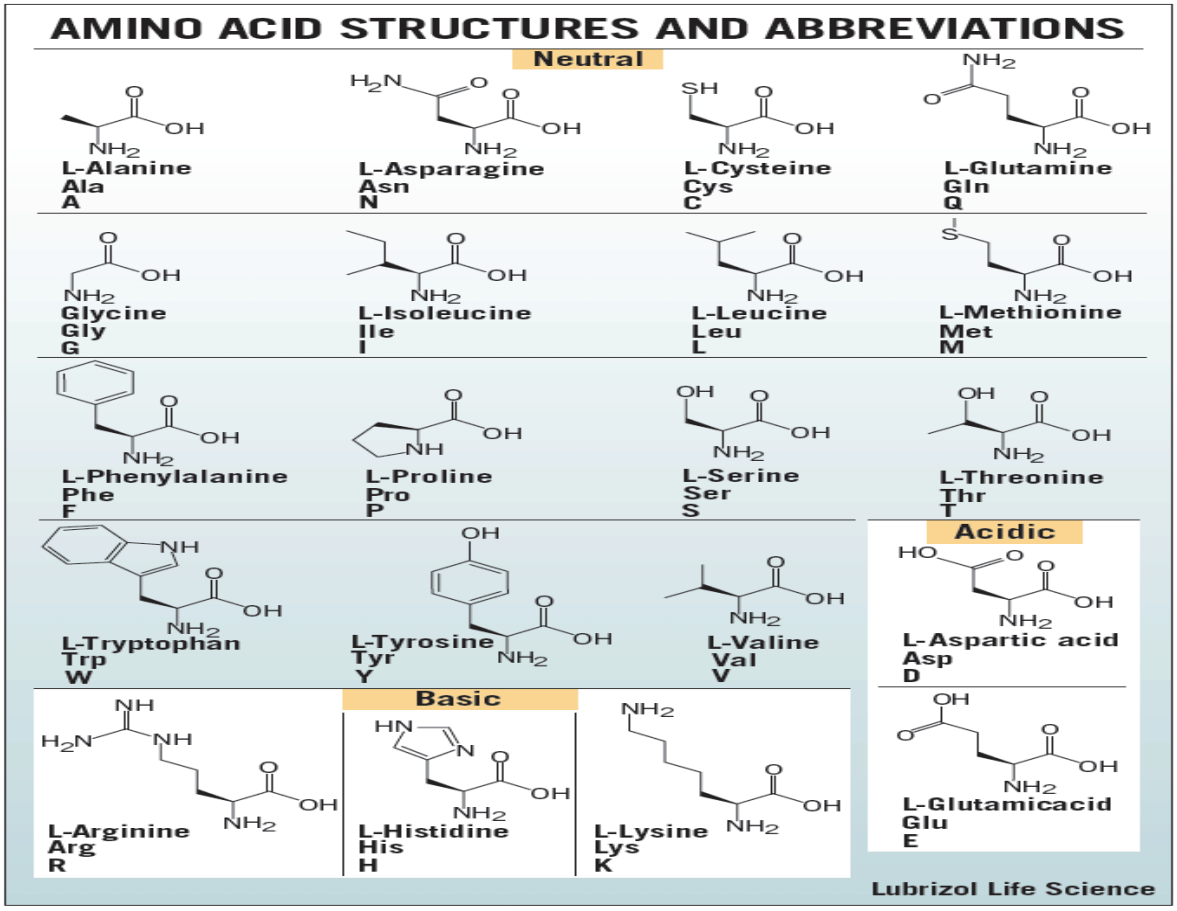


Figure 1

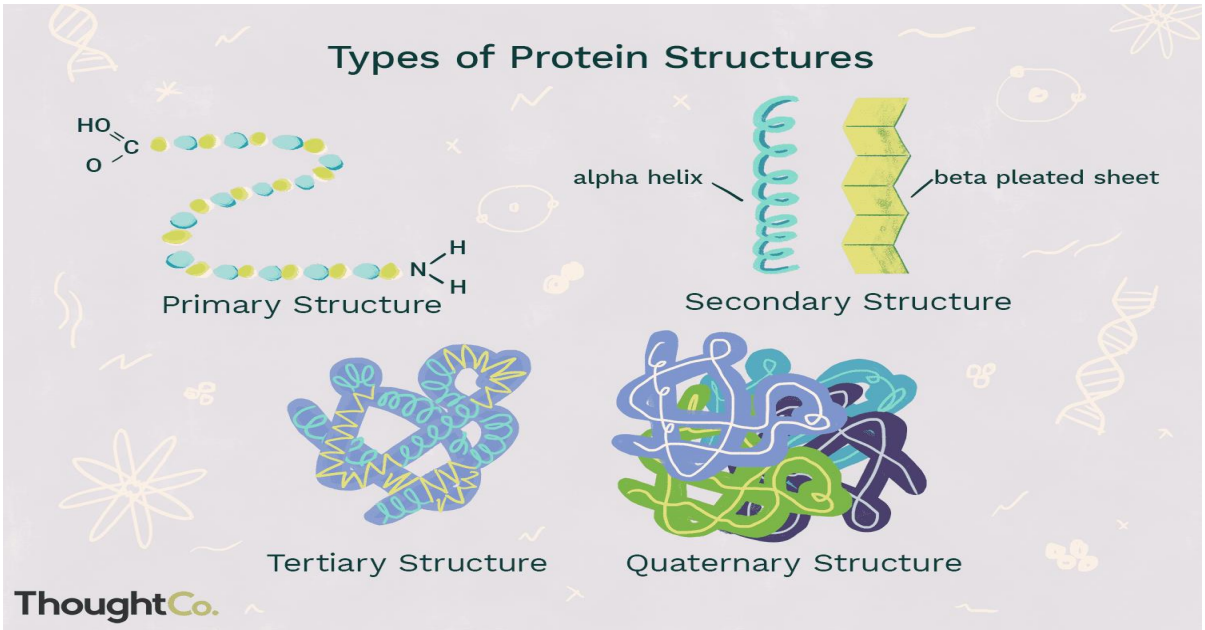


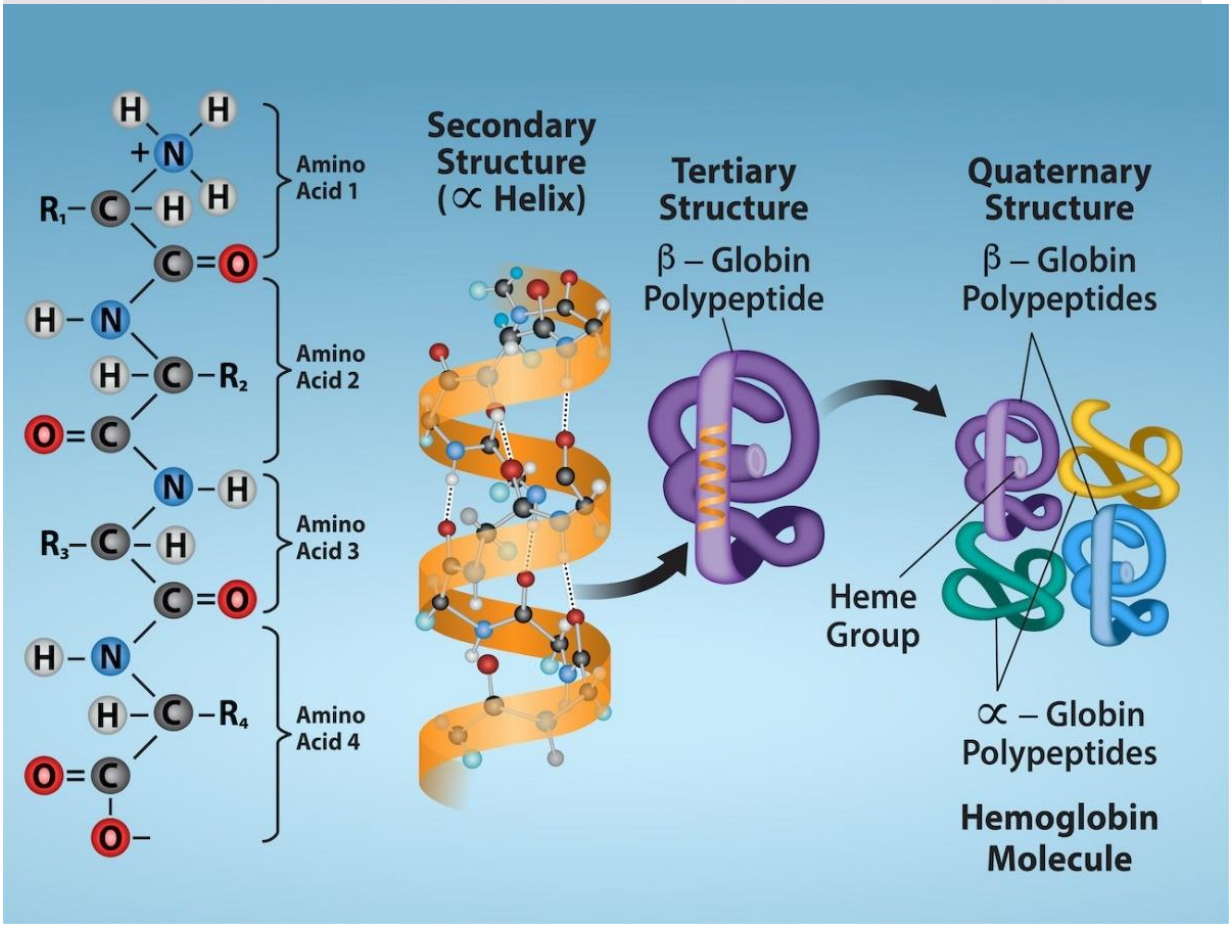
Levels of Structure:

- Primary: Amino acid sequence.
- Secondary: Alpha helices and beta sheets formed by hydrogen bonding.
- Tertiary: Overall three-dimensional folding driven by hydrophobic interactions, disulfide bridges, and ionic bonds.
- Quaternary: Association of multiple polypeptide chains.

Mnemonic:

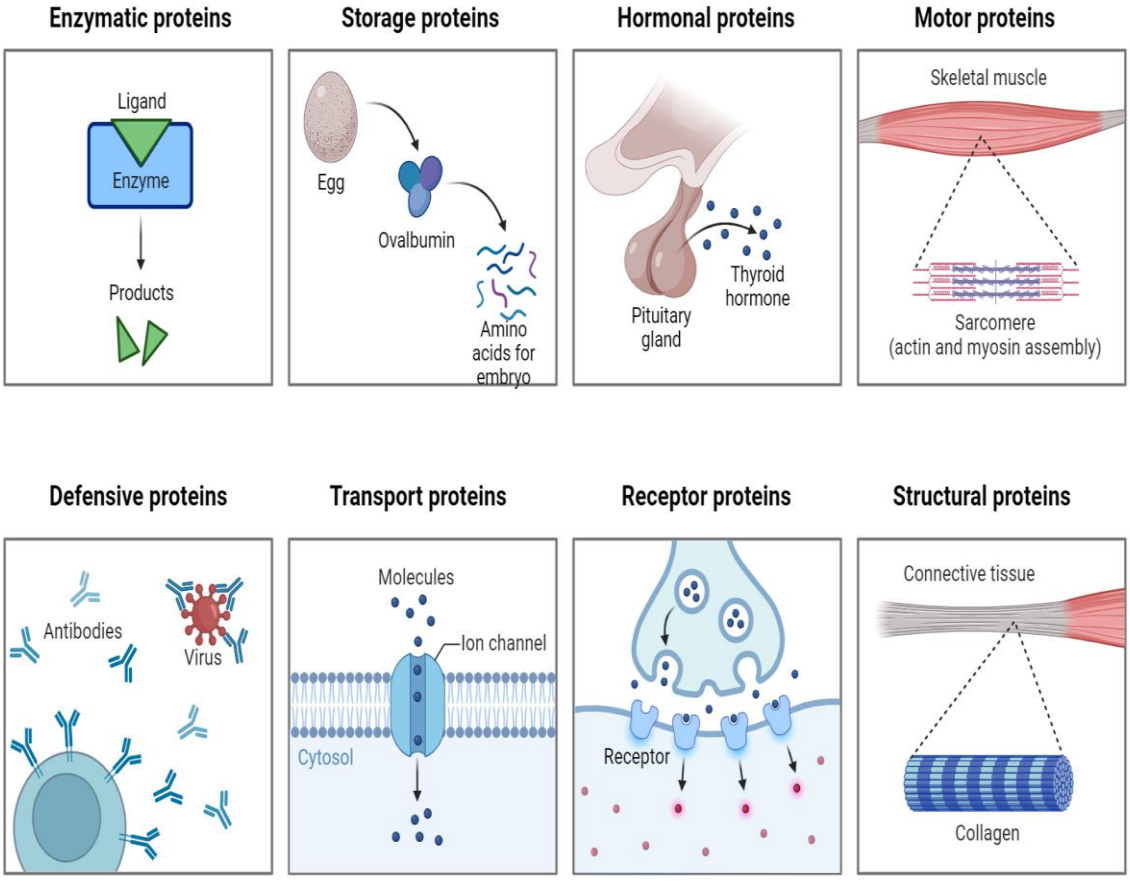
"P-STQ": Primary, Secondary, Tertiary, Quaternary – A quick way to remember the hierarchy of protein structure.

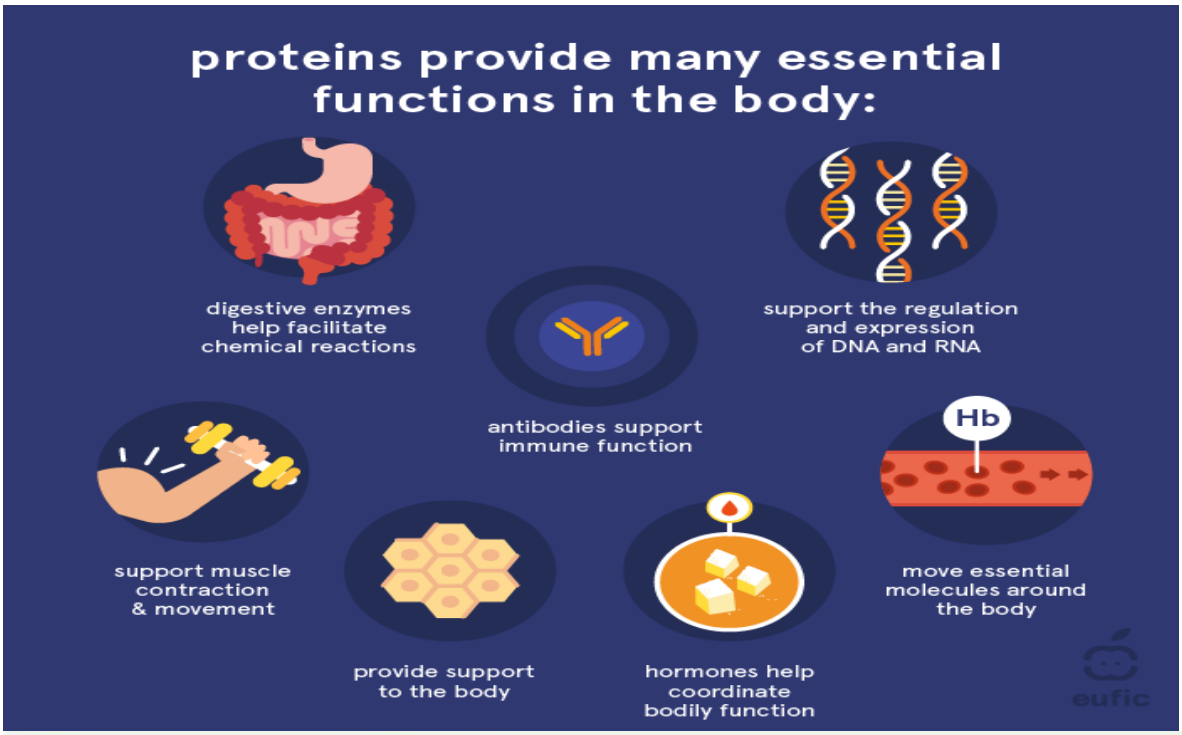




Roles in Cellular Function:

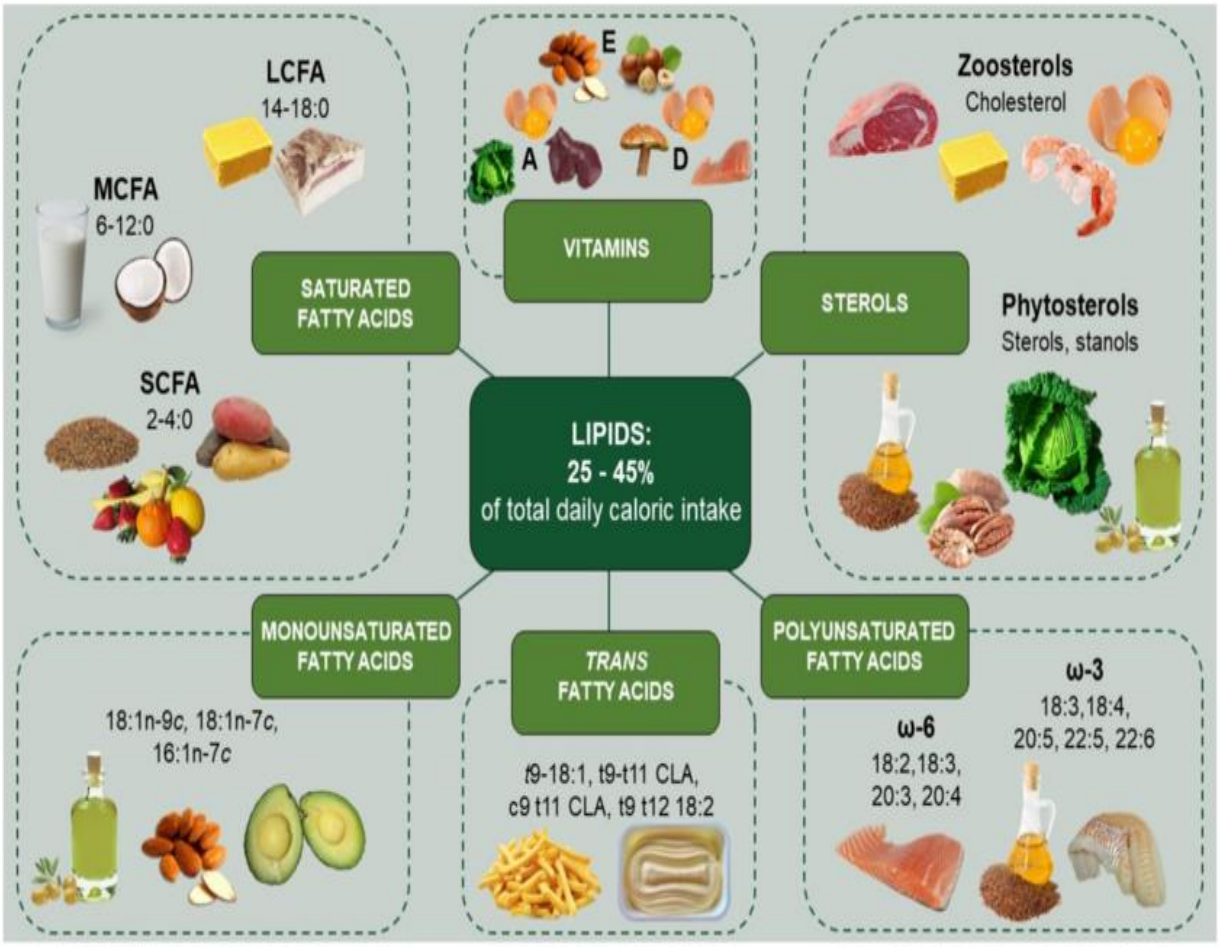
- Catalysts (Enzymes): Speed up biochemical reactions (e.g., DNA polymerase, lactase).
- Structural Components: Provide support and shape (e.g., actin, tubulin, collagen).
- Transport: Carry molecules (e.g., hemoglobin transports oxygen).
- Signaling: Function as receptors and hormones (e.g., insulin, G-protein coupled receptors).
- Immune Response: Antibodies protect against pathogens.


Enzymatic proteins
Ligand
Enzyme
Products
Storage proteins
Egg
Ovalbumin
Amino acids for embryo
Hormonal proteins
Thyroid hormone
Pituitary gland
Motor proteins
Skeletal muscle
Sarcomere (actin and myosin assembly)
Defensive proteins
Antibodies
Virus
Transport proteins
Molecules
Ion channel
Cytosol
Receptor proteins
Receptor
Structural proteins
Connective tissue
Collagen



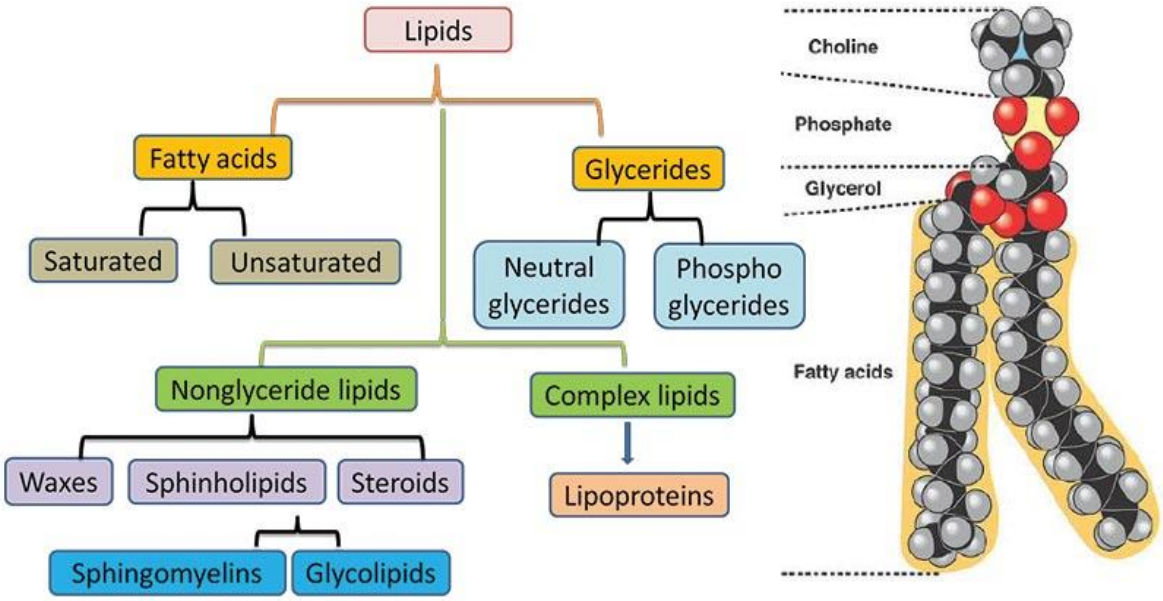
Function	Examples
Structural	Keratin (forms hair, nails, scales, feathers, and horns); silk (forms webs and cocoons)
Movement	Actin and myosin (found in muscle cells; allow contraction)
Defense	Antibodies (found in the bloodstream; fight disease organisms, some neutralize venoms); venoms (found in venomous animals; deter predators and disable prey)
Storage	Albumin (in egg white; provides nutrition for an embryo)
Signaling	Insulin (secreted by the pancreas; promotes glucose uptake into cells)
Catalyzing reactions	Amylase (found in saliva and the small intestine; digests carbohydrates)

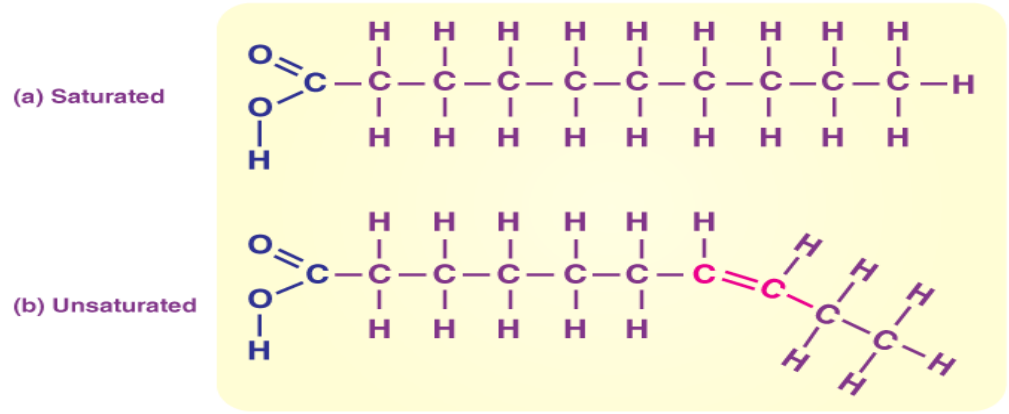
3. Lipids

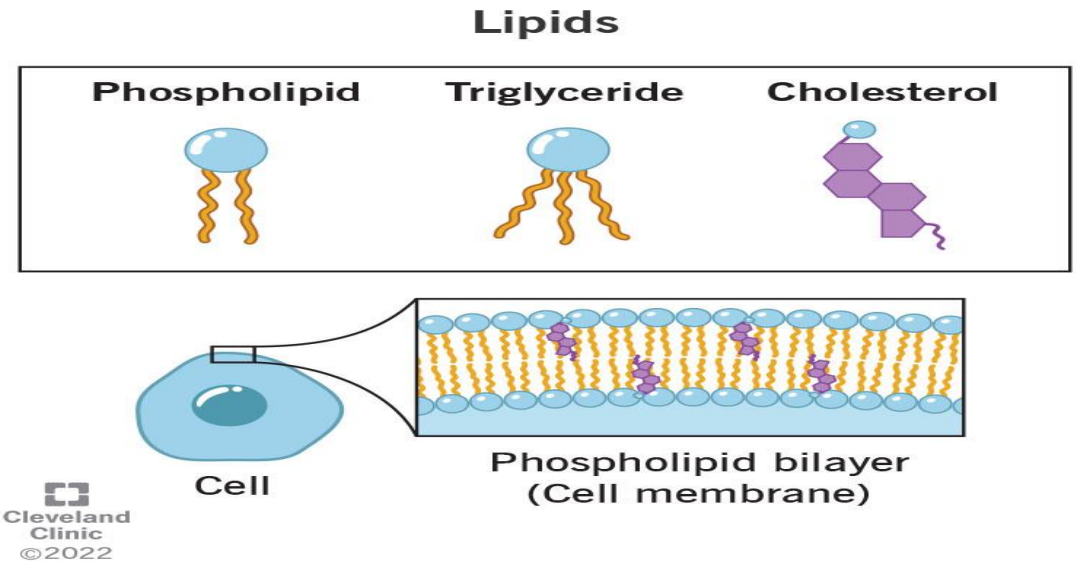


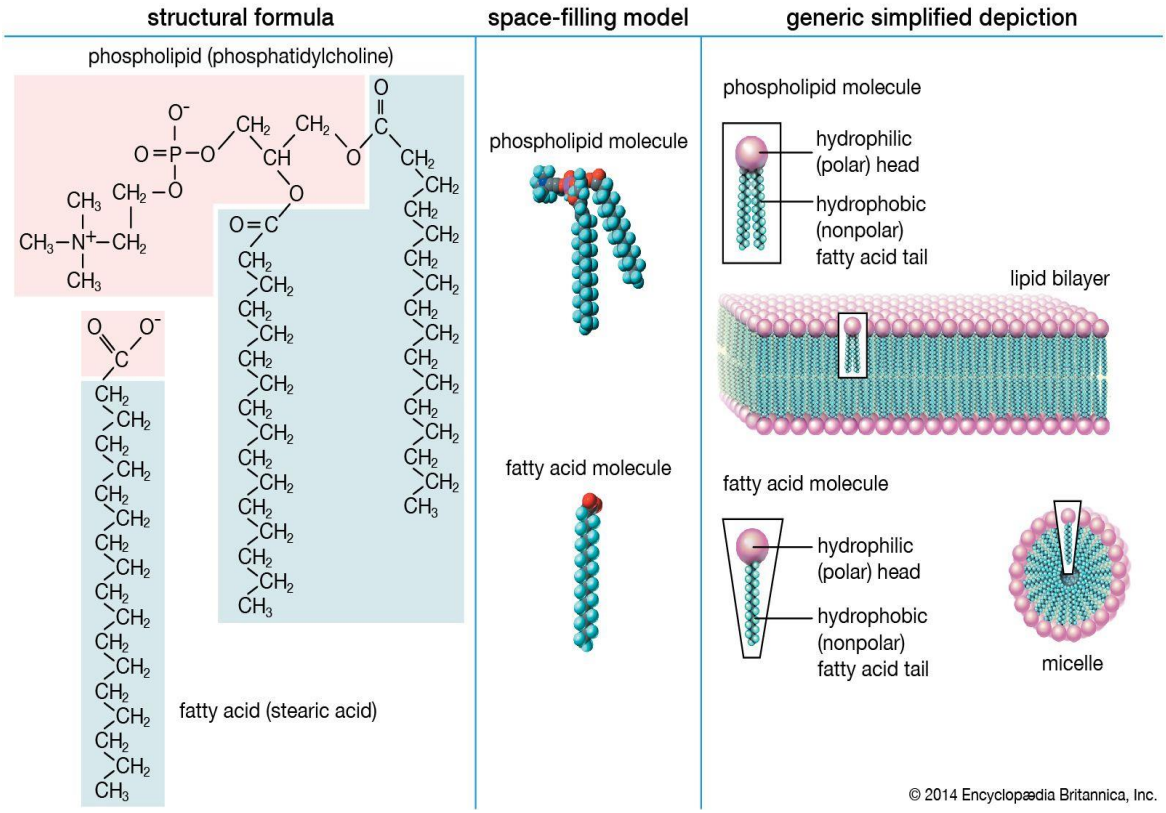
Structure:

- Fatty Acids and Glycerol: Building blocks of triglycerides (fats and oils).
- Phospholipids: Contain a glycerol backbone, two fatty acid tails, and a phosphate group; form bilayers in cell membranes.
- Steroids: Composed of four fused rings; include cholesterol and steroid hormones.
- Waxes: Long-chain fatty acids linked to alcohols; used for protection and waterproofing.


Lipids
Fatty acids
Glycerides
Saturated
Unsaturated
Neutral glycerides
Phospho glycerides
Nonglyceride lipids
Complex lipids
Waxes
Sphinholipids
Steroids
Lipoproteins
Sphingomyelins
Glycolipids
Choline
Phosphate
Glycerol
Fatty acids
BYJU'S
The Learning App


(a) Saturated
(b) Unsaturated


Lipids
Phospholipid
Triglyceride
Cholesterol
Cell
Phospholipid bilayer
(Cell membrane)
Cleveland Clinic
©2022


structural formula
space-filling model
generic simplified depiction
phospholipid (phosphatidylcholine)
fatty acid (stearic acid)
phospholipid molecule
fatty acid molecule
phospholipid molecule
hydrophilic (polar) head
hydrophobic (nonpolar) fatty acid tail
lipid bilayer
fatty acid molecule
hydrophilic (polar) head
hydrophobic (nonpolar) fatty acid tail
micelle
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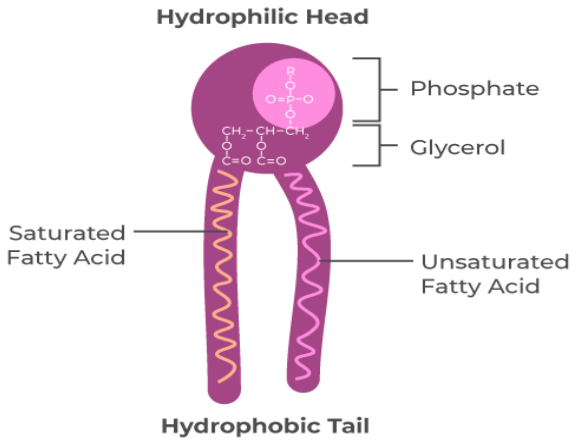
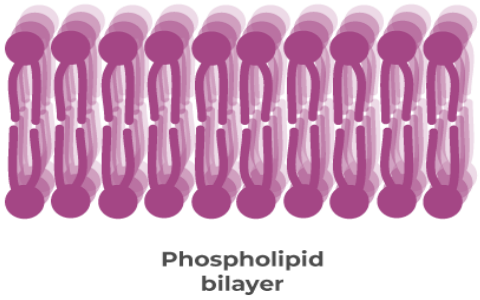
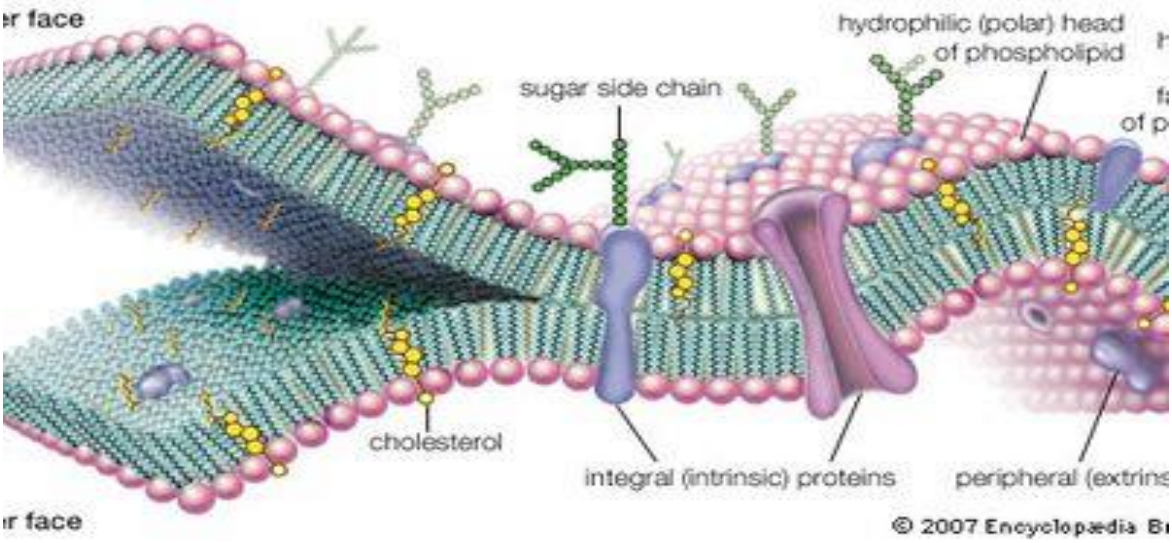

Hydrophilic Head
Phosphate
Glycerol
Saturated Fatty Acid
Unsaturated Fatty Acid
Hydrophobic Tail


Phospholipid bilayer



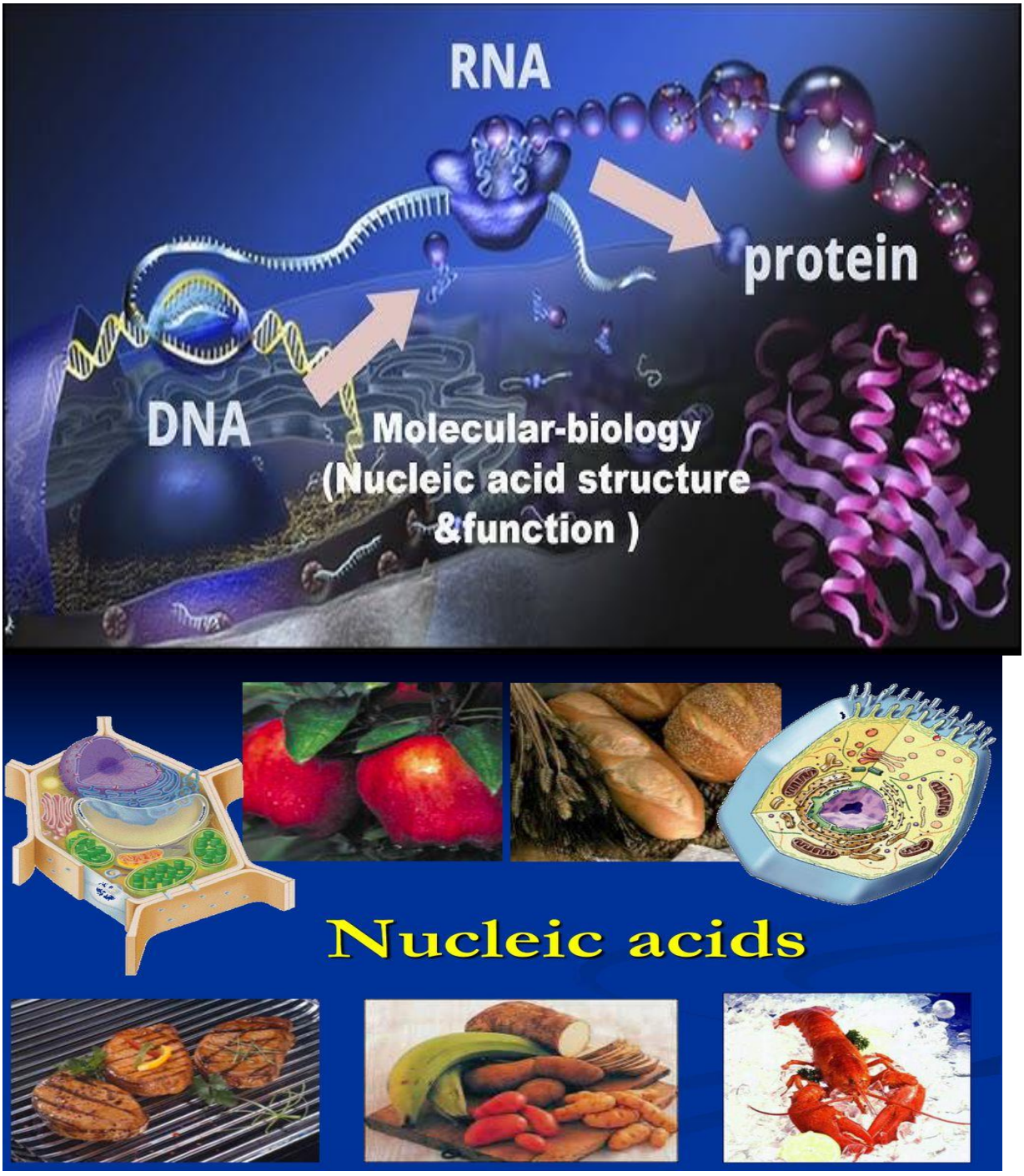
Roles in Cellular Function:

- Energy Storage: Triglycerides are stored in adipose tissue as a dense energy reserve.
- Membrane Structure: Phospholipids create the semi-permeable barrier of the cell membrane.
- Signaling: Steroid hormones regulate various physiological processes (e.g., estrogen, testosterone).
- Insulation and Protection: Lipids provide thermal insulation and protect organs.

Mnemonic:

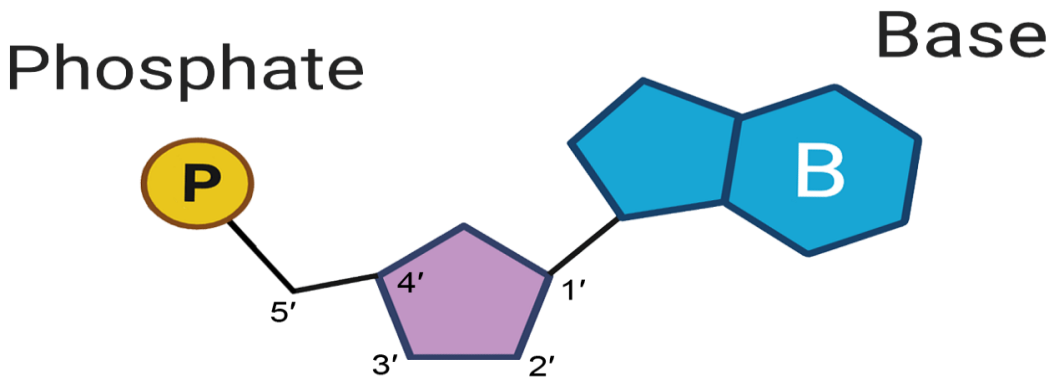
"F-P-S": Fat storage, Phospholipid membrane, Steroid signaling.

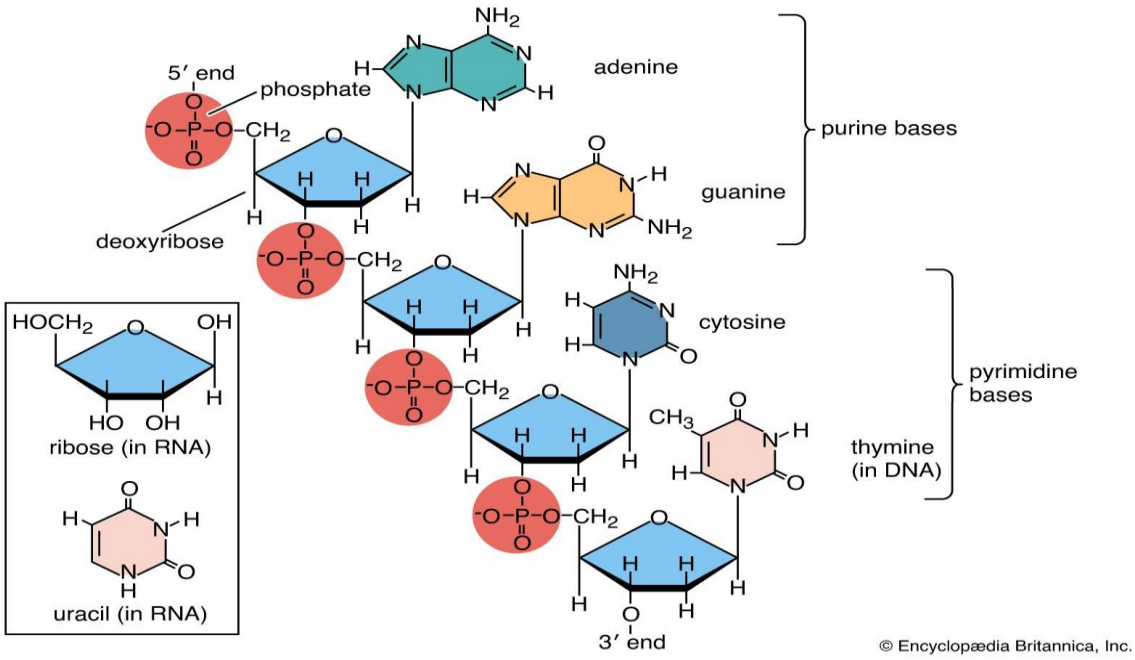
4. Nucleic Acids



Structure:

- Nucleotides: Composed of a sugar (deoxyribose in DNA, ribose in RNA), a phosphate group, and a nitrogenous base (adenine, thymine/uracil, cytosine, guanine).
- DNA: Double-stranded helix that stores genetic information.
- RNA: Typically single-stranded; involved in protein synthesis and regulation (e.g., mRNA, tRNA, rRNA).


Phosphate
Base
P
B
4′
5′
1′
3′
2′
Sugar


5′ end
phosphate
adenine
purine bases
guanine
deoxyribose
cytosine
pyrimidine bases
thymine (in DNA)
ribose (in RNA)
uracil (in RNA)
3′ end
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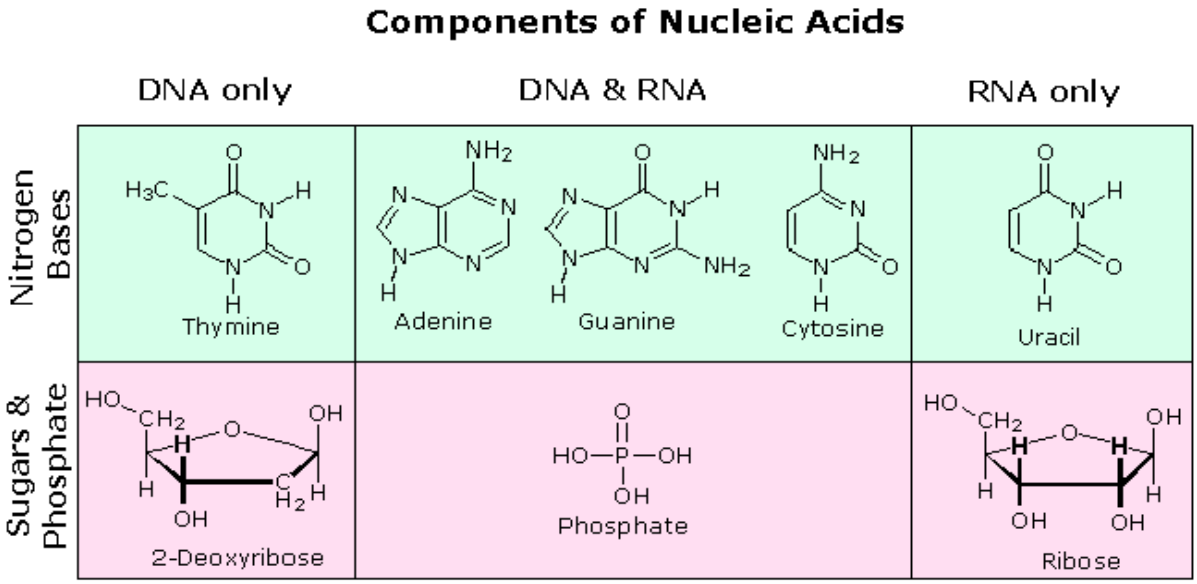
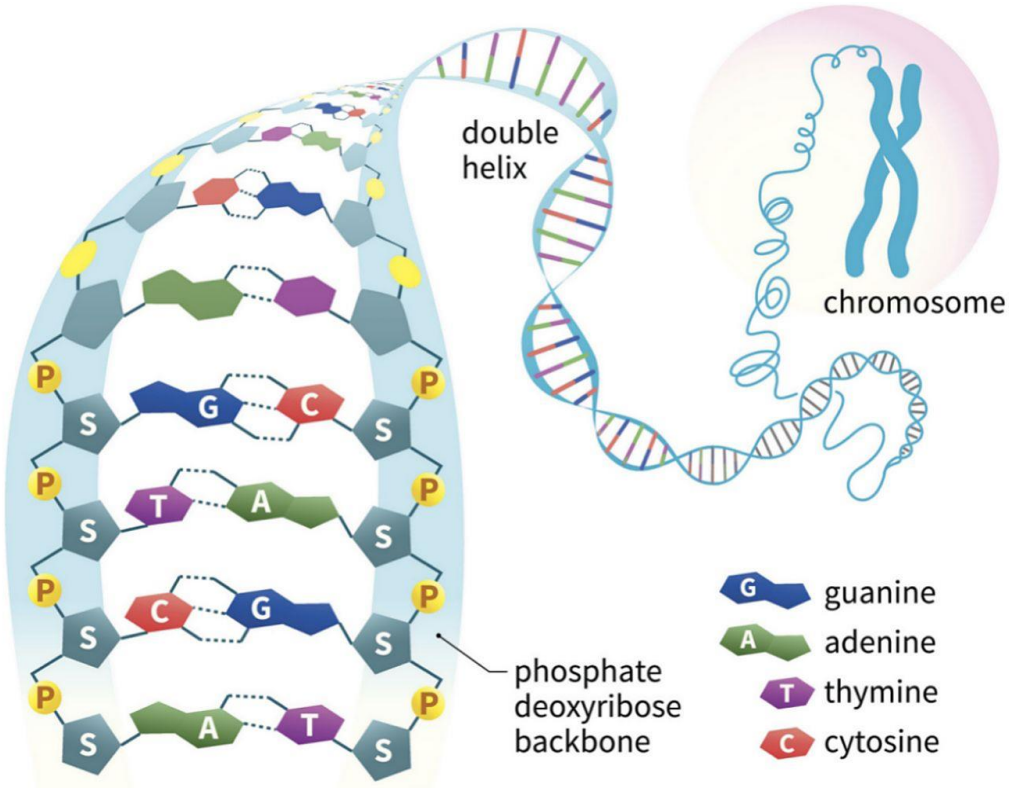




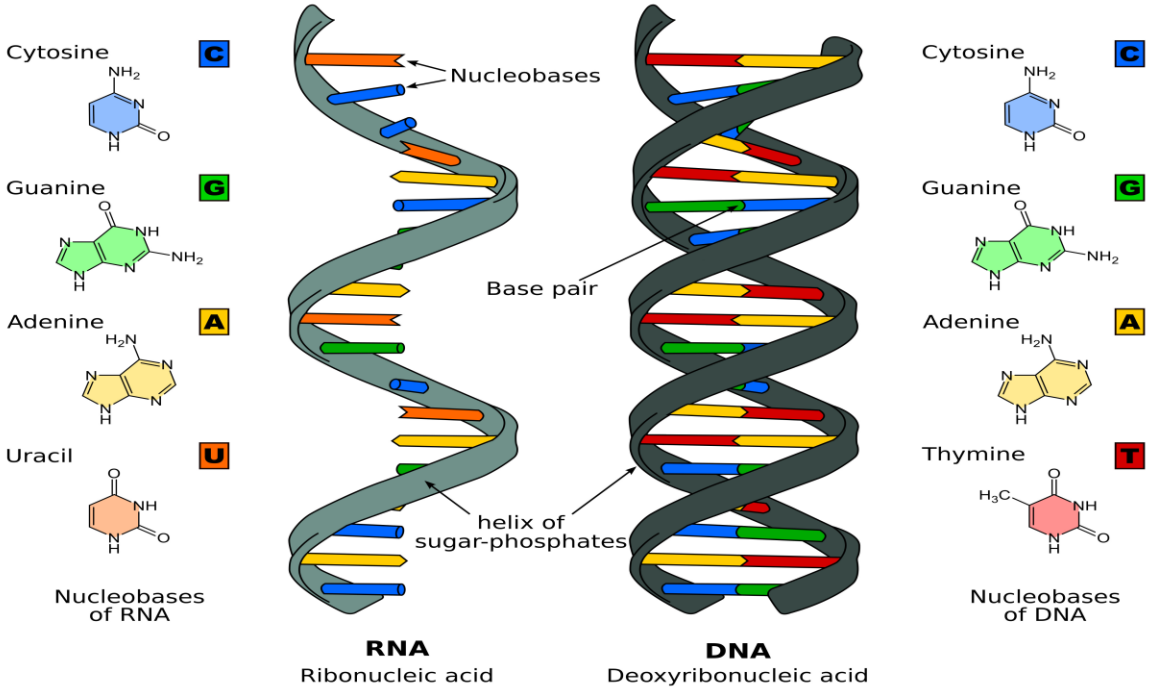
Roles in Cellular Function:

- Genetic Information Storage: DNA holds the instructions for building and maintaining the cell.

- Protein Synthesis: RNA transfers genetic information from DNA to ribosomes (translation process).
- Regulation: Various forms of RNA (e.g., microRNA) regulate gene expression and cellular processes.

Mnemonic:

"DR. NA": DNA has Deoxyribose and is the Reservoir of NAtural information.



Self-Assessment:

Fill in the Blanks:

1. Glucose is a _____ (monosaccharide/disaccharide/polysaccharide) that serves as a key energy source.
2. Glycogen is the storage form of glucose found in _____ (plants/animals).
3. The sequence of amino acids in a protein is called its _____ structure.
4. _____ proteins, such as hemoglobin, are essential for transporting oxygen in the blood.
5. _____ lipids form the structural basis of the cell membrane by arranging into a bilayer.
6. Triglycerides are primarily used for _____ in cells.
7. The sugar found in DNA is _____, whereas RNA contains _____.
8. DNA is typically a _____-stranded molecule.

MCQ:

Which of the following carbohydrates provides structural support in plant cell walls?

A) Glycogen

B) Cellulose

C) Starch

D) Sucrose

(Answer: B) Cellulose

Which level of protein structure involves the formation of alpha helices and beta sheets?

A) Primary

B) Secondary

C) Tertiary

D) Quaternary

(Answer: B) Secondary

Which lipid is most directly involved in cell signaling?

A) Triglyceride

B) Phospholipid

C) Steroid

D) Wax

(Answer: C) Steroid

Which nucleic acid is responsible for transferring the genetic code from DNA to the ribosome?

A) DNA

B) mRNA

C) tRNA

D) rRNA

(Answer: B) mRNA

Fun Fact:

- The human brain uses about 120 grams of glucose per day to function efficiently!
- There are more possible protein sequences than there are atoms in the known universe, highlighting the vast potential of protein diversity.
- The average human body stores enough fat to create nearly 7 bars of soap!
- One gram of fat provides more than twice the energy of carbohydrates or proteins!
- If uncoiled, the DNA in one human cell would stretch to about 2 meters in length!
- Engage with interesting facts about biomolecules to reinforce your memory (e.g., the surprising lengths of DNA, the rapid catalytic rates of enzymes).

Additional Study Tips & Tricks

Flowcharts & Diagrams:

- Create visual summaries for each biomolecule class. Flowcharts that connect structure to function can be especially helpful. For example, a flowchart linking "phospholipids" to "cell membrane formation" and then to "cell signaling" illustrates the continuum from structure to function.

Flashcards:

- Make flashcards for key terms (e.g., “monosaccharide,” “phospholipid,” “nucleotide”) with definitions and functions.

□ 3. Biochemical Composition of Cell Membrane & The Fluid Mosaic Model

□ Key Concepts

✓Phospholipid Bilayer: Hydrophilic head, Hydrophobic tail → Barrier for selective permeability

✓Proteins: Integral (embedded) & Peripheral (surface) → Transport & signaling

✓Cholesterol: Maintains membrane fluidity

✓Carbohydrates: Glycoproteins & glycolipids → Cell recognition & communication

 Mnemonic: "People Can Love Carbs"

P - Proteins

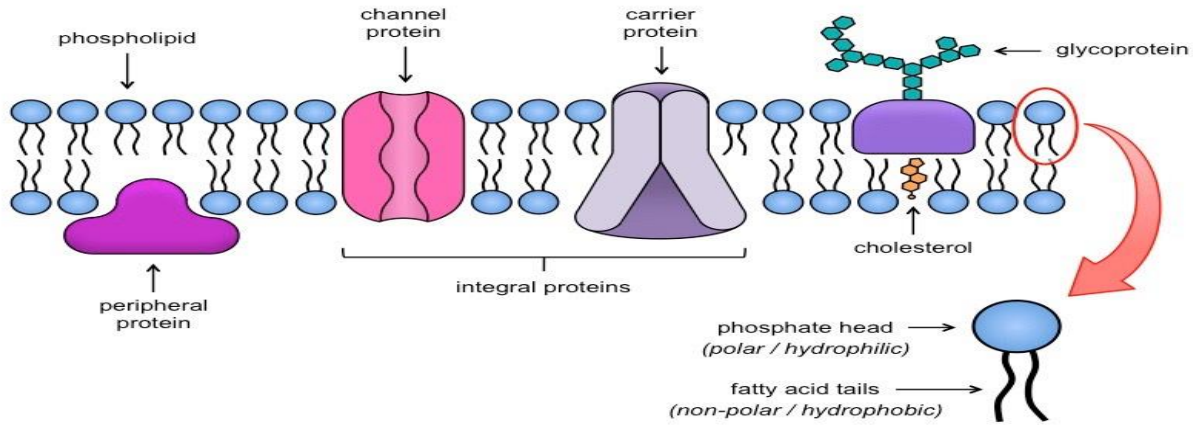
C - Cholesterol

L - Lipids

C - Carbohydrates

The Fluid Mosaic Model

Definition: The Fluid Mosaic Model describes the structure of the cell membrane as a dynamic, fluid structure in which a phospholipid bilayer forms the basic framework. Within this bilayer, various proteins (integral and peripheral), cholesterol, and carbohydrate chains are interspersed, creating a “mosaic” pattern.



"Fluid" Aspect:

- Dynamic Lipids: The phospholipids are not fixed; they can move laterally within the layer. This fluidity allows the membrane to be flexible, facilitating processes like vesicle formation, cell signaling, and membrane protein redistribution.
- Temperature and Composition: The degree of fluidity depends on factors such as temperature and the lipid composition (saturated vs. unsaturated fatty acids) and cholesterol content.

"Mosaic" Aspect:

- Embedded Proteins: Integral proteins (which span the membrane) and peripheral proteins (which are attached to the surface) are scattered throughout the lipid bilayer. These proteins serve various functions, including transport, signal transduction, cell recognition, and enzymatic activity.
- Carbohydrate Conjugates: Carbohydrates attached to proteins (glycoproteins) or lipids (glycolipids) extend from the extracellular surface and participate in cell–cell interactions and immune responses.

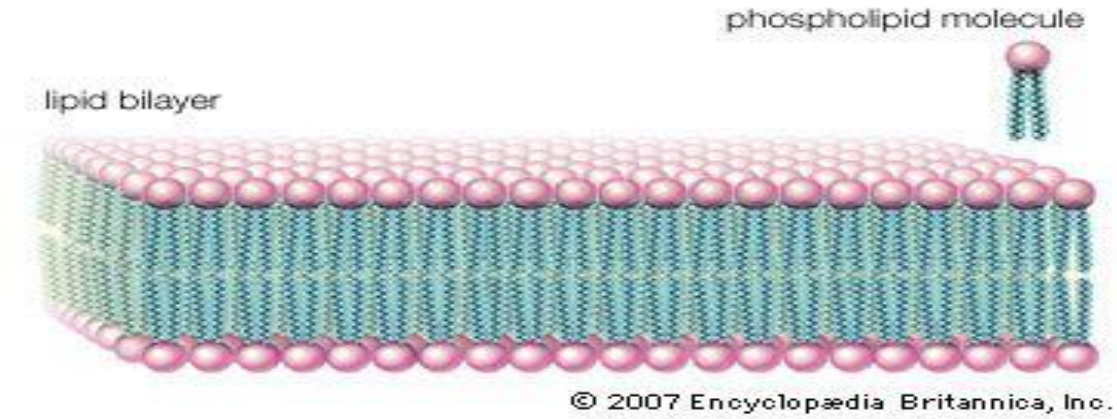
Functional Significance:

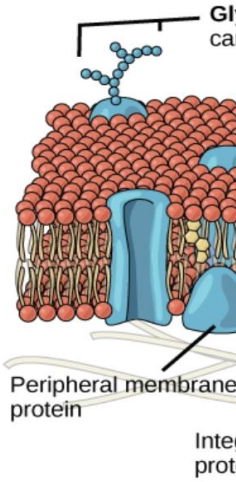
- Selective Permeability: The fluid nature of the membrane allows for the selective passage of molecules, which is essential for maintaining the internal environment of the cell.
- Cell Signaling: The mobility of membrane proteins facilitates rapid changes in response to signals and the formation of specialized regions (like lipid rafts) that organize signaling molecules.
- Adaptability: This dynamic organization allows cells to adjust to environmental changes, repair damaged areas, and enable processes like endocytosis and exocytosis.

Mnemonic : "F-MAP"

- Fluid
- Mosaic
- Assembly of lipids, proteins, and carbohydrates
- Protein mobility

This mnemonic reminds you that the membrane is Fluid, has a Mosaic pattern, is composed of various components, and that protein movement is key to its function.





The plasma membr
phospholipids, chol
(gl

Flowchart Idea:

- Create a flowchart starting with "Phospholipid Bilayer" branching into "Protein Insertion" (integral vs. peripheral), "Cholesterol Regulation," and "Carbohydrate Attachment" to illustrate how these components create the mosaic structure.

Biochemical Composition and Functions of the Components of the Cell Membrane

The cell membrane, also called the plasma membrane, is a semi-permeable structure that surrounds the cell, providing protection, communication, and selective transport of molecules. The biochemical composition of the cell membrane determines its structure and function, making it a critical component for cellular survival and interaction.

1. Biochemical Composition of the Cell Membrane

The cell membrane is primarily composed of lipids, proteins, and carbohydrates, each contributing to its function:

A. Lipids (50% of the Membrane) – The Structural Component

Lipids provide the basic framework of the membrane and contribute to its fluidity and permeability.

1. Phospholipids – The Bilayer Backbone

Structure: Composed of hydrophilic heads (phosphate group) and hydrophobic tails (fatty acid chains). Arranged in a bilayer, with the hydrophobic tails facing inward and the hydrophilic heads facing outward.

Function:

- Forms a selective barrier that controls the entry and exit of molecules.
- Provides membrane fluidity, allowing proteins to move and function properly.

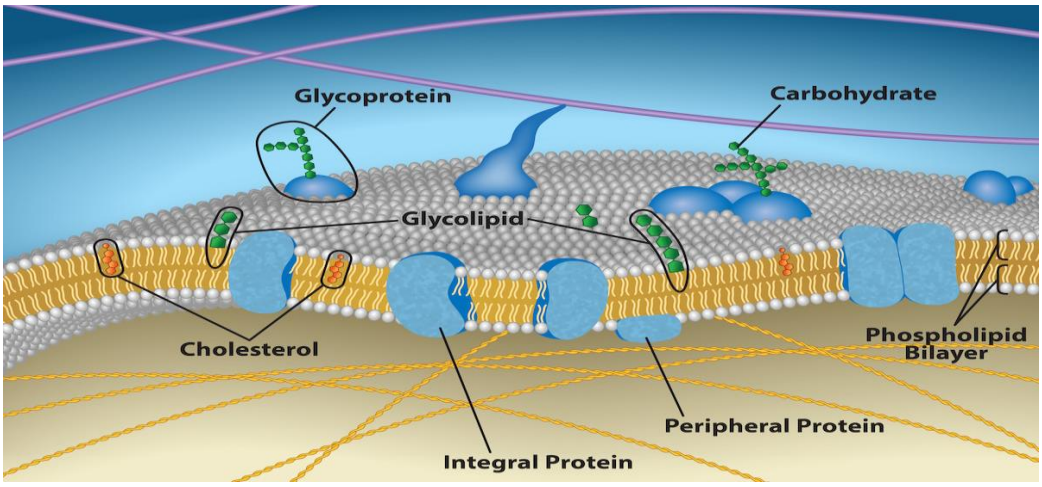
2. Cholesterol – The Fluidity Regulator

Structure: Interspersed between phospholipids. Rigid ring structure that interacts with fatty acid chains.

Function:

- Maintains fluidity: Prevents phospholipids from packing too tightly at low temperatures and stabilizes the membrane at high temperatures.
- Enhances membrane stability and prevents breakage.

3. Glycolipids – The Cell Communication Molecules



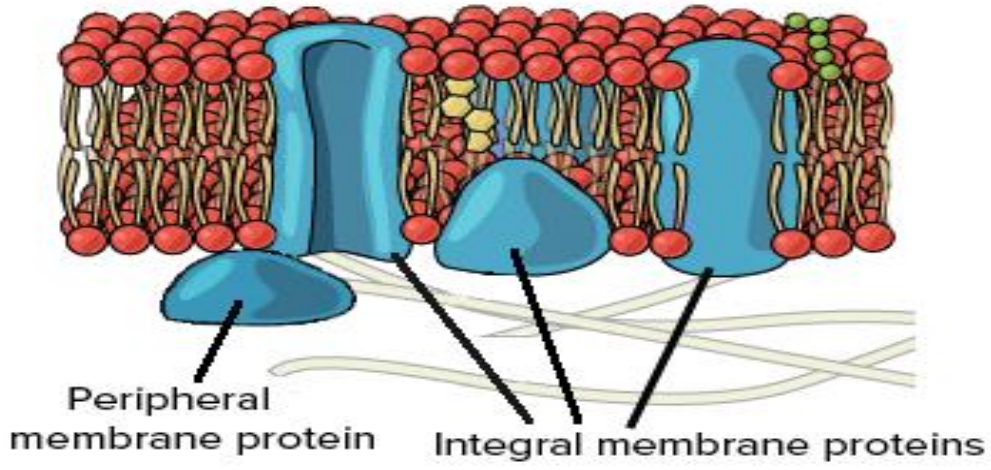
Structure: Lipids with carbohydrate chains attached, found on the outer surface of the membrane.

Function:

- Cell recognition – Helps in immune responses and blood group determination.
- Provides membrane stability and protection.

B. Proteins (50% of the Membrane) – The Functional Component

Membrane proteins play a crucial role in transport, signaling, and cell-cell interactions.



1. Integral (Transmembrane) Proteins – Transporters & Signalers

Structure: Embedded within the lipid bilayer, spanning across the membrane.

Function:

- Transporters & Channels: Move molecules across the membrane (e.g., Na^+/K^+ pump, GLUT transporters).
- Receptors: Bind to signaling molecules (e.g., insulin receptor).
- Cell Adhesion Proteins: Help in cell-cell interactions and communication.

2. Peripheral Proteins – Support & Signaling

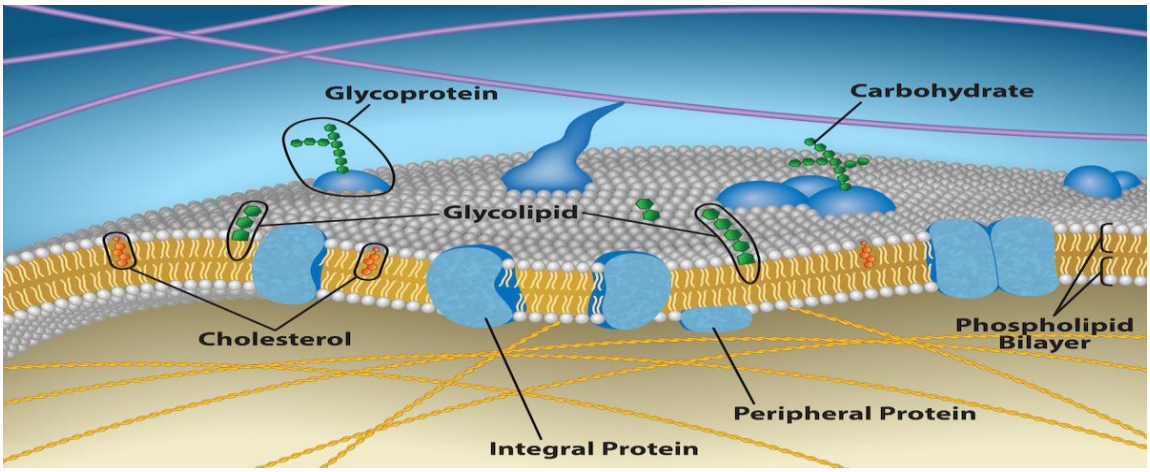
Structure: Loosely attached to the inner or outer surface of the membrane.

Function:

- Enzymatic Activity: Speed up chemical reactions.
- Cytoskeletal Anchors: Provide structural support by linking to the cytoskeleton.

C. Carbohydrates (1-5% of the Membrane) – The Identifiers

- Carbohydrates are attached to lipids (glycolipids) or proteins (glycoproteins) and are found on the outer surface of the membrane.



Function:

- Cell Recognition: Helps the immune system distinguish self from non-self (e.g., ABO blood group antigens).
- Intercellular Communication: Allows cells to interact with each other.

2. Functions of the Cell Membrane Components

1. Selective Permeability

- Phospholipids control the passage of molecules:
- Small, nonpolar molecules (O_2, CO_2) diffuse freely.
- Large, charged molecules (glucose, Na^+, K^+) require transport proteins.

2. Transport of Molecules

- **Passive Transport (No ATP required):**
  - Simple Diffusion: Movement of molecules down a concentration gradient (O_2, CO_2).
  - Facilitated Diffusion: Transport via channels or carriers (GLUT transporters for glucose).
  - Osmosis: Movement of water via aquaporins.
- **Active Transport (Requires ATP):**
  - Primary Active Transport: Uses ATP to move molecules against a gradient (Na^+/K^+ pump).
  - Secondary Active Transport: Uses energy from ion gradients (SGLT for glucose transport).

3. Cell Signaling & Communication

- Receptors on Integral Proteins bind to hormones and neurotransmitters to trigger cellular responses.

- Example: Insulin binds to its receptor, stimulating glucose uptake.

4. Cell Recognition & Immune Response

- Glycoproteins and glycolipids act as "ID tags" for immune system recognition (e.g., blood groups, MHC proteins).

5. Structural Support & Cell Shape

- Peripheral proteins link to the cytoskeleton, maintaining cell shape and integrity.

Mnemonic to Remember Membrane Components:

"P.C.P. – Proteins, Carbohydrates, Phospholipids"

Mnemonic for Membrane Protein Types:

“TIP” – Transporters, Integral proteins, Peripheral proteins

Flowchart Idea:

- Create a flowchart linking each membrane component to its function, e.g.,
  - Lipids → Structure & Fluidity
  - Proteins → Transport & Signaling
  - Carbohydrates → Recognition & Communication

Self-Assessment

Fill in the Blanks

1. The cell membrane is composed of a _____ bilayer.

(Answer: phospholipid)

2. _____ proteins are embedded throughout the membrane, while _____ proteins are attached to its surface.

(Answer: Integral; peripheral)

3. The dynamic movement of phospholipids within the membrane is described as its _____ nature.

(Answer: fluidity)

4.The cell membrane is composed mainly of _____, _____, and _____.

(Answer: lipids, proteins, carbohydrates)

5..The component responsible for regulating membrane fluidity is _____.

(Aswer: cholesterol)

6. Glycoproteins and glycolipids function primarily in _____.

(Answer: cell recognition and signaling)

Multiple Choice Question

Which of the following components primarily contributes to the regulation of membrane fluidity?

A) Carbohydrates

B) Cholesterol

C) Peripheral proteins

D) Glycoproteins

(Correct Answer: B) Cholesterol

Which of the following is a function of integral proteins?

A) Energy storage

B) Signal transduction

C) Structural support

D) Lipid synthesis

(Answer: B) Signal transduction

What is the role of cholesterol in the cell membrane?

A) It acts as a transporter

B) It provides energy

C) It regulates fluidity

D) It forms the glycocalyx

(Answer: C) It regulates fluidity

True/False

The Fluid Mosaic Model implies that membrane proteins are fixed in place.

(False – They can move laterally within the lipid bilayer.)

Study Tips:

- Use analogy: Think of the membrane as a “fluid border with gates” where:
    - Lipids are the flexible walls
    - Proteins are the doors
    - Carbohydrates are name tags
- Flashcards: Create flashcards with key terms (e.g., phospholipid, integral protein, cholesterol) and their roles.Use flashcards with each membrane component and its function.
- Interactive Diagram: Draw the cell membrane and label each component. Re-draw it several times to reinforce your memory.
- Group Discussion: Explain the fluid mosaic model to a peer to reinforce your understanding.

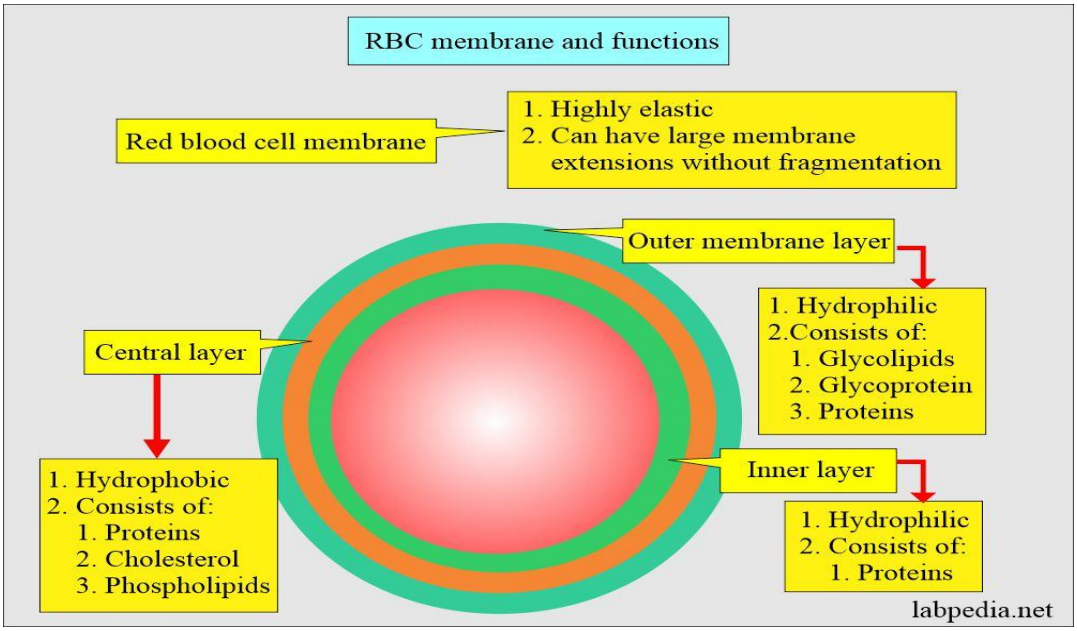
Fun Fact

- If you could "unfreeze" all the membranes in your body, you’d see more than 100 trillion individual molecules moving and interacting dynamically, all contributing to the life of your cells!
- Your body has 37.2 trillion cells, each surrounded by a lipid bilayer!
- Did you know? The total surface area of all the cell membranes in a human body is estimated to be around 100,000 square meters, roughly the size of a football field!

Comparison of the Biochemical Significance of Different Types of Membranes

Cellular membranes play a crucial role in maintaining compartmentalization, biochemical reactions, transport, and signaling. Different organelles have specialized membranes with unique biochemical compositions and functions tailored to their roles

1. Red Blood Cell (RBC) Membrane – Gas Exchange & Flexibility



Biochemical Composition:

- Phospholipids: Phosphatidylcholine (PC), Phosphatidylethanolamine (PE), Phosphatidylserine (PS), and Sphingomyelin (SM).
- High Cholesterol Content: Maintains membrane fluidity and prevents rupture.

Membrane Proteins:

- Band 3: Anion exchanger (Cl^-/HCO_3^- exchange for CO_2 transport).
- Glycophorin: Prevents RBC aggregation.
- Spectrin & Actin Cytoskeleton: Provides shape and elasticity.

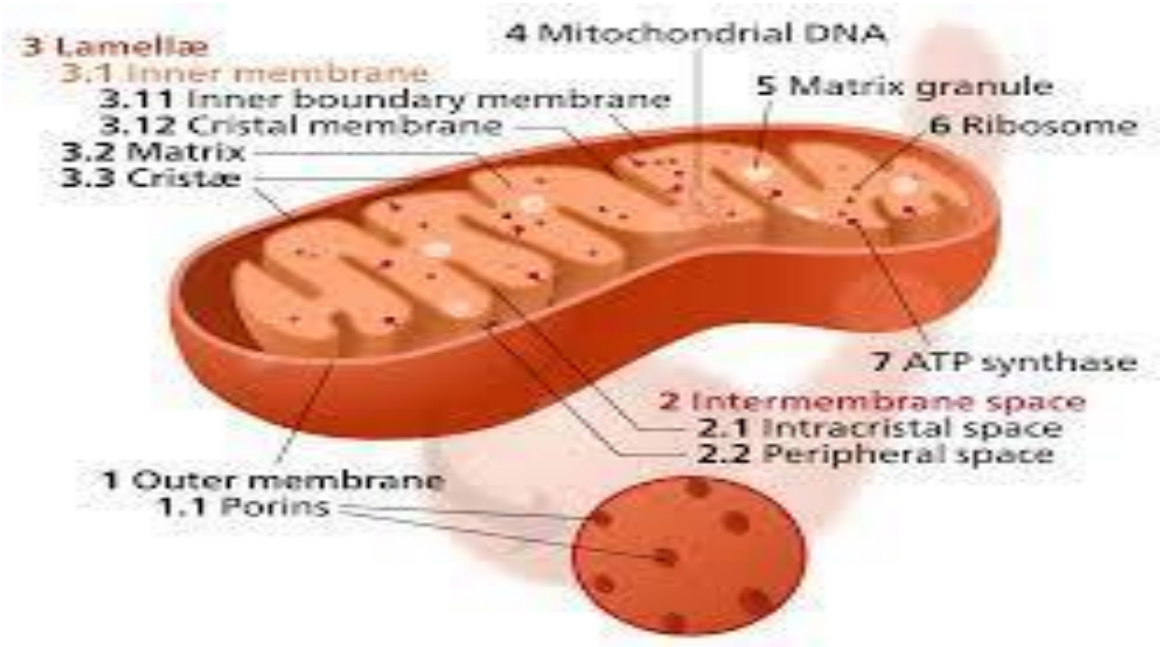
Biochemical Significance:

- Maintains flexibility and deformability for squeezing through capillaries.
- Facilitates gas exchange (O_2 and CO_2 transport) via hemoglobin.
- Provides immune recognition through blood group antigens (ABO, Rh).

Clinical Relevance:

- Hereditary Spherocytosis: Defect in spectrin, leading to RBC rigidity and hemolysis.
- Sickle Cell Anemia: Mutant hemoglobin (HbS) affects membrane integrity.

2. Mitochondrial Membrane – Energy Production & Metabolism



Biochemical Composition:

- Outer Membrane: Contains porins, making it permeable to small molecules.
- Inner Membrane:
- Cardiolipin (a unique phospholipid) maintains mitochondrial structure.
- Electron Transport Chain (ETC) Proteins: ATP synthase, Complex I-IV.

Biochemical Significance:

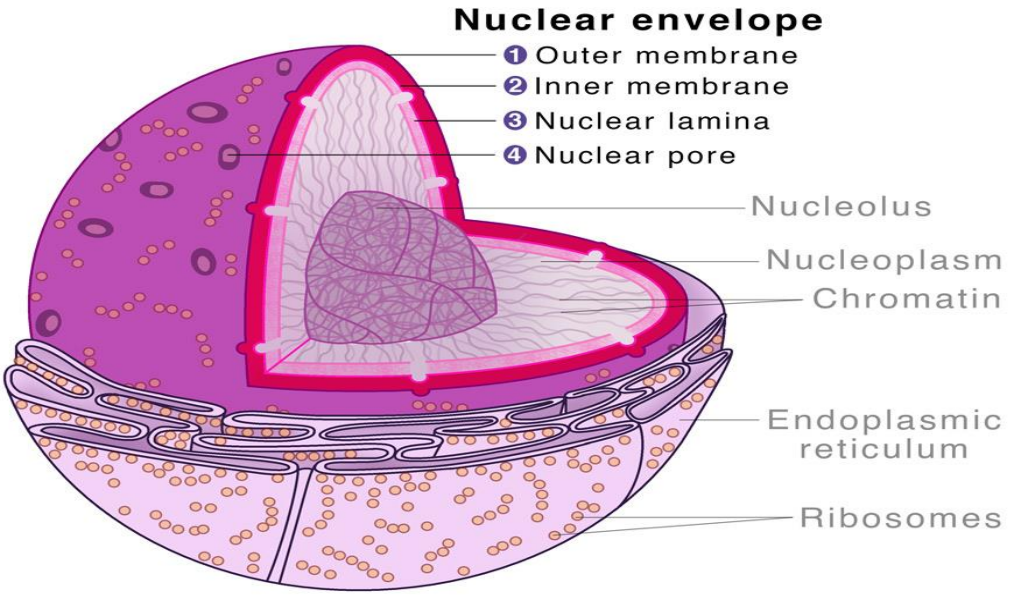
- Oxidative Phosphorylation: ATP production via Electron Transport Chain (ETC).
- Fatty Acid Oxidation: Generates acetyl-CoA for energy.
- Apoptosis Regulation: Cytochrome c release triggers cell death.

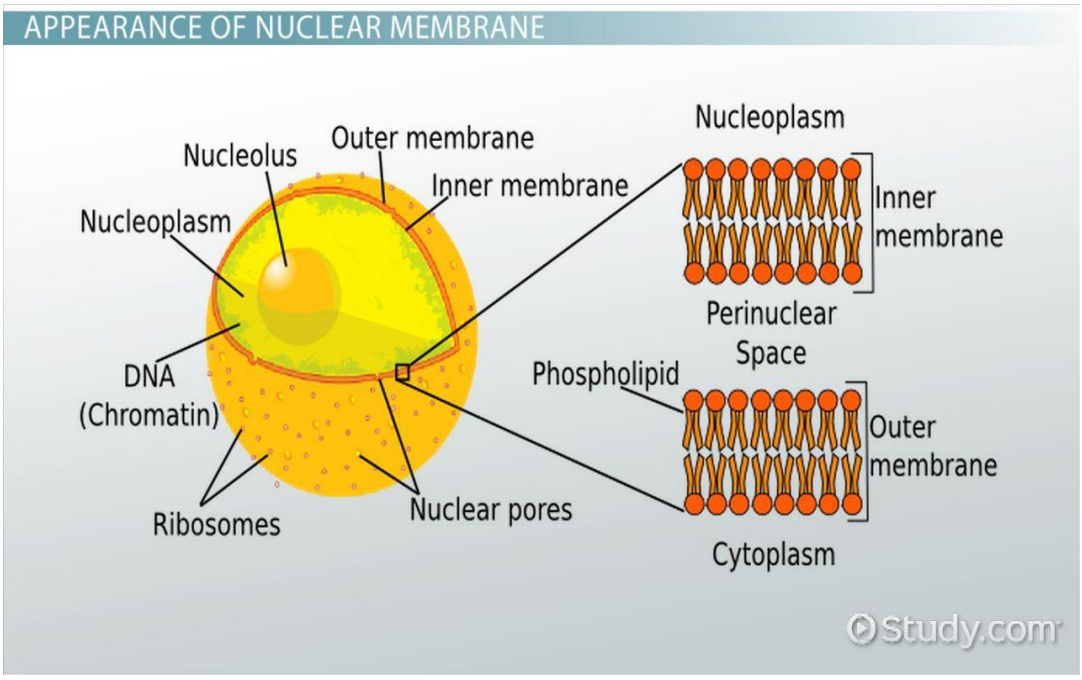
Clinical Relevance:

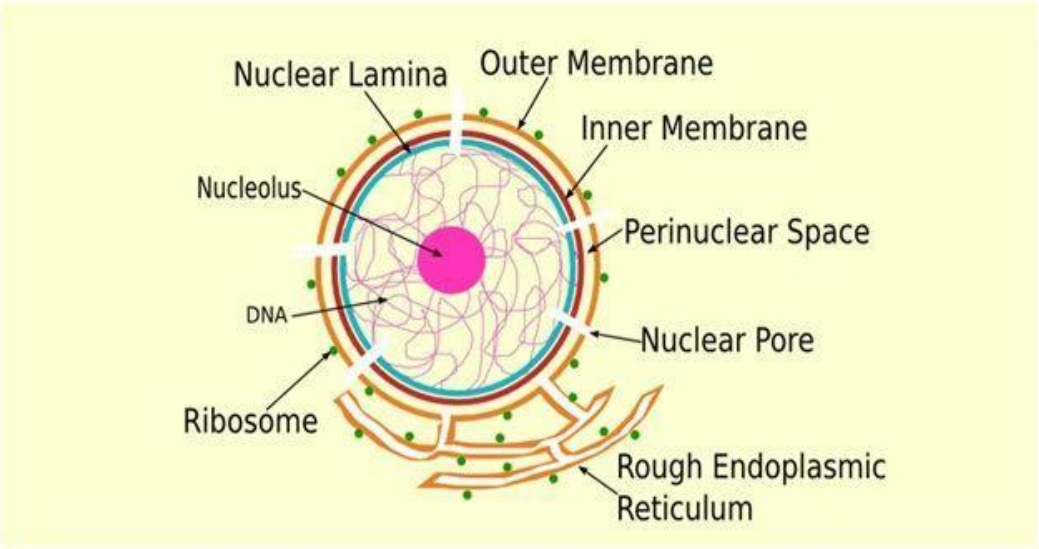
- Leigh Syndrome: Defective ETC proteins → mitochondrial dysfunction.
- Mitochondrial Myopathies: Energy deficiency in muscles.

3. Nuclear Membrane (Nuclear Envelope) – DNA Protection & Transport

Nuclear Envelope







Biochemical Composition:

- Double Membrane: Inner and outer lipid bilayers.
- Nuclear Pores: Contain importins & exportins for selective molecule transport.
- Nuclear Lamina: Composed of lamins, providing structural support.

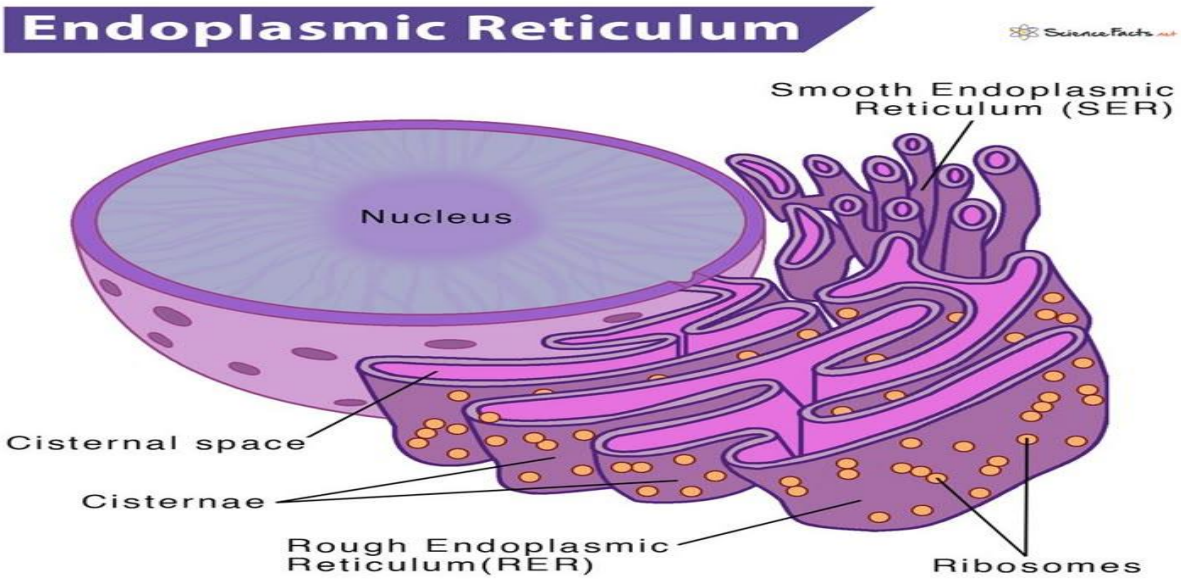
Biochemical Significance:

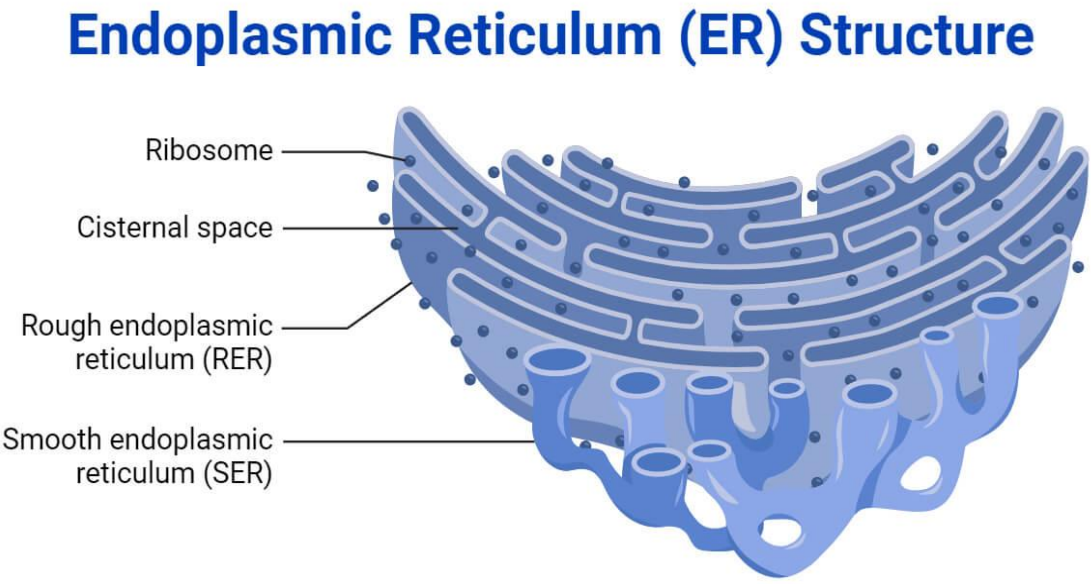
- Protects DNA from cytoplasmic enzymes.
- Selective Transport: Controls entry of transcription factors, ribosomal RNA, and signaling molecules.
- Regulates Gene Expression: By controlling nuclear transport.

Clinical Relevance:

- Hutchinson-Gilford Progeria Syndrome (HGPS): Mutation in lamin A causes premature aging.
- Cancer: Irregular nuclear shape in aggressive tumors.

4. Endoplasmic Reticulum (ER) Membrane – Protein & Lipid Synthesis





Biochemical Composition:

- Phospholipid bilayer with embedded enzymes.
- Ribosomes (Rough ER): Site of protein synthesis.
- Calcium Pumps (SER): Store and regulate calcium levels.

Biochemical Significance:

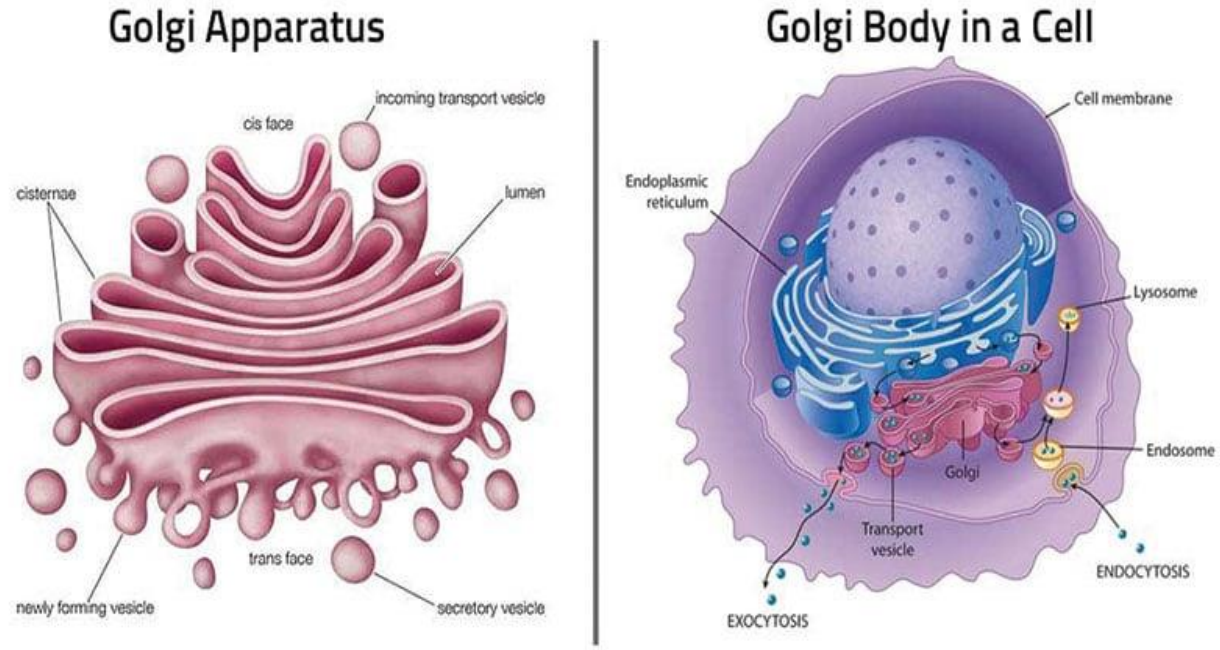
- Rough ER (RER):
    - Synthesizes secretory proteins (e.g., insulin).
    - Facilitates protein folding and post-translational modifications.

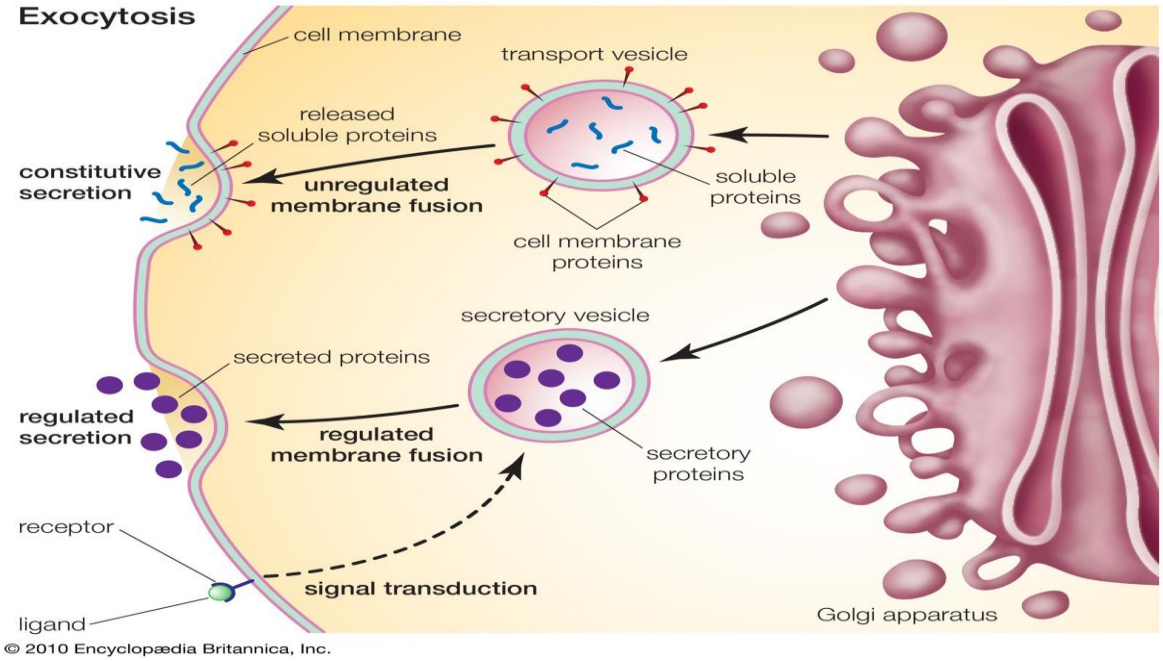
- Smooth ER (SER):
    - Lipid & steroid hormone synthesis (e.g., cholesterol, testosterone).
    - Detoxification (liver SER metabolizes drugs).
    - Calcium Storage for muscle contraction.

Clinical Relevance:

- Cystic Fibrosis: Misfolded CFTR protein accumulates in the ER.
- Non-Alcoholic Fatty Liver Disease (NAFLD): Dysfunctional lipid metabolism in SER.

5. Golgi Apparatus Membrane – Protein Sorting & Vesicle Formation





Biochemical Composition:

- Stacks of membrane-bound cisternae (cis, medial, and trans faces).
- Glycosyltransferases & Glycosidases for post-translational modifications.

Biochemical Significance:

- Protein Modification: Glycosylation, phosphorylation, sulfation.
- Sorting & Packaging:

- Lysosomal enzymes are tagged with mannose-6-phosphate.
- Secretory proteins (e.g., hormones) are packed into vesicles.
- Membrane Recycling: Supplies new plasma membrane components.

Clinical Relevance:

- I-Cell Disease: Defective Golgi tagging leads to lysosomal enzyme deficiency.
- Congenital Disorders of Glycosylation (CDG): Impaired protein glycosylation.

Mnemonics to Remember Membrane Functions

"Really Mighty Nucleus Enjoys Golgi"

RBC – Rigid & flexible

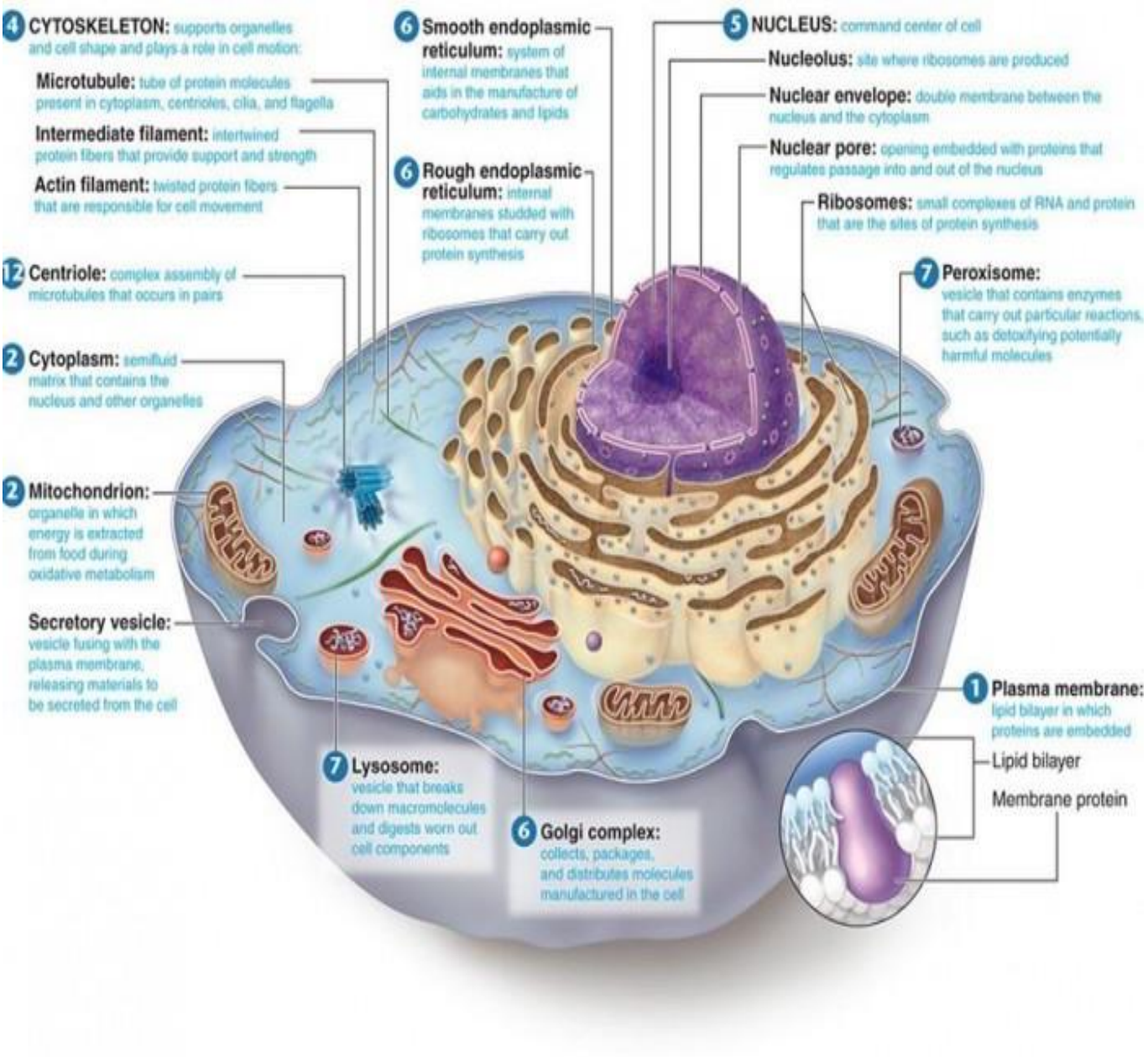
Mitochondria – Makes ATP

Nucleus – Nucleotide storage (DNA)

ER – Enzyme and protein synthesis

Golgi – Glycosylation and sorting

Cell Organelles: Biochemistry, Functions & Marker Enzymes



 Study Tip:

 Think of the cell as a city!

- Nucleus = City Hall (controls everything, stores information)
- Mitochondria = Power Plant (produces energy)
- Rough ER = Factory (makes proteins)
- Golgi = Post Office (sorts & delivers)

- Lysosomes = Recycling Center (breaks down waste)
- Peroxisomes = Detox Plant (cleans up toxic waste)
- Endosomes = Transport Hub (moves cargo within the cell)

1. Nucleus: The Command Center

Structure & Biochemical Composition

- Double membrane with nuclear pores for transport.
- Nucleoplasm (contains chromatin: DNA + histones).
- Nucleolus (produces rRNA for ribosomes).

Function

- ✅Stores genetic material & controls gene expression.
- ✅Regulates cell division (mitosis & meiosis).
- ✅Synthesizes ribosomal RNA (rRNA).

Marker Enzymes

- DNA Polymerase – Replicates DNA.
- RNA Polymerase I – Transcribes rRNA.

Clinical Connection

- Hutchinson-Gilford Progeria Syndrome: Mutation in lamin A (nuclear envelope protein) causes premature aging.

Mnemonic:

- "Nucleolus = Makes ribosomes; Nucleus = Controls cell"

2. Ribosomes: The Protein Factory

Structure & Biochemical Composition

- Made of rRNA + proteins.
- Two subunits: 40S + 60S = 80S (Eukaryotic).

Function

- ✅Synthesizes proteins from mRNA.

Marker Enzyme

- Peptidyl Transferase – Catalyzes peptide bond formation.

Clinical Connection

- Diamond-Blackfan Anemia (DBA): Defective ribosomal proteins cause low RBC production.

Fun Fact:

- Eukaryotic ribosomes (80S) differ from prokaryotic ribosomes (70S), making them a target for antibiotics (e.g., tetracyclines, macrolides).

3. Mitochondria: The Powerhouse

Structure & Biochemical Composition

- Double membrane: Outer (smooth) + Inner (folded into cristae).
- Matrix: Contains TCA cycle enzymes, mtDNA, ribosomes.

Function

- ✓Generates ATP via Oxidative Phosphorylation (Electron Transport Chain - ETC).
- ✓Regulates apoptosis (cytochrome c release).

Marker Enzyme

- Succinate Dehydrogenase (SDH) – Functions in both TCA cycle & ETC.

Clinical Connection

- Leigh Syndrome: Mitochondrial dysfunction leads to neurological degeneration.

Mnemonic:

"Mighty Mitochondria Make Energy"

(Imagine a flowchart showing Glycolysis → TCA Cycle → Electron Transport Chain → ATP Production.)

4. Golgi Apparatus: The Post Office

Structure & Biochemical Composition

- Stacked cisternae with enzymes for glycosylation, phosphorylation.

Function

- ✓Modifies, sorts, and packages proteins for secretion.
- ✓Produces lysosomes & glycoproteins.

Marker Enzyme

- Galactosyltransferase – Involved in glycosylation.

Clinical Connection

- I-Cell Disease (Inclusion Cell Disease): Defective Mannose-6-Phosphate tagging prevents lysosomal enzyme transport, leading to storage disorders.

Fun Fact:

- Golgi can expand during cell activity – it's like a warehouse adjusting to shipping demand!

5. Lysosomes: The Recycling Center

Structure & Biochemical Composition

- Single membrane with acidic pH (4.5-5).
- Contains hydrolytic enzymes for digestion.

Function

- ✅Breaks down waste, organelles, and foreign particles.
- ✅Plays a role in pathogen destruction (immune function).

Marker Enzyme

- Acid Phosphatase – Key lysosomal enzyme.

Clinical Connection

- Gaucher Disease: Glucocerebrosidase deficiency → Accumulation of glucocerebroside in macrophages → Hepatosplenomegaly, bone pain.

Mnemonic:

- "Lysosomes Lysis Large Molecules"

6. Peroxisomes: The Detox Unit

Structure & Biochemical Composition

- Single membrane with oxidative enzymes (catalase, peroxidases).

Function

- ✅Breaks down very-long-chain fatty acids (VLCFAs) via β-oxidation.
- ✅Detoxifies hydrogen peroxide (H_2O_2) using catalase.

Marker Enzyme

- Catalase – Breaks down H_2O_2 into water + oxygen.

Clinical Connection

- Zellweger Syndrome: Peroxisome biogenesis defect causes VLCFA accumulation → severe neurological issues.

Fun Fact:

- Liver cells have high numbers of peroxisomes because of their role in detoxification!

7. Endoplasmic Reticulum (ER): The Production Line

Structure & Biochemical Composition

- Rough ER (RER): Ribosome-studded, synthesizes proteins.
- Smooth ER (SER): Lacks ribosomes, synthesizes lipids & detoxifies drugs.

Function

- ✅RER: Protein synthesis & folding.
- ✅SER: Lipid metabolism & detoxification.

Marker Enzyme

- Glucose-6-Phosphatase (SER) – Important in gluconeogenesis.

Clinical Connection

- Cystic Fibrosis: Misfolded CFTR protein accumulates in RER → Thick mucus formation.

TIP

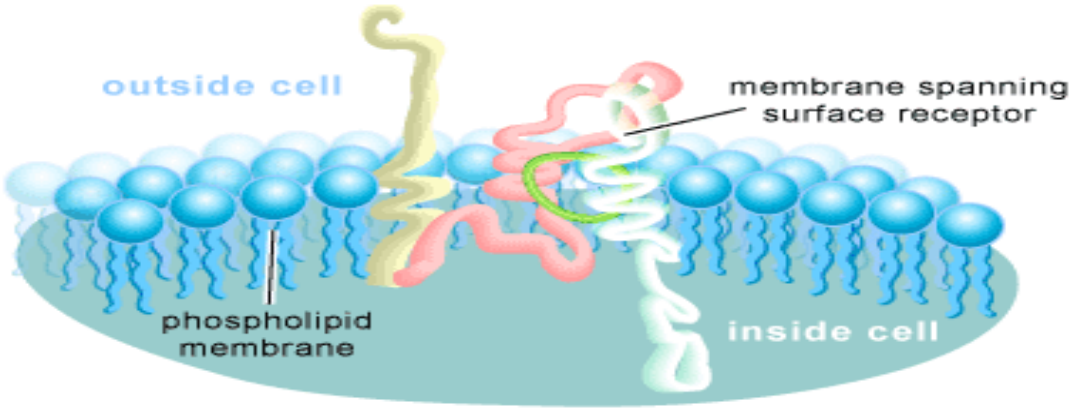
(Imagine a flowchart: DNA → mRNA → RER → Golgi → Secreted Protein.)

Chemistry of Cell Surface Receptors and Associated Signaling Mechanisms

Cell surface receptors are specialized proteins embedded in the plasma membrane that detect and transmit extracellular signals to the cell's interior. These receptors play a crucial role in cell communication, homeostasis, and response to external stimuli such as hormones, neurotransmitters, and growth factors.

The chemistry of cell surface receptors involves protein-ligand interactions, conformational changes, and biochemical cascades that lead to cellular responses. These receptors exhibit specificity for their ligands and function through signaling pathways that amplify and regulate cellular processes.

Chemical Composition and Structure of Cell Surface Receptors



Cell surface receptors are primarily composed of glycoproteins with distinct domains that facilitate ligand binding, signal transduction, and intracellular communication. Their structure typically includes:

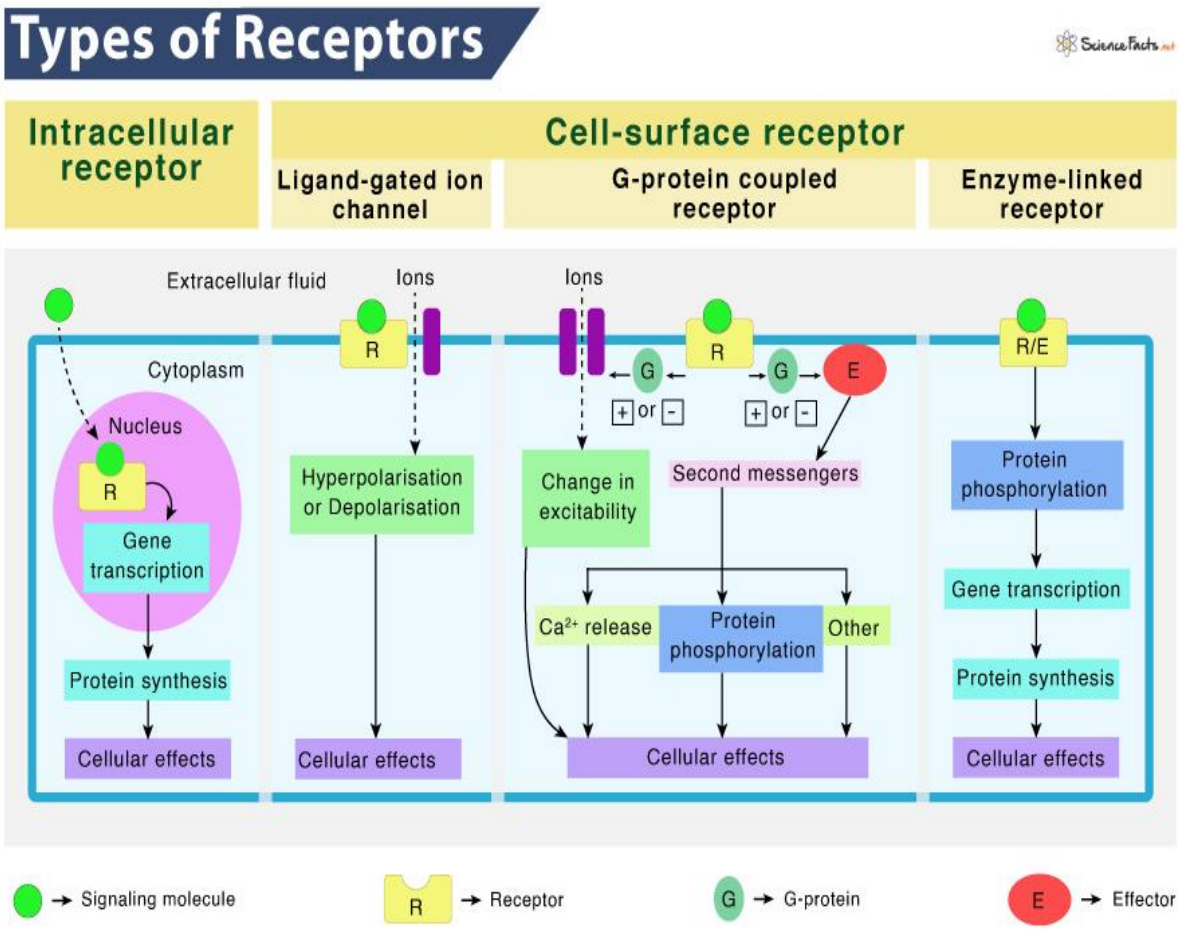
1. Extracellular Domain – Binds to the ligand (e.g., hormones, cytokines, neurotransmitters).

2. Transmembrane Domain – Anchors the receptor in the membrane and transduces signals across the bilayer.

3. Intracellular Domain – Interacts with intracellular signaling proteins to propagate the response.

Receptor proteins are composed of amino acids linked by peptide bonds, often containing disulfide bridges to stabilize their tertiary structure. Many receptors undergo post-translational modifications, such as phosphorylation, glycosylation, and ubiquitination, which regulate their function and lifespan.

Types of Cell Surface Receptors and Their Signaling Mechanisms

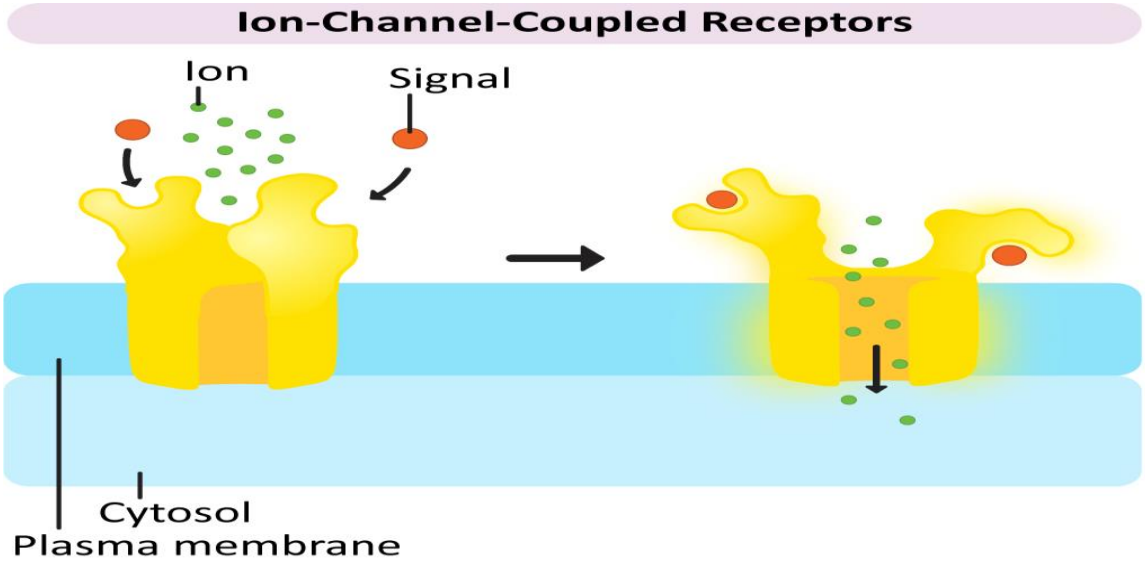


1. Ion Channel-Linked Receptors (Ligand-Gated Ion Channels): These receptors function as ion channels that open or close upon ligand binding, allowing ions such as Na^+, K^+, Ca^{2+}, or Cl^- to pass through the membrane.

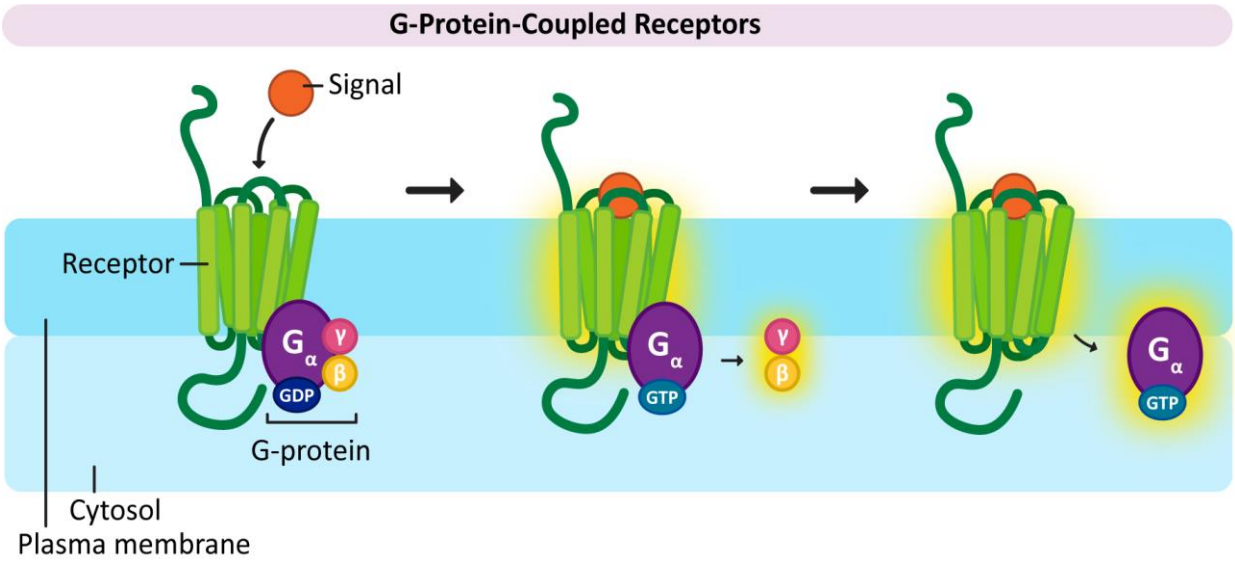
- **Example:** Nicotinic Acetylcholine Receptor (nAChR)
- **Structure:** Five subunits forming a pore.
- **Mechanism:** When acetylcholine (ACh) binds to the receptor, it induces a conformational change, opening the channel and allowing Na^+ influx, leading to membrane depolarization and muscle contraction.
- **Clinical Relevance:**
    - Myasthenia Gravis: Autoimmune disease where antibodies block nAChRs, leading to muscle weakness.
    - Neurotoxins like Curare: Block nAChRs, causing paralysis.

2. G Protein-Coupled Receptors (GPCRs): GPCRs are the largest family of cell surface receptors and are involved in hormone signaling, neurotransmission, and sensory perception. These receptors contain seven transmembrane α-helices and function via intracellular G proteins (GTP-binding proteins).

- **Example:** β-Adrenergic Receptor (β-AR)
- **Mechanism:**
    - 1. Ligand Binding: Epinephrine binds to the β-adrenergic receptor.
    - 2. G Protein Activation: The receptor activates a heterotrimeric G protein (Gs) by exchanging GDP for GTP.
    - 3. Second Messenger Cascade: The activated G protein stimulates adenylyl cyclase, increasing cAMP levels.
    - 4. Cellular Response: cAMP activates protein kinase A (PKA), leading to glycogen breakdown and energy release.
- **Clinical Relevance:**

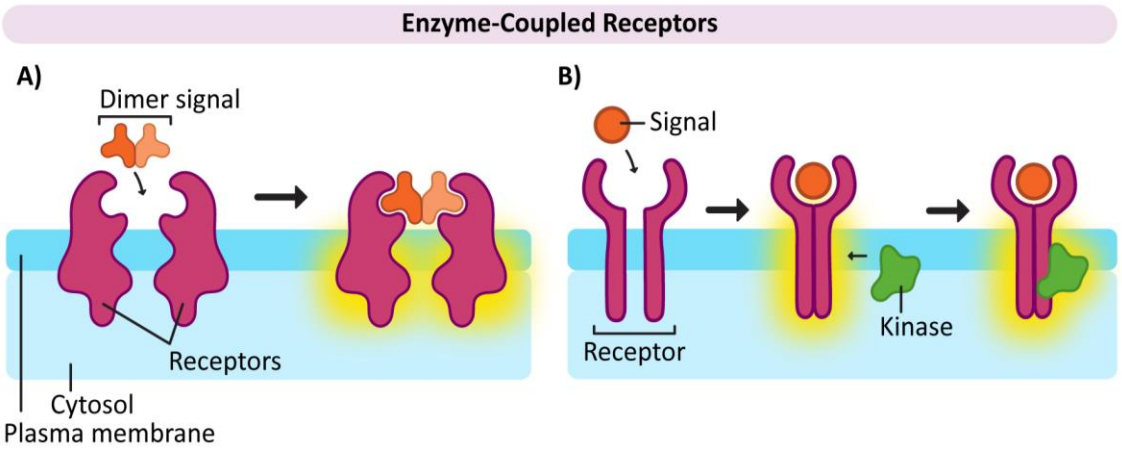


    - β-Blockers (e.g., Propranolol): Inhibit β-adrenergic receptors to reduce heart rate in hypertension.
    - Cholera Toxin: Permanently activates Gs proteins, leading to excessive cAMP and severe diarrhea.



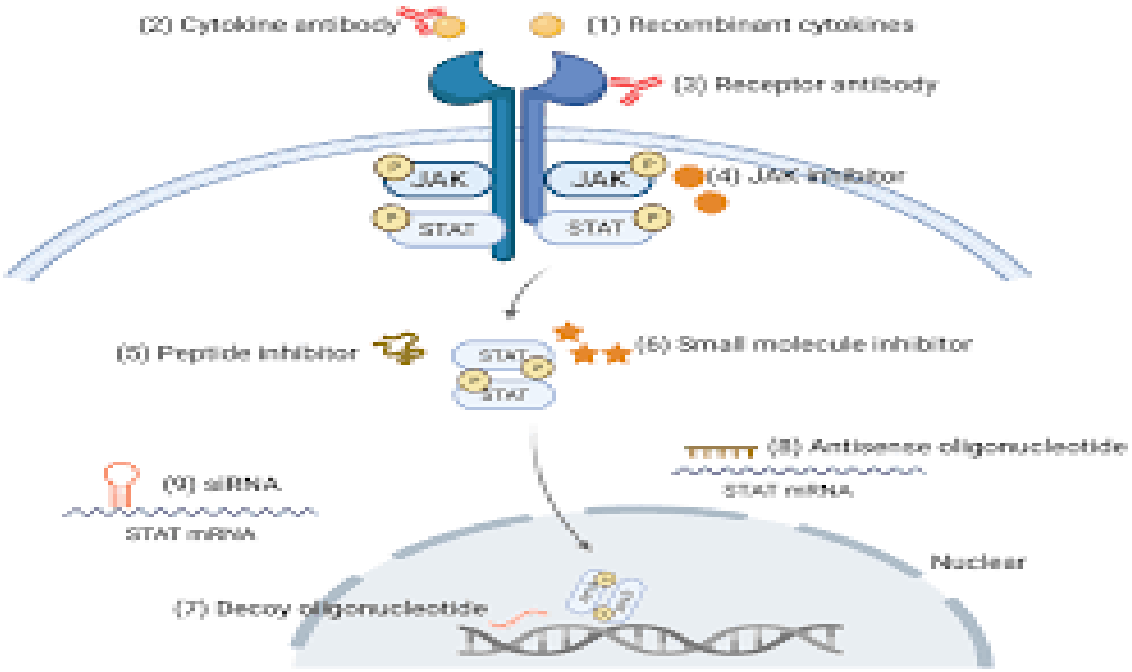
3. Enzyme-Linked Receptors (Tyrosine Kinase Receptors – RTKs): These receptors possess intrinsic enzyme activity or associate with intracellular kinases to mediate growth, differentiation, and metabolism.

- **Example:** Insulin Receptor
- **Mechanism:**
    - 1. Insulin Binding: Triggers autophosphorylation of tyrosine residues.
    - 2. Recruitment of Adapter Proteins: IRS (Insulin Receptor Substrate) proteins are phosphorylated.
    - 3. Downstream Signaling: Activates the PI3K-Akt pathway, leading to glucose uptake via GLUT4 transporters.
- **Clinical Relevance:**
    - Type 2 Diabetes Mellitus (T2DM): Insulin resistance due to defects in insulin receptor signaling.
    - Cancer (e.g., Breast Cancer): Overexpression of HER2, a tyrosine kinase receptor, promotes uncontrolled cell growth.



4. Cytokine Receptors (JAK-STAT Pathway): These receptors lack intrinsic enzyme activity but activate Janus Kinases (JAKs) upon ligand binding, leading to signal transduction via STAT (Signal Transducers and Activators of Transcription) proteins.

- **Example:** Interleukin-6 (IL-6) Receptor
- **Mechanism:**
    - 1. IL-6 binds to its receptor.
    - 2. JAK phosphorylates STAT proteins.
    - 3. STAT dimerizes and translocates to the nucleus to regulate gene expression.
- **Clinical Relevance:**
    - Autoimmune Diseases (e.g., Rheumatoid Arthritis): Excessive cytokine signaling leads to inflammation.
    - JAK Inhibitors (e.g., Tofacitinib): Used to treat rheumatoid arthritis by blocking JAK-STAT signaling.



- **Signal Amplification and Regulation**
  - Second Messengers: Small molecules like cAMP, Ca^{2+}, IP_3, and DAG amplify the signal inside the cell.
  - Phosphorylation Cascades: Protein kinases phosphorylate downstream proteins to propagate and amplify signals.
  - Feedback Mechanisms: Negative feedback loops turn off signals to prevent overstimulation.
    - Example: cAMP is broken down by phosphodiesterase (PDE) to terminate the signal in GPCR pathways.

Mnemonics for Cell Surface Receptors:

"G-E-C-I" – Major Types of Receptors

- **G-protein coupled**
- **Enzyme-linked (Tyrosine Kinase)**
- **Cytokine receptors (JAK-STAT)**
- **Ion-channel linked**

"I-G-E-C" – Order of Signaling Speed

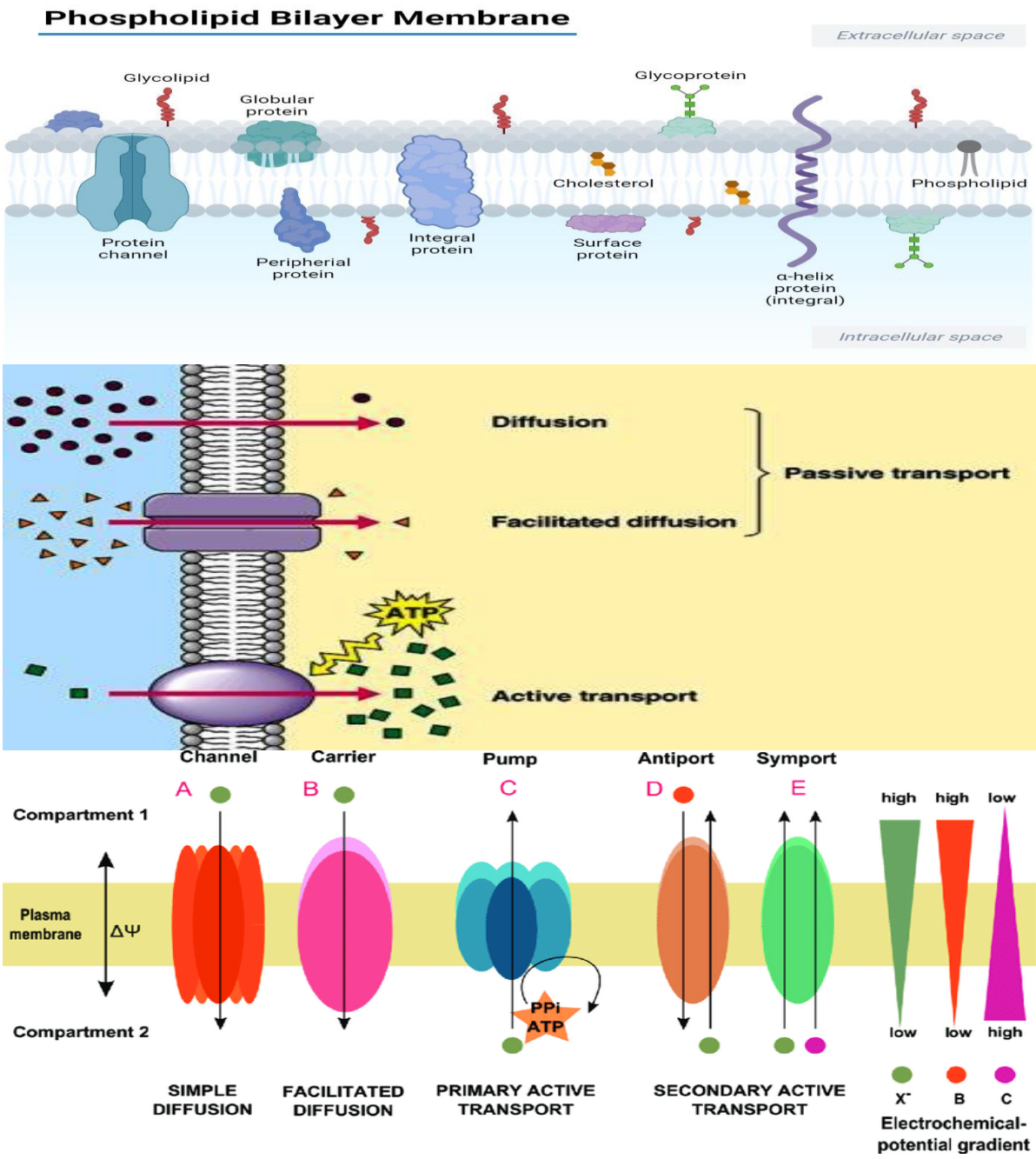
- **Ion channels (milliseconds)**
- **GPCRs (seconds)**
- **Enzyme-linked (minutes)**

- **Cytokine receptors (hours)**

Fun Facts!

- 70% of all drugs target GPCRs due to their involvement in diverse physiological processes.
- The olfactory system (sense of smell) relies entirely on GPCRs.
- Botulinum toxin (Botox) blocks neurotransmitter release by preventing vesicle docking at GPCR-regulated synapses.

Comparison of the Biochemical Basis of Various Membrane Transport Mechanisms



Membrane transport mechanisms regulate the movement of ions, nutrients, and metabolites across biological membranes. These processes are essential for cellular metabolism, signal transduction, homeostasis, and energy production. The transport mechanisms differ in their biochemical properties, including energy dependency, specificity, and directionality.

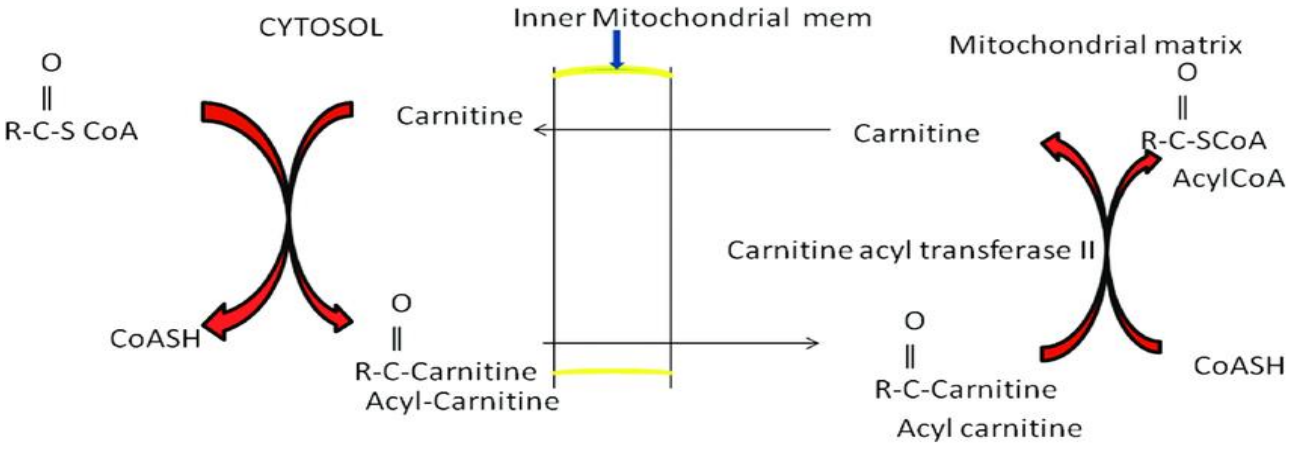
1. GLUTs (Glucose Transporters) – Facilitated Diffusion

- Biochemical Basis: GLUTs transport glucose passively via facilitated diffusion, meaning they do not require ATP. They utilize a concentration gradient, moving glucose from a region of high concentration to low concentration.
- **Key Features:**
    - Carrier-mediated transport (undergoes conformational change).
    - Works via uniport (transports glucose alone, without coupling to other molecules).
    - GLUT1 (RBCs, brain), GLUT2 (liver, pancreas), GLUT4 (insulin-sensitive, muscle, fat).
- **Clinical Relevance:**
    - Diabetes Mellitus: Impaired GLUT4 translocation reduces glucose uptake.
    - GLUT1 Deficiency Syndrome: Neurological disorder due to defective glucose transport into the brain.

2. SGLT (Sodium-Glucose Linked Transporters) – Secondary Active Transport

- Biochemical Basis: SGLT transporters couple glucose transport to sodium (Na^+) movement, using the Na^+ gradient generated by the Na^+/K^+ ATPase pump. This process is an example of secondary active transport, where the energy from Na^+ movement drives glucose uptake against its concentration gradient.
- **Key Features:**
    - Symport mechanism (transports glucose and Na^+ in the same direction).
    - SGLT1 (intestines, kidney) and SGLT2 (proximal tubule of the kidney).
- **Clinical Relevance:**
    - SGLT2 Inhibitors (e.g., Empagliflozin): Used in type 2 diabetes to reduce glucose reabsorption in kidneys.
    - Glucose-Galactose Malabsorption: Defective SGLT1 causes severe diarrhea due to impaired intestinal glucose uptake.

3. Carnitine Shuttle – Fatty Acid Transport into Mitochondria



- Biochemical Basis: The carnitine shuttle transports long-chain fatty acids into the mitochondrial matrix for β-oxidation. Since fatty acyl-CoA cannot cross the inner mitochondrial membrane, it is first converted into fatty acyl-carnitine by carnitine palmitoyltransferase I (CPT-I).
- **Key Features:**
  - CPT-I (Outer membrane): Converts fatty acyl-CoA to fatty acyl-carnitine.
  - Carnitine-Acylcarnitine Translocase: Transports fatty acyl-carnitine across the inner membrane.
  - CPT-II (Inner membrane): Converts fatty acyl-carnitine back to fatty acyl-CoA.
- **Clinical Relevance:**
  - Carnitine Deficiency: Leads to impaired fatty acid oxidation, causing muscle weakness and hypoglycemia.
  - CPT-I Deficiency: Affects liver metabolism, leading to hypoketotic hypoglycemia.

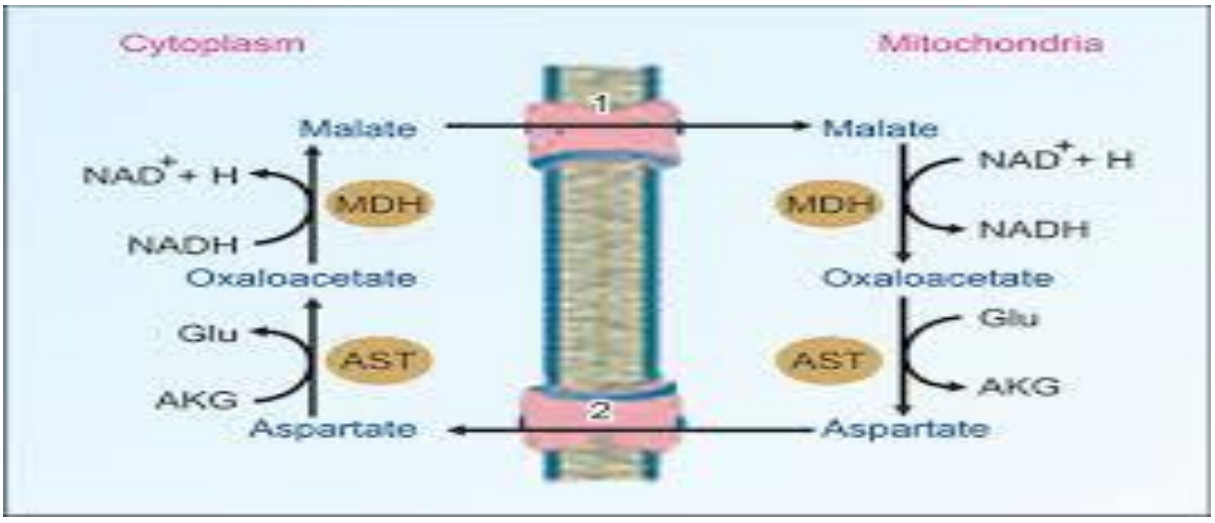
4. H^+/K^+ ATPase Pump – Primary Active Transport

- Biochemical Basis: This ATP-dependent pump exchanges intracellular H^+ for extracellular K^+, maintaining gastric acid secretion in parietal cells of the stomach. The energy required is derived from ATP hydrolysis, making it an example of primary active transport.
- **Key Features:**
  - Antiport mechanism (H^+ out, K^+ in).
  - Located in gastric parietal cells for acid secretion.
- **Clinical Relevance:**
  - Proton Pump Inhibitors (PPIs) (e.g., Omeprazole): Inhibit H^+/K^+ ATPase to treat GERD and peptic ulcers.
  - Hypochlorhydria: Reduced acid secretion due to pump dysfunction.

5. Cl^- Ion Channels – Passive Ion Transport

- Biochemical Basis: Chloride (Cl^-) channels allow the passive movement of Cl^- ions down their electrochemical gradient. They regulate membrane potential, fluid secretion, and neuronal excitability.
- **Key Features:**
  - Found in epithelial cells, neurons, and muscle cells.
  - Involved in Cl^- secretion in sweat glands, lungs, and intestines.
- **Clinical Relevance:**
  - Cystic Fibrosis (CF): Mutations in the CFTR (Cystic Fibrosis Transmembrane Conductance Regulator) gene impair Cl^- transport, leading to thick mucus production in the lungs and digestive tract.

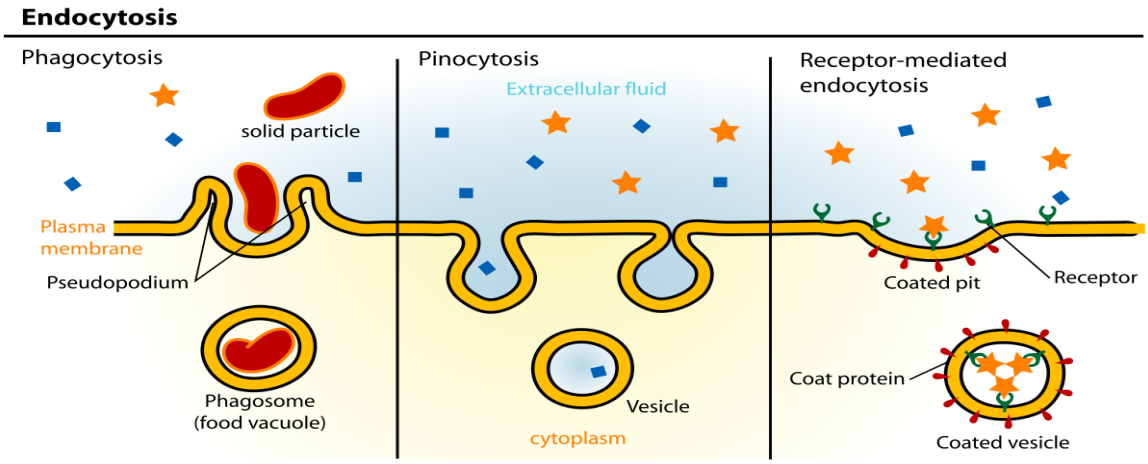
6. Malate Shuttle – NADH Transport Between Cytoplasm and Mitochondria



- Biochemical Basis: Since NADH cannot cross the mitochondrial membrane, the malate shuttle transfers reducing equivalents (electrons) into the mitochondria to facilitate oxidative phosphorylation.
- **Key Features:**
    - Malate crosses into mitochondria, where it is oxidized to oxaloacetate, regenerating NADH.
    - Aspartate returns to the cytoplasm, completing the cycle.
- **Clinical Relevance:**
    - Essential for ATP production in cells lacking direct NADH transport.
    - Defects impair energy metabolism, leading to lactic acidosis.

7. Receptor-Mediated Endocytosis – Selective Uptake of Macromolecules

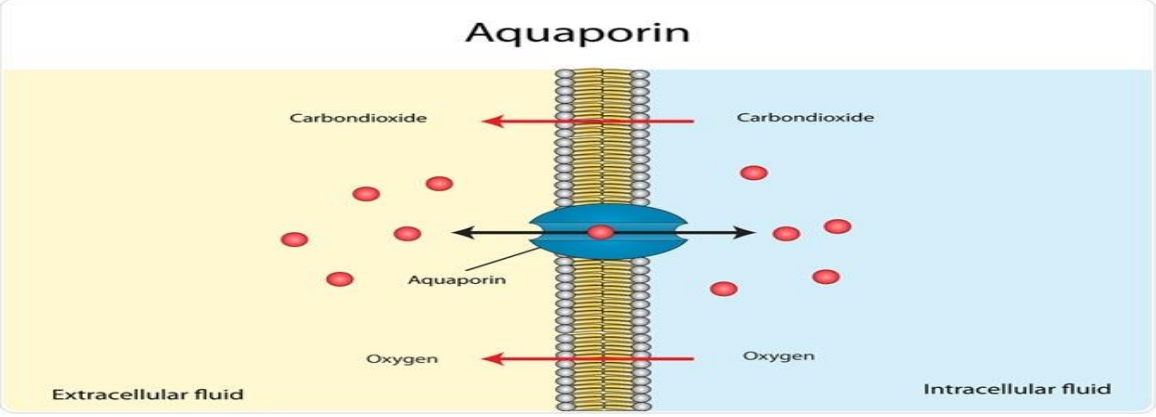
- Biochemical Basis: This clathrin-dependent process enables cells to internalize specific ligands via receptor binding. Ligand-receptor complexes are internalized into clathrin-coated vesicles, which later fuse with endosomes for processing.



- **Key Features:**
  - Used for LDL cholesterol uptake, iron transport (via transferrin), and hormone signaling.
  - Involves clathrin-coated pits on the plasma membrane.
- **Clinical Relevance:**
  - Familial Hypercholesterolemia (FH): Defective LDL receptors impair cholesterol uptake, leading to atherosclerosis.

8. Aquaporins – Water Channels for Osmotic Balance

- Biochemical Basis: Aquaporins are passive water channels that allow the movement of water molecules down their concentration gradient, facilitating rapid osmosis.



- **Key Features:**
  - Found in kidneys, brain, and red blood cells.
  - Regulate water homeostasis.
- **Clinical Relevance:**
  - Diabetes Insipidus: Defective Aquaporin-2 (AQP2) results in excessive water loss and polyuria.

- Brain Edema: AQP4 regulates water balance in brain cells.

9. ATP-Sensitive K^+ (KATP) Channels – Metabolic Sensors

- Biochemical Basis: KATP channels open or close in response to ATP levels, linking cell metabolism to electrical activity.
- **Key Features:**
  - Found in pancreatic β-cells, cardiac myocytes, and neurons.
  - Regulated by ATP/ADP ratio.
- **Clinical Relevance:**
  - Sulfonylurea Drugs (e.g., Glibenclamide): Block KATP channels in pancreatic β-cells to increase insulin secretion in type 2 diabetes.

□ SECTION II: ENZYMES

⚡ 1. Classification & Mechanism of Enzyme Action

□ Key Concepts

✓Enzymes are biological catalysts that lower activation energy.

✓Lock & Key vs. Induced Fit Model – How enzymes bind to substrates.

✓Classes of Enzymes (Mnemonic: LIL HOT)

1. Lyases → Break bonds without water

2. Isomerases → Rearrange molecular structure

3. Ligases → Join molecules using ATP

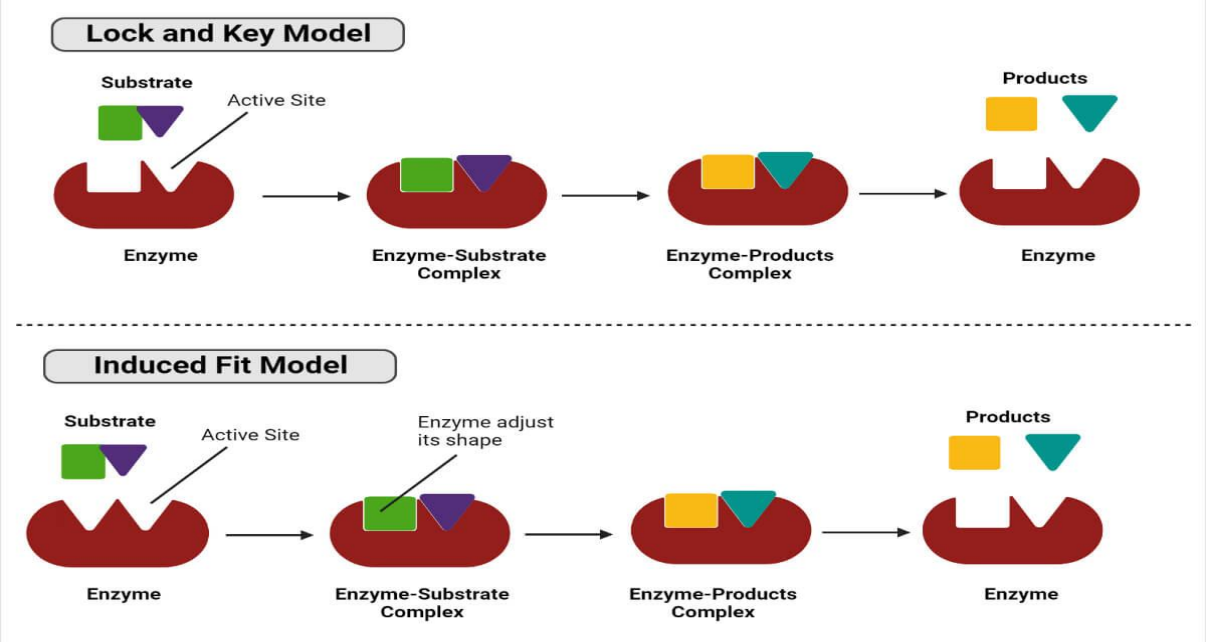
4. Hydrolases → Break bonds using water

5. Oxidoreductases → Redox reactions

6. Transferases → Transfer functional groups

Enzymes are the biological catalysts that accelerate biochemical reactions by lowering activation energy. Their role in metabolism, digestion, cellular regulation, and clinical diagnostics makes them fundamental in medical biochemistry.

Lock & Key vs. Induced Fit Model – How enzymes bind to substrates.



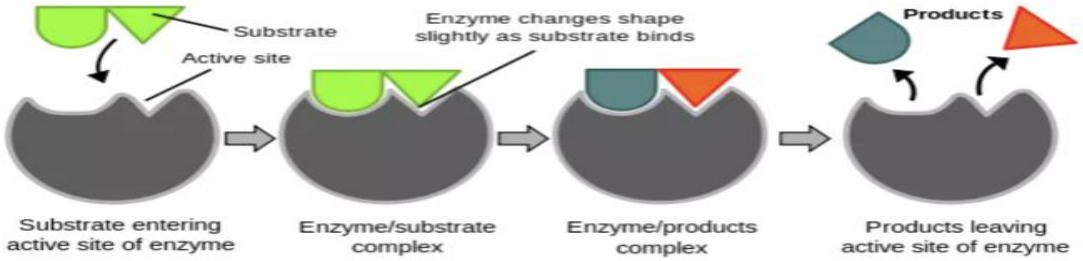


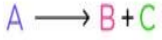
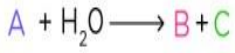
Fig 1. Induced Fit Model. Substrate binds to the enzyme's active site. As substrate binds, the shape of the active site changes slightly. If the substrate enables the active site's shape to change in the right way then the reaction takes place and an enzyme-product complex is formed. The products are then released from the active site.

1. Classification of Enzymes

Biochemical Basis : Enzymes are classified into six major categories based on the type of reaction they catalyze:

- Oxidoreductases – Catalyze redox reactions.
  - Example: Lactate dehydrogenase (LDH) (converts lactate to pyruvate).
- Transferases – Transfer functional groups.
  - Example: Alanine aminotransferase (ALT) (transfers amino groups).
- Hydrolases – Catalyze hydrolysis reactions (break bonds using water).
  - Example: Amylase (digests starch into maltose).

- Lyases – Break bonds without hydrolysis or oxidation.
    - Example: Adenylate cyclase (forms cyclic AMP).
- Isomerases – Catalyze rearrangement within molecules.
    - Example: Phosphoglucomutase (converts glucose-1-phosphate to glucose-6-phosphate).
- Ligases – Join molecules using ATP.
    - Example: DNA Ligase (seals DNA strands during replication).

6 Types of Enzymes	
Enzyme	**Function**
Lyase	Dissociates molecules, breaks covalent bonds without using water, oxidation, or reduction (ex: Decarboxylase) 
Ligase	Joins two molecules together, forms covalent bonds between two molecules (ex: DNA ligase) 
Isomerase	Rearranges bonds of a molecule, a reactant forms one of its isomers (ex: phosphoglucose isomerase, mutase) 
Transferase	Transfers functional group from one molecule to another (ex: kinase, phosphorylase, peptidyl transferease) 
Hydrolase	Uses water to cleave a molecule, breaks covalent bonds with water (ex: hydrolase, phosphatase, protease) 
Oxidoreductase	Transfers electrons from one molecule to another, alters oxidation state of reactants (ex: lactate dehydrogenase) 

Mnemonic: "Over The HILL"

- **Oxidoreductases**
- **Transferases**
- **Hydrolases**
- **Isomerases**
- **Lyases**
- **Ligases**

□ THINK TANK:

Why are oxidoreductases vital for energy production?

How do hydrolases contribute to digestion?

□ Fill in the Blanks:

1. Enzymes that catalyze oxidation-reduction reactions are called _____.

(Answer: Oxidoreductases)

2. Ligases require _____ to form bonds between molecules.

(Answer: ATP)

?MCQ:

Which class of enzymes catalyzes the transfer of phosphate groups?

A) Lyases

B) Hydrolases

C) Transferases

D) Isomerases

(Answer: C) Transferases

2. Mechanism of Enzyme Action

Key Concepts

- **Substrate binds to the active site forming an enzyme-substrate complex.**
- **The enzyme stabilizes the transition state, lowering activation energy.**
- **The product is released, and the enzyme remains unchanged.**

Models of Enzyme Action

- Lock and Key Model – The substrate fits perfectly into the active site.
- Induced Fit Model – The enzyme undergoes conformational change upon binding.

Clinical Relevance:

- HIV Protease Inhibitors block the active site of viral proteases.
- Aspirin irreversibly inhibits cyclooxygenase (COX) to reduce inflammation.

□ Fun Fact:

- The fastest enzyme is Carbonic Anhydrase! It can catalyze one million reactions per second to convert CO_2 into bicarbonate.

□ Short Answer Question (SAQ):

Explain how enzymes lower activation energy.

3. Components of Enzymes

The Parts of an Enzyme

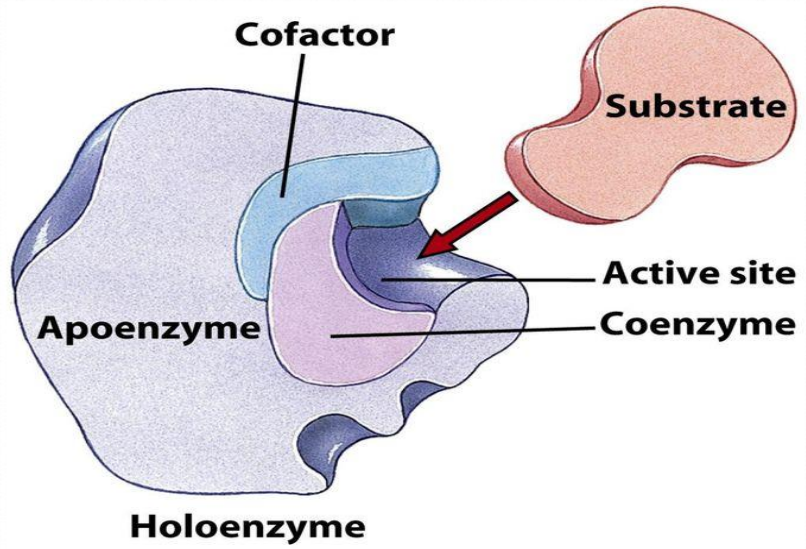


Figure 5-6 Microbiology, 6/e
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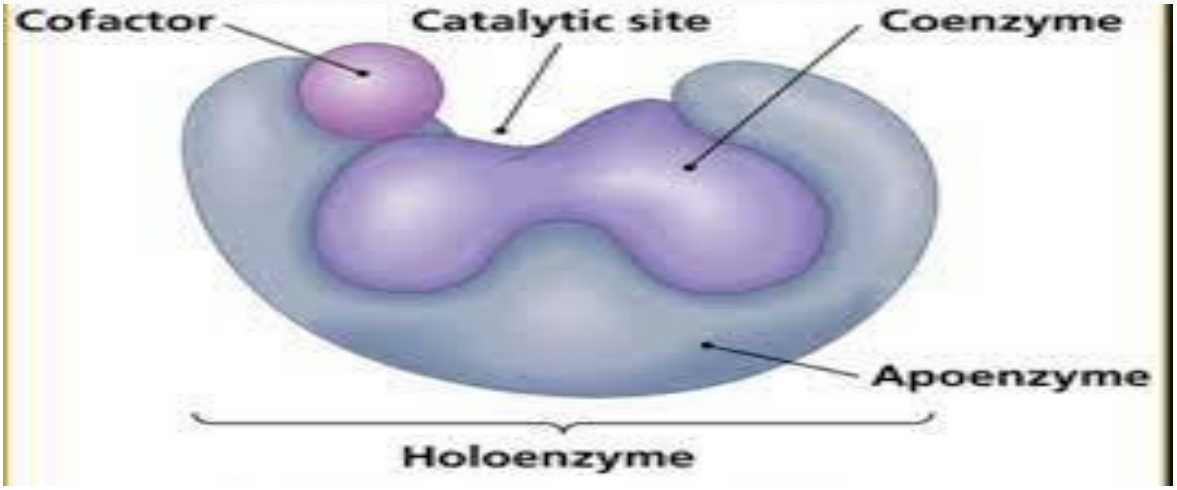


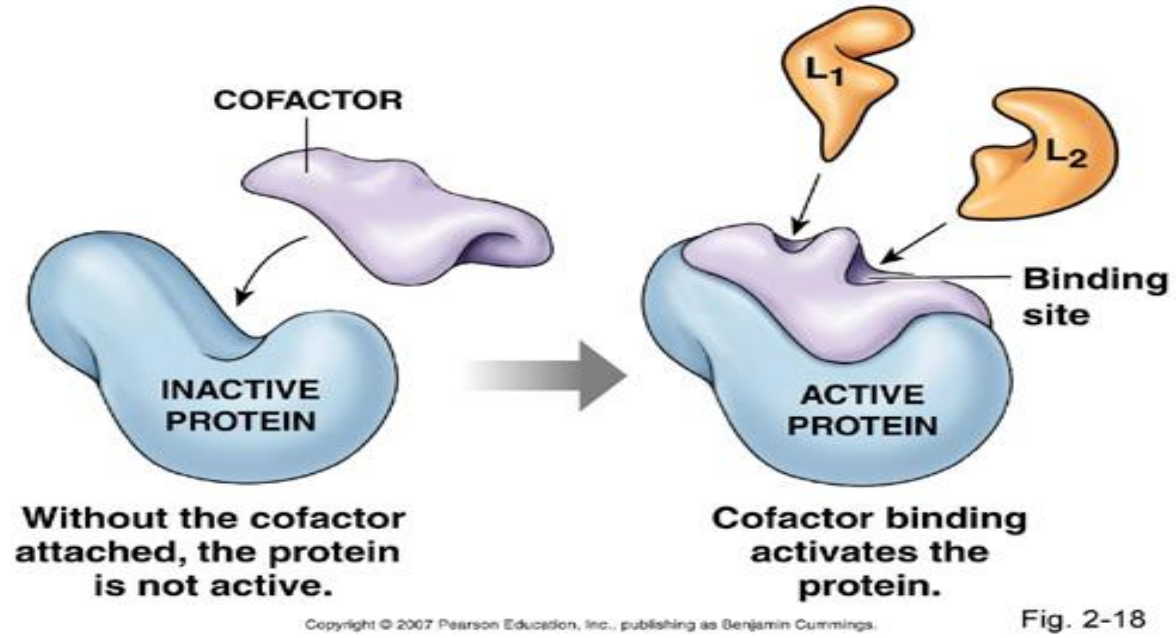
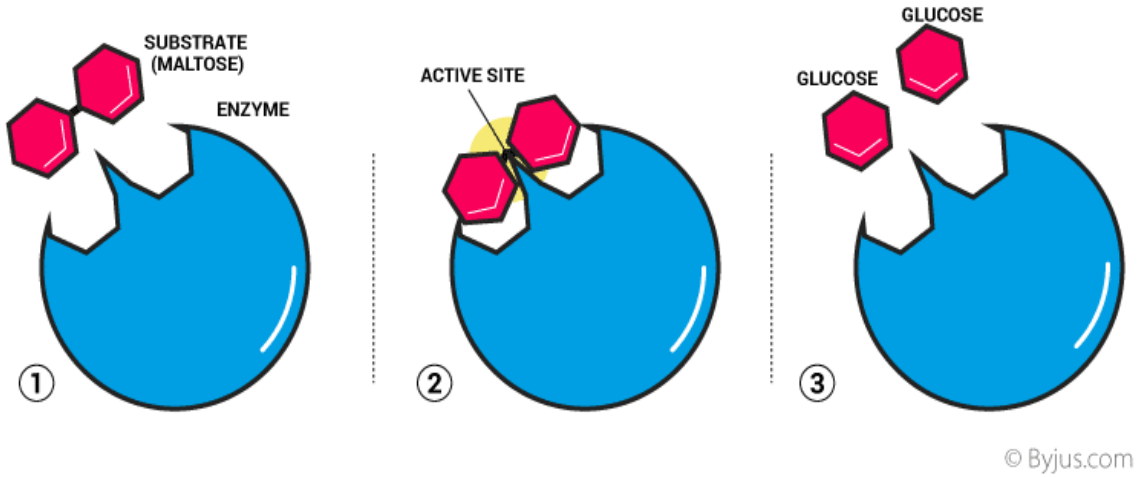


Fig. 2-18



Key Terms:

- **Apoenzyme – Protein part of an enzyme (inactive alone).**
- **Holoenzyme – Active enzyme with a cofactor or coenzyme.**
- **Cofactors – Metal ions (Mg^{2+}, Zn^{2+}, Fe^{2+}) needed for enzyme function.**
- **Coenzymes – Organic molecules (NAD^{+}, FAD, biotin) required for enzyme activity.**
- **Prosthetic Group – A permanently bound coenzyme (e.g., FAD in succinate dehydrogenase).**

Clinical Relevance:

- Zinc Deficiency → Affects carbonic anhydrase, impairing CO_2 removal.
- Vitamin B Deficiency → Affects enzymes involved in energy metabolism.

✍ Fill in the Blanks:

1. The protein part of an enzyme that requires a cofactor is called _____.

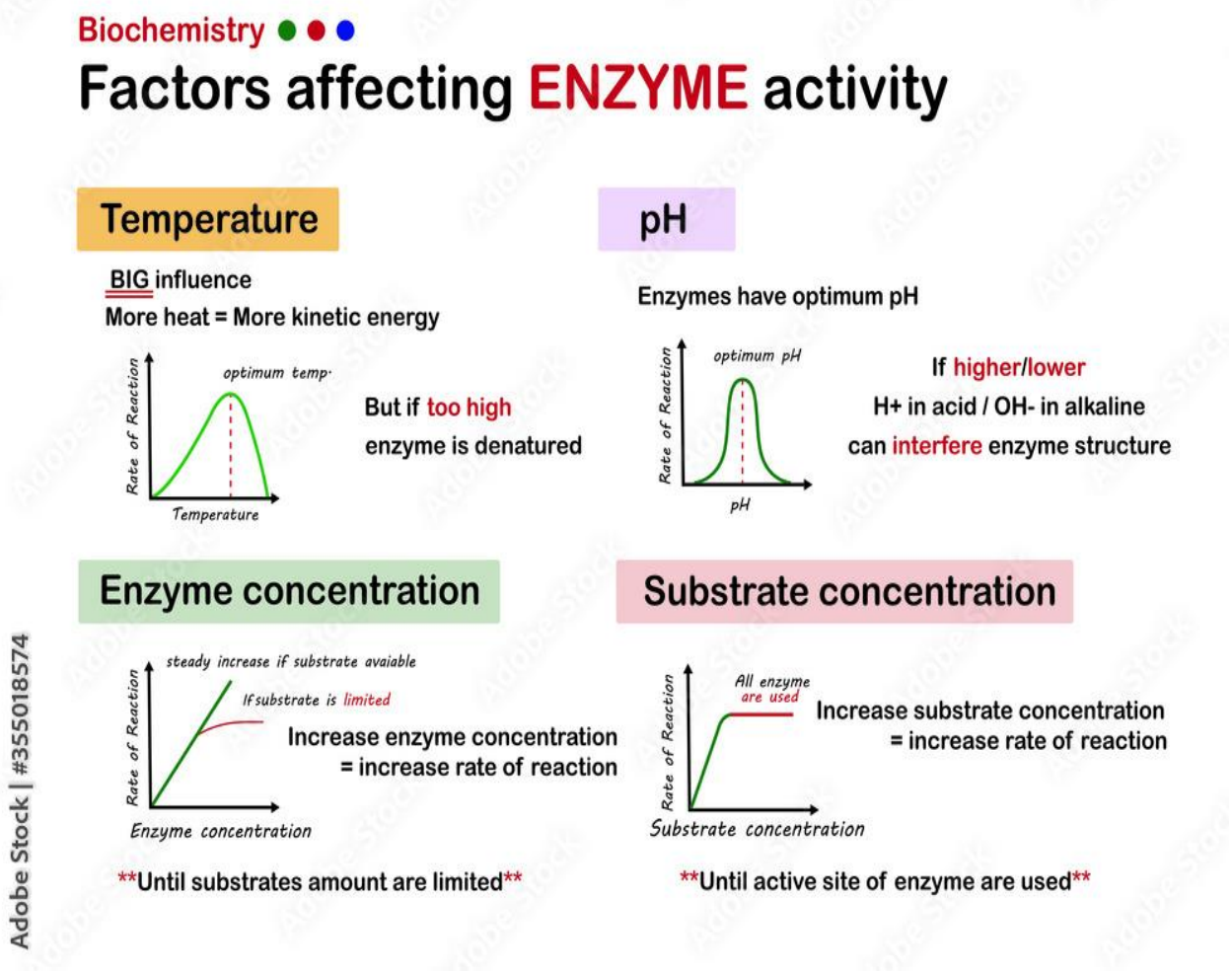
(Answer: Apoenzyme)

2. _____ is a permanently bound coenzyme. (Answer: Prosthetic group)

4. Factors Affecting Enzyme Activity

Key Factors:

- **1. Temperature – Optimal at 37°C; too high causes denaturation.**
- **2. pH – Each enzyme has an optimal pH (Pepsin: pH 2, Amylase: pH 7).**
- **3. Substrate Concentration – Increases activity until saturation.**
- **4. Enzyme Concentration – More enzyme increases reaction rate.**
- **5. Inhibitors – Competitive and non-competitive inhibitors reduce activity.**



Clinical Relevance:

- Hypochlorhydria affects pepsin function leading to digestive issues.

❓ SAQ:

How does temperature affect enzyme activity?

5. ? Enzyme Kinetics & The Michaelis-Menten Equation

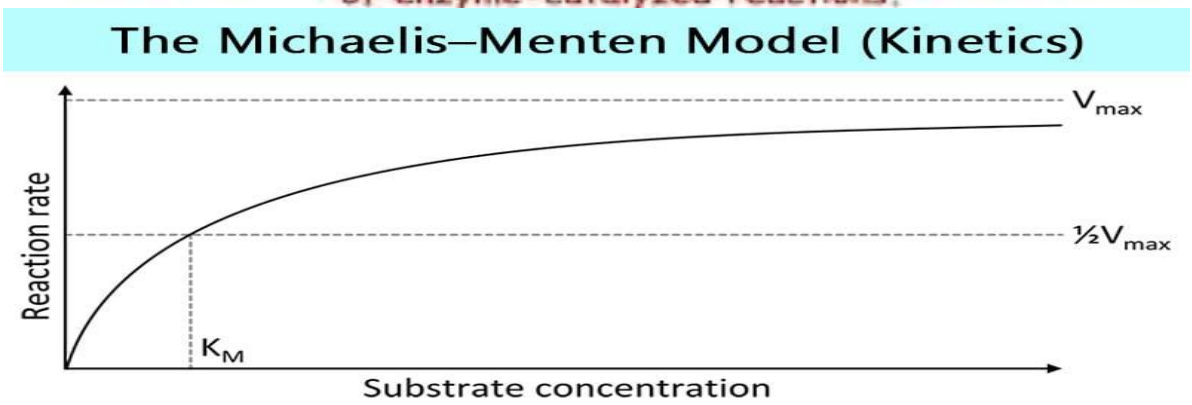
Key Concepts:

- **Michaelis-Menten Equation: Describes the relationship between substrate concentration (S) and enzyme velocity (V_o).**
- **Km (Michaelis constant) – Measures enzyme affinity for the substrate.**
- **Lineweaver-Burk Plot: A double-reciprocal graph used to determine Km and Vmax.**

Michaelis-Menten Equation

$$V_0 = \frac{V_{max}[S]}{K_m + [S]}$$

The Michaelis-Menten equation describes the relationship between substrate and enzyme concentrations and the rates of enzyme-catalyzed reactions.



Clinical Relevance:

- Hexokinase (Low Km) → Active at low glucose levels.
- Glucokinase (High Km) → Active when glucose levels are high in the liver.

Self-Assessment:

Fill in the blanks:

The Michaelis-Menten equation describes enzyme ____.

Km is the substrate concentration at which the reaction rate is ____ of Vmax.

Answers: kinetics, half

Mnemonic: "Km is the Key to Affinity" (Lower Km = Higher Affinity)

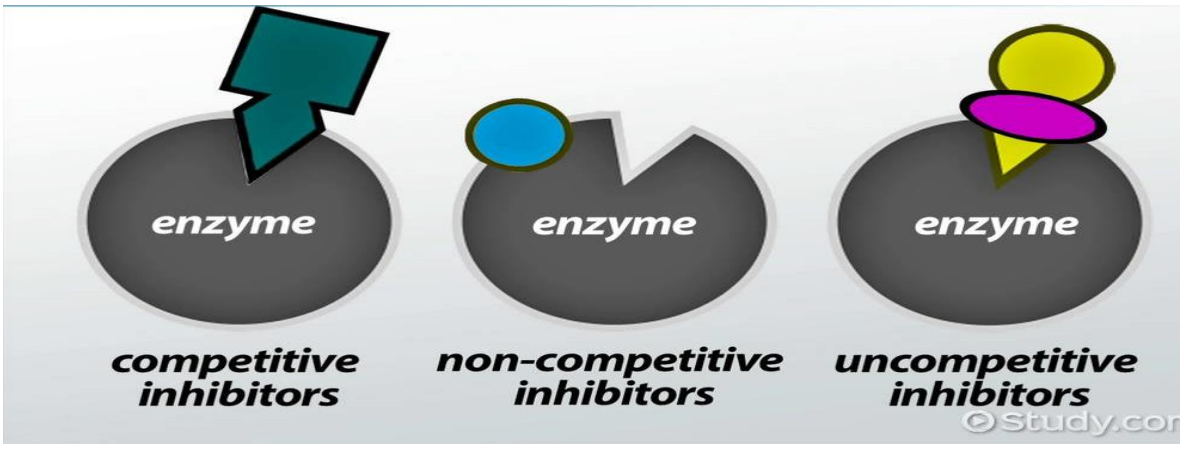
Fun Fact:

One molecule of catalase can break down 40 million hydrogen peroxide molecules per second!

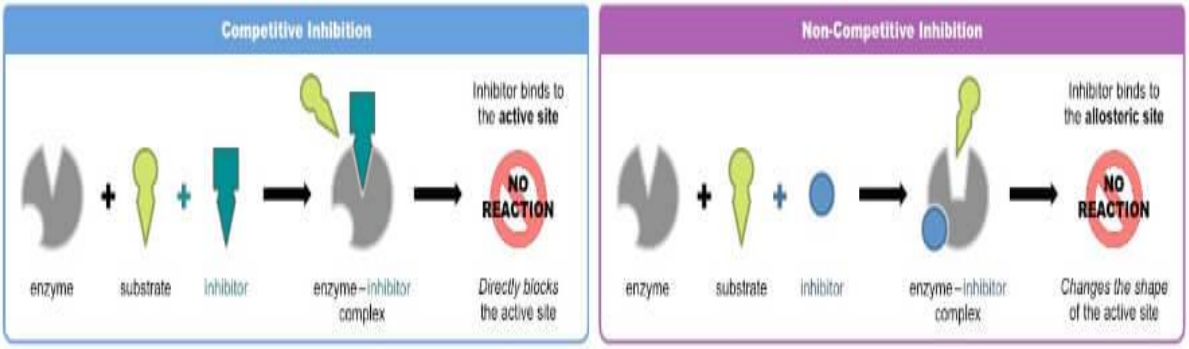
THINK TANK:

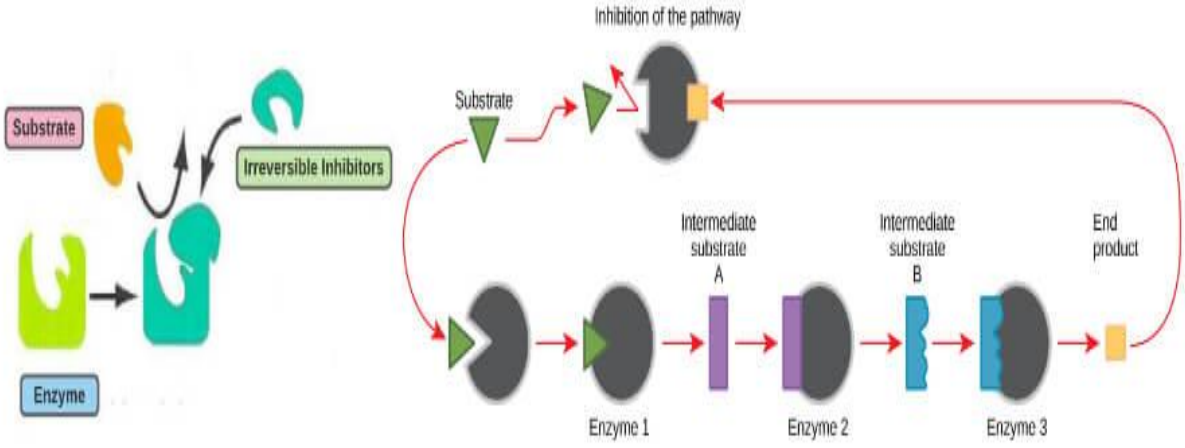
Why is the Lineweaver-Burk plot useful in enzyme kinetics?

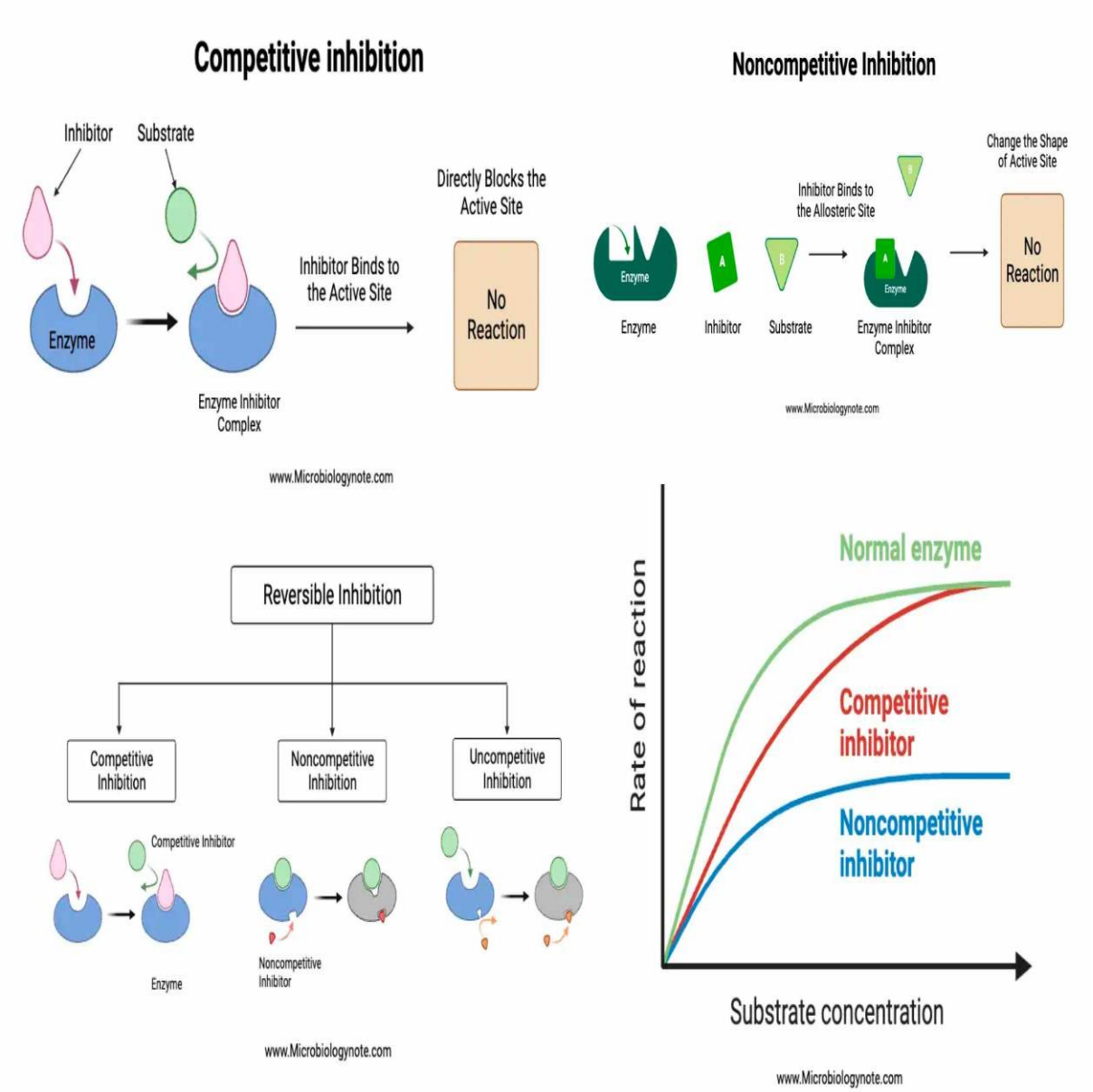
6. Types of Enzyme Inhibition



Enzyme Inhibitors and Enzyme Inhibition







1. Competitive Inhibition – Inhibitor competes with the substrate for the active site.

- Example: Statins inhibit HMG-CoA reductase (cholesterol synthesis).

2. Non-Competitive Inhibition – Inhibitor binds elsewhere, reducing enzyme function.

- Example: Cyanide inhibits cytochrome oxidase, blocking respiration.

Clinical Relevance:

- Methanol Poisoning → Treated with ethanol, a competitive inhibitor of alcohol dehydrogenase.

❓ MCQ:

Which inhibitor binds at a site other than the active site?

A) Competitive

B) Non-Competitive

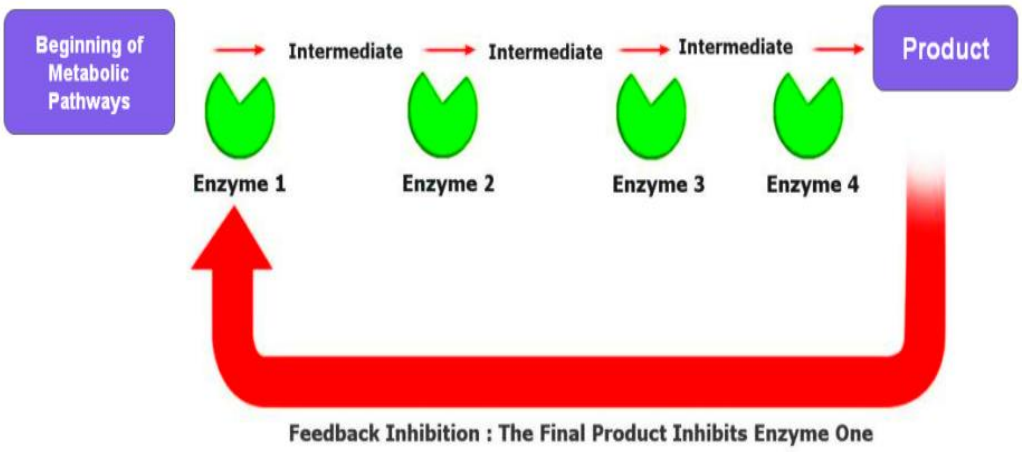
C) Allosteric

D) Reversible

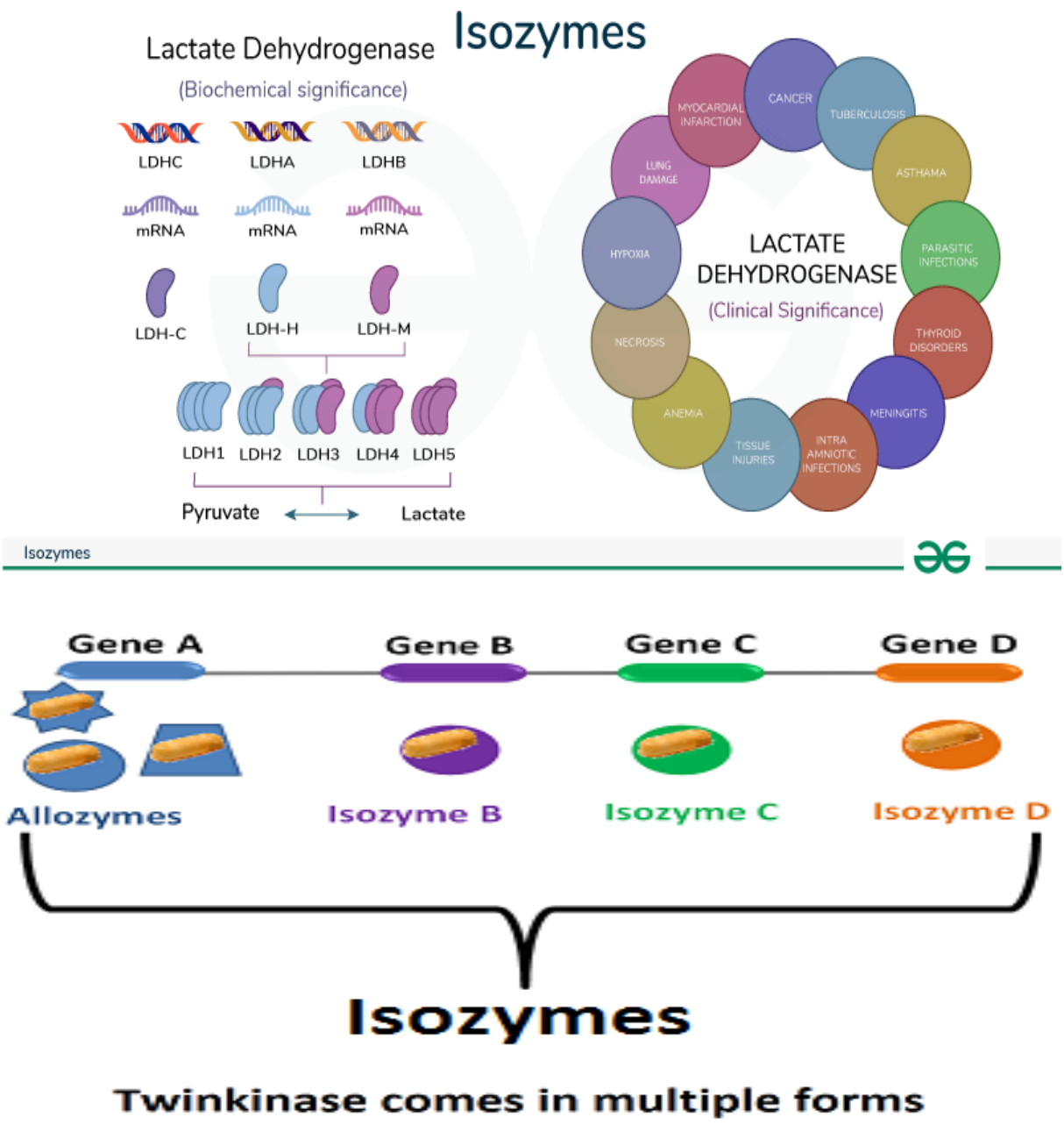
(Answer: B) Non-Competitive

7. Enzyme Regulation & Isoenzymes

- Regulated by feedback inhibition.



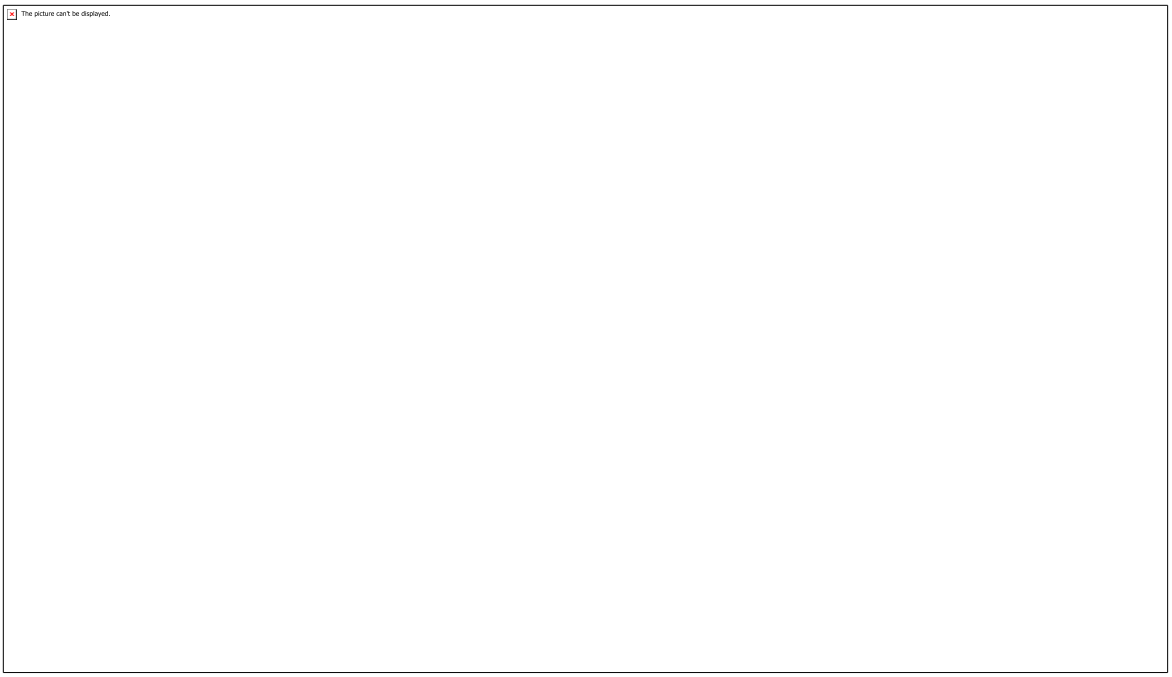
- Isoenzymes → Different forms of an enzyme with tissue-specific activity.
    - CK-MB → Cardiac marker for myocardial infarction.
    - LDH-1 → Elevated in heart attack patients.



Role of Minerals as Cofactors & Vitamins as Coenzymes in Medical Biochemistry

Cofactors and coenzymes are essential for enzymatic function. Minerals (cofactors) and vitamins (coenzymes) play key roles in metabolism, cellular energy production, and enzymatic regulation. Their deficiencies can lead to metabolic disorders, neurological dysfunction, and cardiovascular diseases.

1. Role of Minerals as Cofactors



Biochemical Basis: Minerals act as inorganic cofactors for enzymes, facilitating catalysis, electron transfer, and structural stability. Some enzymes require metal ions to function properly.

Essential Minerals and Their Functions

□ Magnesium (Mg^{2+})

- Activates ATP-dependent enzymes (e.g., Hexokinase, DNA polymerase).
- Stabilizes ribosomes and DNA structure.

Clinical Relevance: Deficiency leads to muscle cramps, arrhythmias, and seizures.

□ Calcium (Ca^{2+})

- Acts as a second messenger in muscle contraction and neurotransmission.
- Essential for blood clotting (activates clotting factors).

Clinical Relevance: Hypocalcemia causes tetany and osteoporosis.

□ Zinc (Zn^{2+})

- Required for DNA polymerase, carbonic anhydrase, and superoxide dismutase.
- Essential for wound healing and immune function.

Clinical Relevance: Deficiency leads to delayed wound healing and growth retardation.

□ Iron (Fe^{2+}/Fe^{3+})

- Component of hemoglobin, myoglobin, and cytochromes (oxidative phosphorylation).

Clinical Relevance: Deficiency causes iron-deficiency anemia.

□ Copper (Cu^{2+})

- Needed for cytochrome c oxidase (electron transport chain) and collagen synthesis.

Clinical Relevance: Wilson's disease (copper accumulation), Menkes disease (copper deficiency).

□ Selenium (Se^{2-})

- Part of glutathione peroxidase (antioxidant enzyme).

Clinical Relevance: Deficiency leads to Keshan disease (cardiomyopathy).

Mineral	Some Important Functions	Food Sources
Boron Unknown	Important in bone retention.	Fruits, leafy vegetables, nuts, legumes, beans.
Calcium 1,000 - 1,300 mg.	Essential for growth and structural integrity of bones and teeth; nerve conduction; muscle contraction and relaxation.	Yogurt, milk, cheese, tofu, fortified juices, green leafy vegetables.
Chromium[1] 50 - 200 μg.	Participates in CHO and fat metabolism; muscle function; increases effectiveness of insulin.	Whole grains, cheese, yeast.
Copper[1] 1.5 - 3 mg.	Essential for red blood cell production, pigmentation, and bone health.	Nuts, liver, lobster, cereals, legumes, dried fruit.
Iron[2] 10 -15 mg.	Essential for the production of hemoglobin in red blood cells and myoglobin in skeletal muscle, and enzymes that participate in metabolism.	Liver, clams, oatmeal, farina, fortified cereals, soybeans, apricot, green leafy vegetables.
Magnesium 280 - 350 mg.	Essential for nerve impulse conduction; muscle contraction and relaxation; enzyme activation.	Whole grains, artichoke, beans, green leafy vegetables, fish, nuts, fruit.
Manganese[1] 2 - 5 mg.	Essential for formation and integrity of connective tissue and bone, sex hormone production, and cell function.	Nuts, legumes, whole grains.
Phosphorous 800 - 1,200 mg.	Essential for metabolism and bone development. Involved in most biochemical reactions in the body.	Fish, milk, meats, poultry, legumes, nuts.
Potassium[3] 2,000 mg.	Essential for nerve impulse conduction, fluid balance, and for normal heart function.	Squash, potatoes, beans, fresh fruits (bananas, oranges) and vegetables (tomatoes).
Selenium 55 - 70 μg.	Antioxidant, works with vitamin E to reduce oxidation damage to tissues.	Meats, seafood, cereals.
Sodium[4] 500 - 2,400 mg.	Essential for nerve impulse conduction, muscle contraction, fluid balance, and acid-	Table salt, canned and processed foods.

□ Fill in the Blanks:

1. _____ is a cofactor for ATP-dependent enzymes and stabilizes DNA. (Answer: Magnesium)

2. Hemoglobin contains _____, which is essential for oxygen transport. (Answer: Iron)

□ MCQ:

Which mineral is an essential cofactor for glutathione peroxidase?

A) Iron

B) Copper

C) Selenium

D) Zinc

(Answer: C) Selenium

□ Fun Fact:

The human body contains 4 grams of iron, enough to forge a small nail!

2.Role of Vitamins as Coenzymes

Biochemical Basis: Vitamins act as organic coenzymes, assisting enzymes in metabolism, redox reactions, and DNA synthesis. Many B-complex vitamins serve as precursors for essential coenzymes.

□ Vitamin B1 (Thiamine) – Coenzyme: Thiamine Pyrophosphate (TPP)

Function:

- Coenzyme for pyruvate dehydrogenase (TCA cycle) and transketolase (HMP shunt).
- Helps in carbohydrate metabolism.

Deficiency:

- Beriberi (neuropathy, cardiac failure).
- Wernicke-Korsakoff Syndrome (alcoholism-related memory loss).

Mnemonic:

“ATP” → Alpha-ketoglutarate DH, Transketolase, Pyruvate DH (Thiamine-dependent enzymes).

□ Vitamin B2 (Riboflavin) – Coenzymes: FAD, FMN

Function:

- Electron carrier in redox reactions (TCA cycle, Electron Transport Chain).
- Essential for fatty acid metabolism.

Deficiency:

- Cheilitis (cracked lips), glossitis (inflamed tongue), corneal vascularization.

□ Think Tank:

Why do alcoholics often suffer from vitamin B1 and B2 deficiencies?

□ Vitamin B3 (Niacin) – Coenzymes: NAD^+, $NADP^+$

Function:

- Coenzyme for dehydrogenases (glycolysis, TCA cycle, fatty acid synthesis).
- Required for redox reactions.

Deficiency:

- Pellagra (3 Ds: Diarrhea, Dermatitis, Dementia).

□ Fun Fact:

Niacin is synthesized from tryptophan, requiring B6!

□ Vitamin B6 (Pyridoxine) – Coenzyme: Pyridoxal Phosphate (PLP)

Function:

- Coenzyme for transaminases (ALT, AST) and decarboxylases (neurotransmitter synthesis).
- Essential for heme synthesis and amino acid metabolism.

Deficiency:

- Peripheral neuropathy, seizures, irritability, anemia.

□ Fill in the Blanks:

1. The coenzyme form of Vitamin B6 is _____. (Answer: PLP - Pyridoxal Phosphate)

2. Vitamin B6 is crucial for the synthesis of the neurotransmitter _____. (Answer: GABA, Dopamine, Serotonin)

□ Biotin (Vitamin B7) – Coenzyme: Biotin

Function:

- Coenzyme for carboxylases (pyruvate carboxylase, acetyl-CoA carboxylase).
- Important for fatty acid synthesis and gluconeogenesis.

Deficiency:

- Alopecia, dermatitis, and metabolic acidosis.
- Caused by raw egg consumption (Avidin binds Biotin).

Mnemonic:

"Carboxylase Enzyme Helper = Biotin"

□ SAQ:

Explain the role of biotin in fatty acid metabolism.

□ Pantothenic Acid (Vitamin B5) – Coenzyme: Coenzyme A (CoA)

Function:

- Coenzyme for fatty acid oxidation (β-oxidation) and TCA cycle.
- Required for acetyl-CoA formation.

Deficiency:

- Rare, but causes burning feet syndrome and adrenal insufficiency.

□ MCQ:

Which vitamin is essential for acetyl-CoA synthesis?

A) B1

B) B2

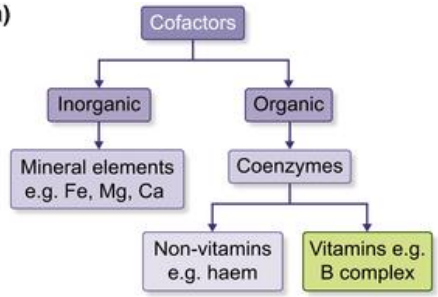
C) B5

D) B12

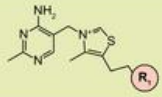
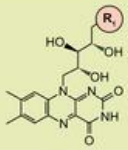
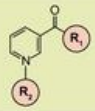
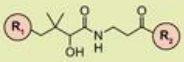
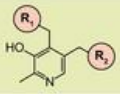
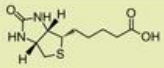
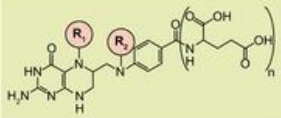
(Answer: C) B5 - Pantothenic Acid

SUMMARY OF VITAMINS

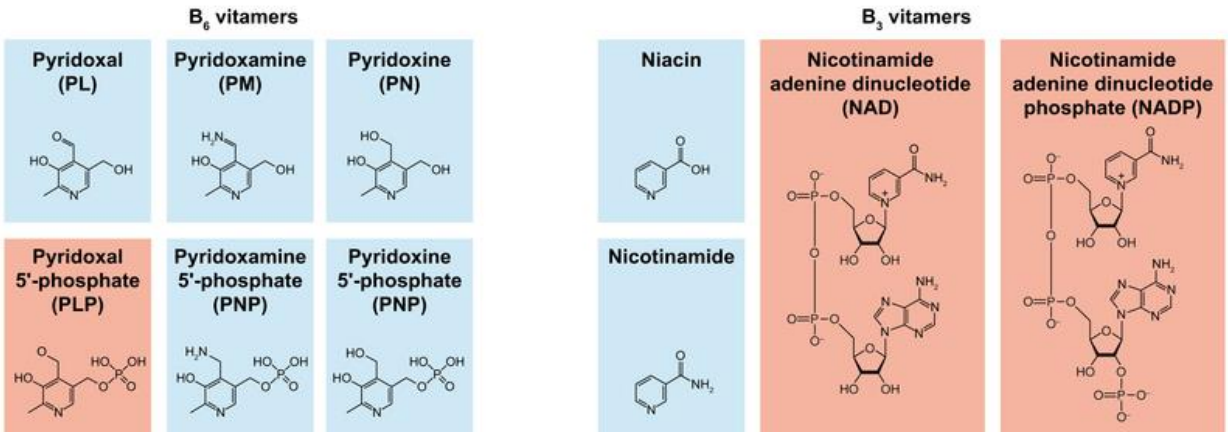
(a)



(b)

B vitamin	Chemical name	Structure	Vitamers	Coenzyme	Coenzyme function	Process
B_1	Thiamine		R_1: −OH, $-OPO_3^{2-}$, $-OP_2O_6^{3-}$, $-OP_3O_9^{4-}$ (+/– adenine nucleotide)	Thiamine diphosphate	Decarboxylation reactions	Cellular respiration, carbohydrate and nucleic acid metabolism
B_2	Riboflavin		R_1: −OH, $-OPO_3^{2-}$ (+/– adenine nucleotide)	Flavin mononucleotide (FMN) and flavin adenine dinucleotide (FAD)	Oxidation–reduction reactions involving two hydrogen atoms	Cellular respiration and fatty acid metabolism
B_3	Niacin		R_1: −OH, $-NH_2$ R_2: ribose (+/– adenine nucleotide diphosphate: +/– $-OPO_3^{2-}$)	NAD⁺ and NADP⁺	Oxidation–reduction reactions involving the hydride ion	Carbohydrate, lipid, nucleic acid and alcohol metabolism
B_5	Pantothenate		R_1: −OH, +/– $-OPO_3^{2-}$, +/– adenine nucleotide diphosphate: +/– $-OPO_3^{2-}$ R_2: cysteamine	Coenzyme A	Acetyl group and other acyl group transfer	Fatty acid and carbohydrate oxidation
B_6	Pyridoxine		R_1: −OH, $-NH_2$ or =O R_2: −OH or $-OPO_3^{2-}$	Pyridoxal 5'-phosphate	Amino and carboxyl group transfer	Amino acid, carbohydrate and lipid metabolism
B_8	Biotin			Biotin	Carboxylation reactions	Lipid, protein and carbohydrate metabolism
B_9	Folate		R_1: −H, −OH, −H, $-CH_3$, $-CH_2^-$, =CH– + R_2: −H, −H, −OH, −H, $-CH_2^-$, =CH–	Tetrahydrofolic acid (THF)	Methyl, formyl, methylene and formimino group transfer	Single carbon unit transfer in nucleic acid and amino acid metabolism

(c)



Tips & Tricks:

✓Mnemonic for B-vitamin Deficiencies:

“The Rich Never Pay Bills Properly” (Thiamine, Riboflavin, Niacin, Pyridoxine, Biotin, Pantothenic Acid).

✓Clinical Tip:

Alcoholics and malnourished patients are often given B-complex supplements to prevent neurological disorders.

□ SECTION III: CLINICAL BIOCHEMISTRY

□ Biochemical Basis of Disease & Cellular Biomarkers

1. Application of Biochemical Functions of Cellular Biomarkers in Clinical Context

Biochemical Basis:Cellular biomarkers are molecules (proteins, enzymes, metabolites) that indicate normal physiological functions or disease states. They are used for:

- Disease diagnosis (e.g., cardiac troponin in myocardial infarction).
- Monitoring treatment response (e.g., HbA1c in diabetes).
- Predicting disease progression (e.g., PSA for prostate cancer).

Key Biomarkers and Their Clinical Significance

- ALT, AST (Liver Function) – Elevated in hepatitis, liver cirrhosis.
- Troponin I, CK-MB (Cardiac Markers) – Elevated in myocardial infarction.
- LDH (Tissue Damage) – Increased in hemolysis, tumors.
- CRP (Inflammation Marker) – High in autoimmune diseases, infections.

Clinical Case:

A 45-year-old male presents with chest pain and shortness of breath. Lab results show elevated troponin I and CK-MB. Diagnosis? Acute Myocardial Infarction (Heart Attack) due to cardiac biomarker elevation.

□ THINK TANK:

Why is troponin I preferred over CK-MB for diagnosing heart attacks?

Correlation of Disorders with Cell Organelles

A. Endoplasmic Reticulum (ER) Disorders

□ Cystic Fibrosis (CF)

- Biochemical Basis: Mutation in CFTR gene → Misfolded CFTR protein accumulates in ER.
- Clinical Features: Thick mucus, chronic lung infections, pancreatic insufficiency.
- Diagnosis: Sweat chloride test, genetic testing.

□ Non-Alcoholic Fatty Liver Disease (NAFLD)

- Biochemical Basis: Lipid accumulation in ER due to insulin resistance.
- Clinical Features: Fatigue, hepatomegaly, increased ALT/AST.
- Diagnosis: Liver biopsy, ultrasound.

Clinical Case:

A 32-year-old obese male with type 2 diabetes has elevated ALT/AST and fatty infiltration in the liver on ultrasound. Diagnosis? NAFLD.

B. Lysosomal Disorders

□ Gaucher Disease

- Biochemical Basis: Glucocerebrosidase deficiency → Accumulation of glucocerebrosides in macrophages.
- Clinical Features: Hepatosplenomegaly, bone pain, anemia.
- Diagnosis: Enzyme assay, genetic testing.

□ Tay-Sachs Disease

- Biochemical Basis: Hexosaminidase A deficiency → Accumulation of GM2 gangliosides in neurons.
- Clinical Features: Cherry-red macula, neurodegeneration, no hepatosplenomegaly.
- Diagnosis: Enzyme assay, genetic testing.

Clinical Case:

A 6-month-old infant presents with progressive neurodegeneration, hyperreflexia, and a cherry-red macula. Diagnosis? Tay-Sachs Disease.

C. Peroxisomal Disorders

□ Zellweger Syndrome

- Biochemical Basis: Defect in peroxisome biogenesis → Accumulation of very-long-chain fatty acids (VLCFAs).
- Clinical Features: Hypotonia, seizures, hepatomegaly.
- Diagnosis: Elevated VLCFAs in plasma.

D. Plasma Membrane Disorders

□ Hereditary Spherocytosis

- Biochemical Basis: Defective spectrin/ankyrin in RBC membrane → Spherocytes form.
- Clinical Features: Hemolytic anemia, jaundice, splenomegaly.
- Diagnosis: Osmotic fragility test.

□ Familial Hypercholesterolemia

- Biochemical Basis: Defective LDL receptors → Increased LDL.
- Clinical Features: Early atherosclerosis, tendon xanthomas.
- Diagnosis: Lipid panel (high LDL levels).

Clinical Case:

A 25-year-old male has xanthomas on tendons, LDL > 300 mg/dL, and a family history of heart disease. Diagnosis? Familial Hypercholesterolemia.

E. Cytoskeleton Disorders

□ Duchenne Muscular Dystrophy

- Biochemical Basis: Dystrophin gene mutation → Weak muscle integrity.
- Clinical Features: Gower's sign, progressive muscle weakness.
- Diagnosis: Genetic testing, elevated CK levels.

F. Cytoplasmic Inclusion Disorders

□ Parkinson's Disease

- Biochemical Basis: Lewy body accumulation (α-synuclein aggregates).
- Clinical Features: Bradykinesia, tremors, rigidity.
- Diagnosis: Clinical exam, dopamine imaging.

Role of Signal Transduction in Health & Disease

Normal Function: Converts external signals (hormones, growth factors) into cellular responses.

Disorders:

- Diabetes (insulin receptor signaling defect).
- Cancer (overactive growth factor signaling).
- Neurodegenerative diseases (defective neurotransmitter signaling).

Clinical Case:

A patient with uncontrolled glucose levels despite normal insulin secretion likely has insulin receptor resistance (Type 2 Diabetes Mellitus).

Membrane Transport Disorders

 Cholera (Vibrio cholerae)

- Biochemical Basis: Toxin permanently activates Gs protein, leading to excess cAMP and severe diarrhea.

 Pertussis (Whooping Cough)

- Biochemical Basis: Pertussis toxin inactivates Gi protein, increasing cAMP levels.

 Cystic Fibrosis

- Biochemical Basis: CFTR mutation → Defective Cl^- transport, thick mucus.

Clinical Significance

- Sugars (Mono-, Di-, Polysaccharides)
- Sorbitol & Mannitol – Osmotic diuretics used in cerebral edema.
- Dextran & Inulin – Plasma expanders in hypovolemia.
- Hyaluronic Acid & Heparin – Used in joint lubrication and anticoagulation.

Porphyrias (Heme Biosynthesis Disorders)

- Acute Intermittent Porphyria (AIP): Deficiency of porphobilinogen deaminase.
    - Symptoms: Abdominal pain, neuropsychiatric symptoms.
- Porphyria Cutanea Tarda (PCT): Uroporphyrinogen decarboxylase deficiency.
    - Symptoms: Blistering photosensitivity.

Hyperbilirubinemia & Jaundice

- Pre-hepatic Jaundice (Hemolysis → ↑ Unconjugated bilirubin).
- Hepatic Jaundice (Liver dysfunction → Mixed bilirubin increase).
- Post-hepatic Jaundice (Obstruction → ↑ Conjugated bilirubin).

Nutritional Anemia: Iron, Vitamin B9 & B12

- Iron Deficiency Anemia – Low iron, microcytic hypochromic RBCs.
- Megaloblastic Anemia (B9/B12 Deficiency) – Macrocytic RBCs, hypersegmented neutrophils.

Role of Vitamin C & K in Bleeding Disorders

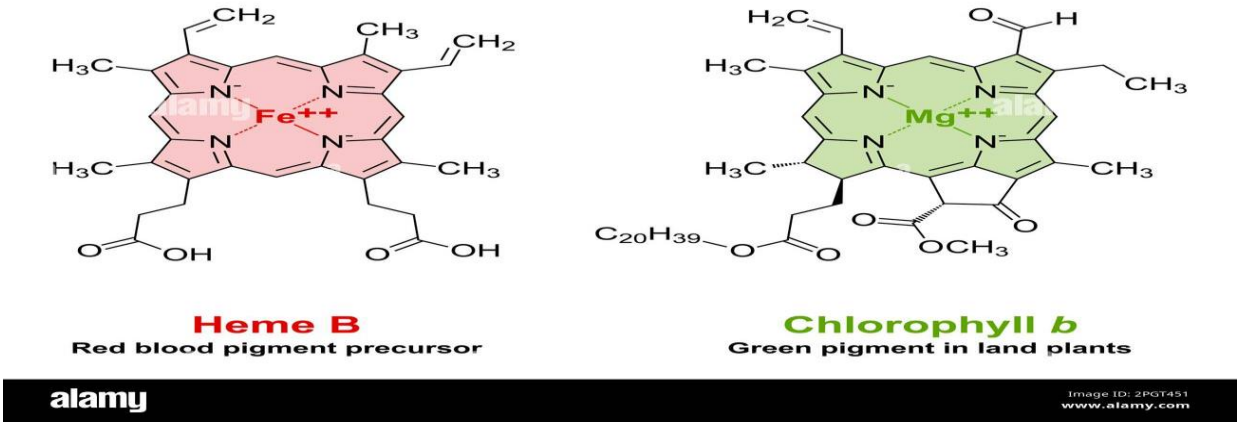
- Vitamin C Deficiency (Scurvy): Defective collagen synthesis → Bleeding gums.
- Vitamin K Deficiency: Defective clotting factors (II, VII, IX, X) → Bleeding disorders.

Biochemistry of Heme & Porphyrin Metabolism + Plasma Proteins

Heme and porphyrins are crucial in oxygen transport, electron transfer, and enzymatic reactions. Plasma proteins, including immunoglobulins, play a vital role in maintaining osmotic pressure, immune defense, and coag**ulation.**

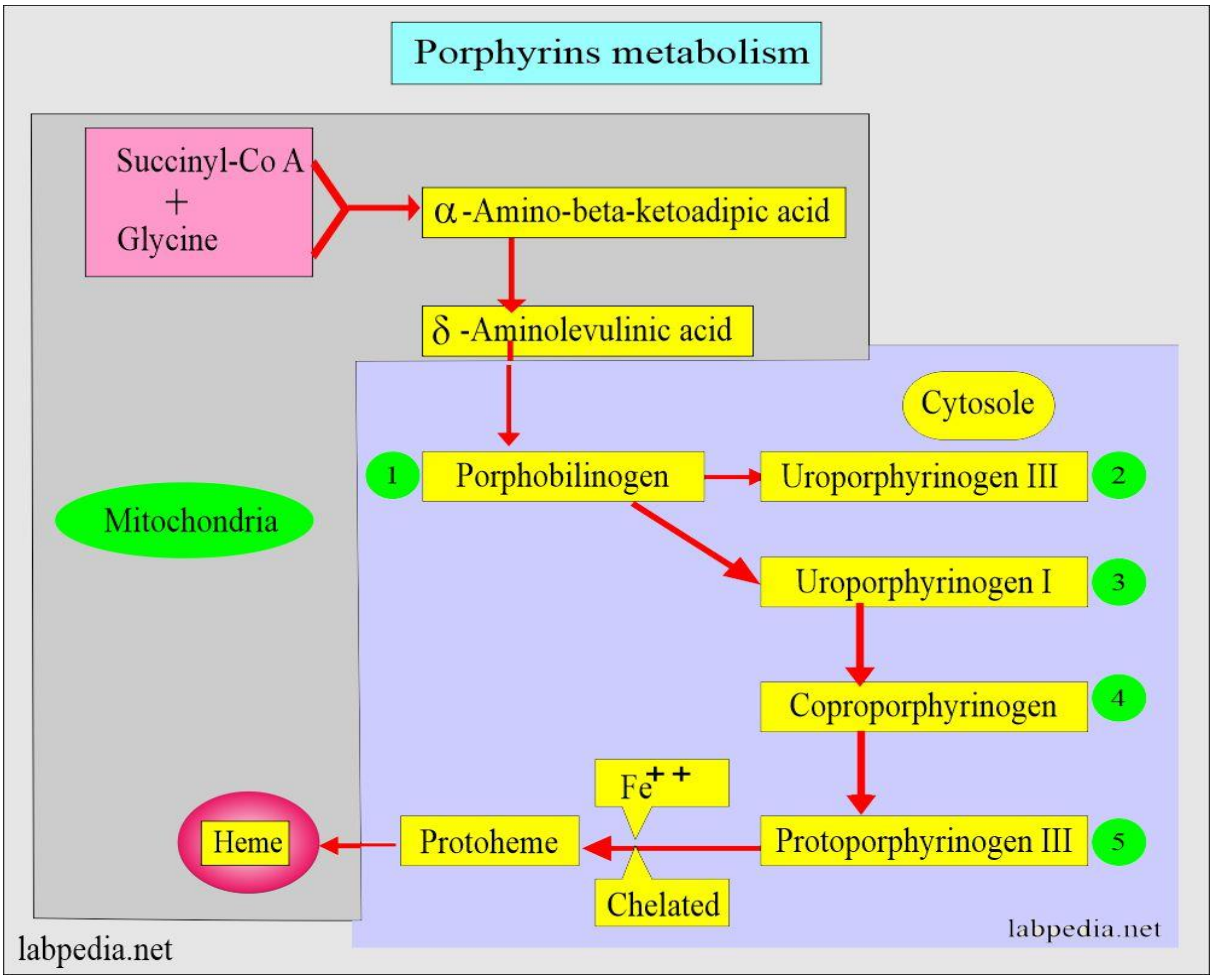
1. Chemistry of Porphyrins

Biochemical Basis: Porphyrins are cyclic organic molecules composed of four pyrrole rings (tetrapyrrole structure) linked by methenyl bridges. The central cavity can bind metal ions, forming metalloporphyrins such as heme (Fe^{2+}) and chlorophyll (Mg^{2+}).



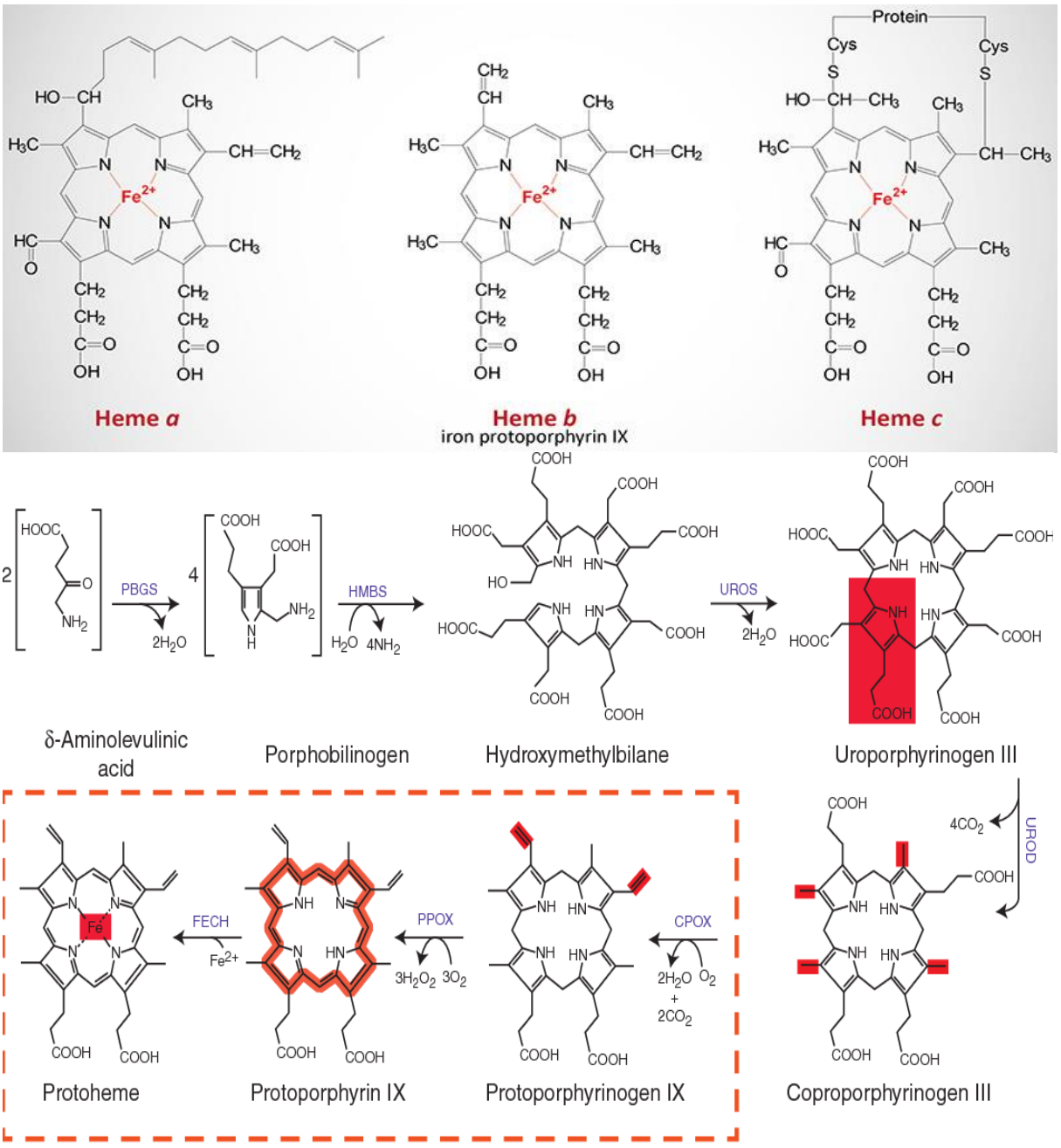
Structure of Porphyrins

- Planar and highly conjugated → Gives red/purple color.
- Substituent groups (acetate, propionate, methyl, vinyl) define different types of porphyrins.
- Uroporphyrin, Coproporphyrin, Protoporphyrin are intermediates in heme biosynthesis.



Clinical Relevance:

Porphyrias are disorders of porphyrin metabolism, leading to accumulation of intermediates and photosensitivity or neurovisceral symptoms.

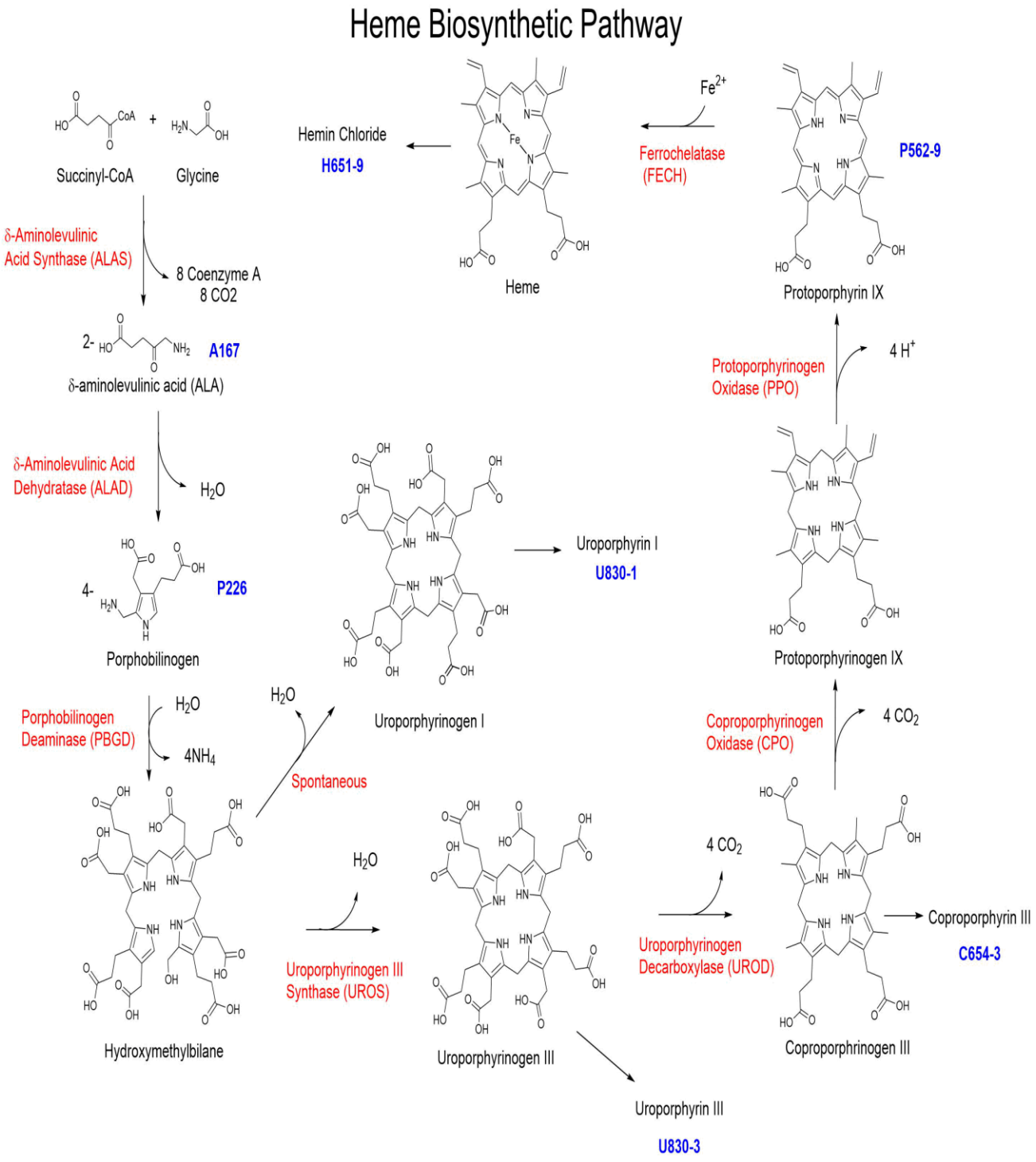


THINK TANK:

Why do porphyrins exhibit fluorescence under UV light?

2. Heme Biosynthesis

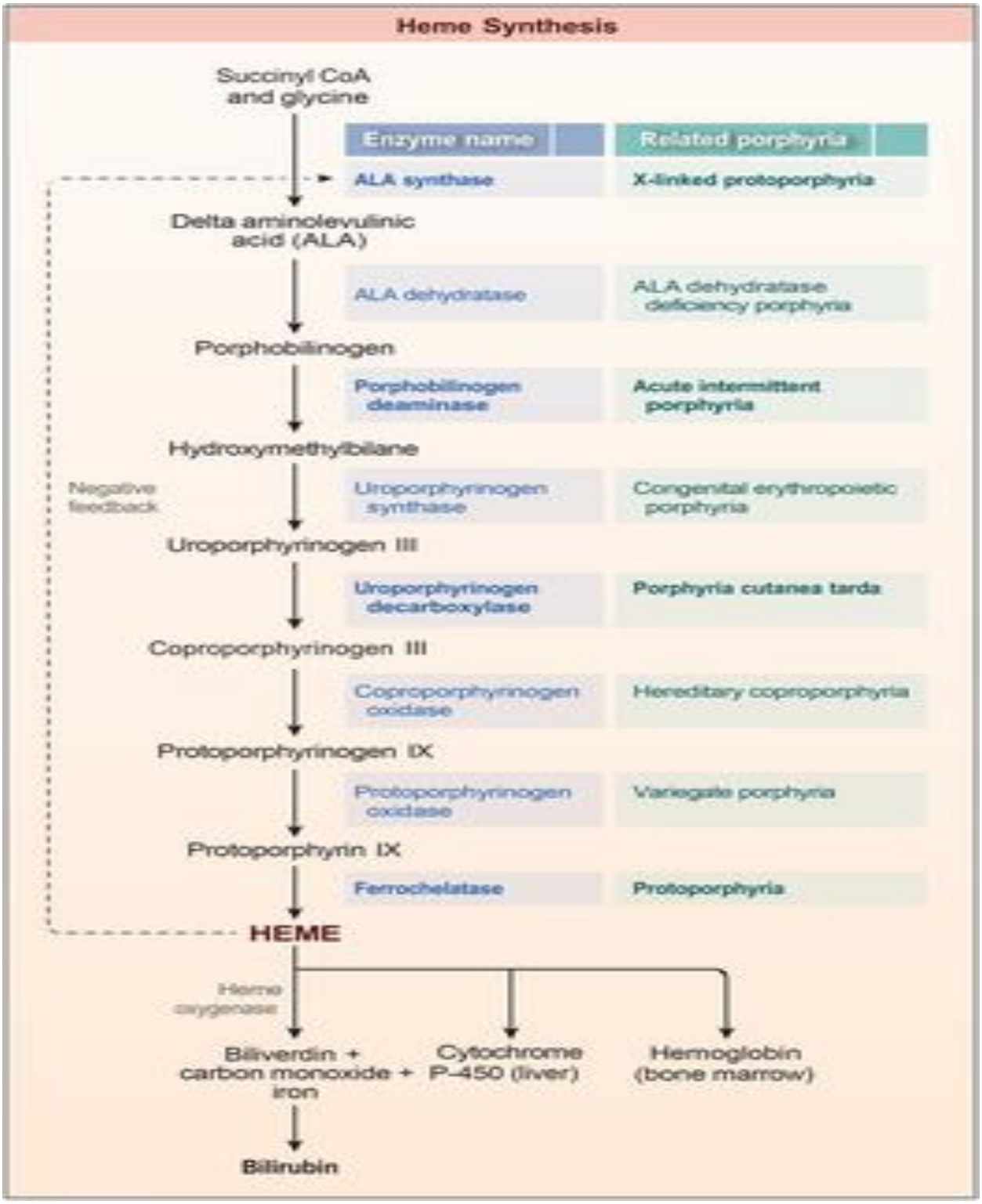
Biochemical Pathway: Heme synthesis occurs in the mitochondria and cytoplasm, primarily in bone marrow (RBCs) and liver (cytochrome enzymes).



Steps in Heme Synthesis

- 1. Formation of δ-Aminolevulinic Acid (ALA) (Rate-limiting step)

    - Enzyme: ALA Synthase
    - Substrates: Glycine + Succinyl-CoA
    - Coenzyme: Pyridoxal phosphate (Vitamin B6)
    - Regulation: Inhibited by heme (feedback inhibition).
- 2. Porphobilinogen (PBG) Formation
    - Enzyme: ALA Dehydratase
    - Inhibited by Lead (Pb^{2+}) → Lead Poisoning.
- 3. Hydroxymethylbilane Formation
    - Enzyme: Porphobilinogen Deaminase
    - Deficiency: Acute Intermittent Porphyria (AIP).
- 4. Uroporphyrinogen → Coproporphyrinogen → Protoporphyrin IX
    - Series of decarboxylation and oxidation reactions.
- 5. Heme Formation
    - Enzyme: Ferrochelatase
    - Fe^{2+} inserted into Protoporphyrin IX to form Heme.
    - Inhibited by Lead → Microcytic Anemia.



Clinical Case:

A 25-year-old factory worker presents with microcytic anemia, abdominal pain, and neurological symptoms. Labs show elevated blood lead levels. Diagnosis? Lead Poisoning (ALA Dehydratase & Ferrochelatase Inhibition).

 MCQ:

Which enzyme inserts Fe^{2+} into Protoporphyrin IX?

A) ALA Synthase

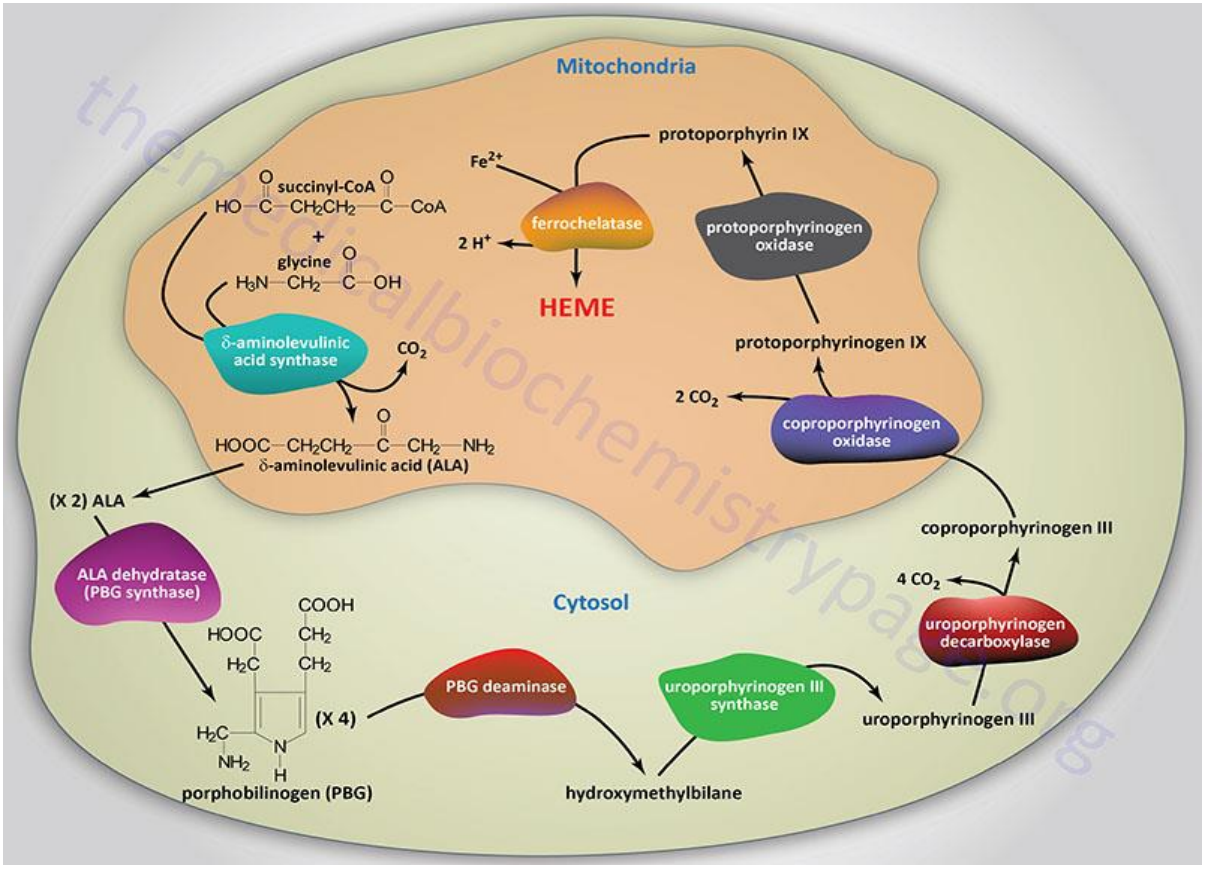
B) Porphobilinogen Deaminase

C) Ferrochelatase

D) Heme Oxygenase

(Answer: C) Ferrochelatase

3. Degradation of Heme & Formation of Bile Pigments



- Step 1: Heme Breakdown (Macrophages of Spleen & Liver)
    - Heme Oxygenase converts heme → biliverdin (green) by opening the porphyrin ring.
    - Biliverdin Reductase converts biliverdin → bilirubin (yellow-orange).
- Step 2: Transport of Bilirubin in Plasma
    - Unconjugated Bilirubin (UCB) is hydrophobic, binds albumin, transported to the liver.

    - Clinical Significance: Excess UCB → Neonatal Jaundice, Kernicterus.
- Step 3: Conjugation in the Liver
    - Enzyme: UDP-Glucuronyltransferase
    - Forms: Conjugated Bilirubin (CB) (water-soluble).
    - Deficiency: Crigler-Najjar Syndrome, Gilbert Syndrome (↑ UCB levels).
- Step 4: Excretion of Bilirubin
    - CB is excreted into bile → intestine → converted to Urobilinogen.
    - Some Urobilinogen is reabsorbed, converted to urobilin (urine) and stercobilin (feces, brown color).
- Types of Jaundice
    - Pre-Hepatic (Hemolysis) → ↑ UCB (e.g., Hemolytic Anemia).
    - Hepatic (Liver Disease) → ↑ Mixed (e.g., Hepatitis).
    - Post-Hepatic (Obstruction) → ↑ CB (e.g., Gallstones).

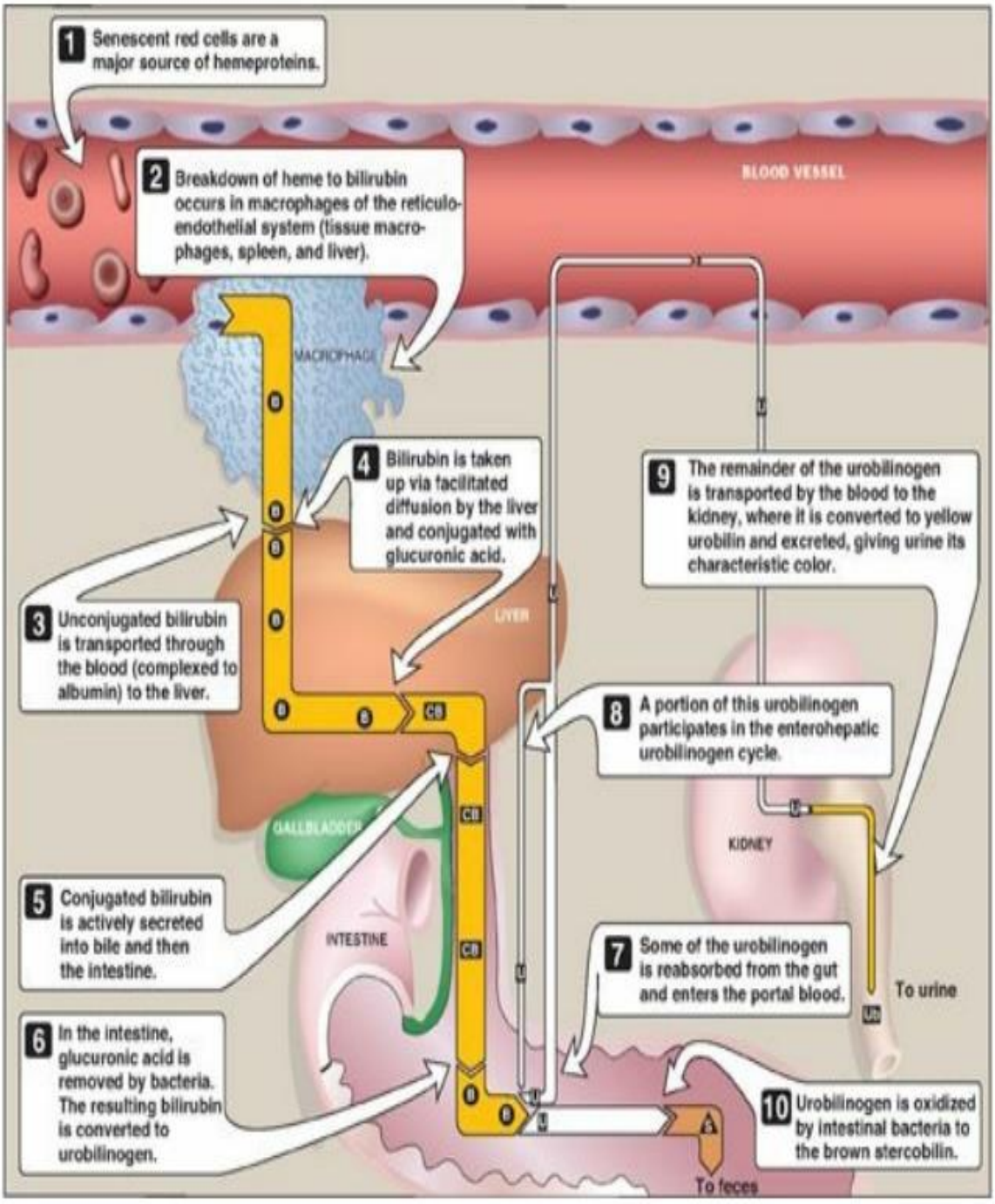


Figure 21.10 Catabolism of heme B = bilirubin; CB = conjugated bilirubin; U = urobilinogen; Ub = urobilin; S = stercobilin.

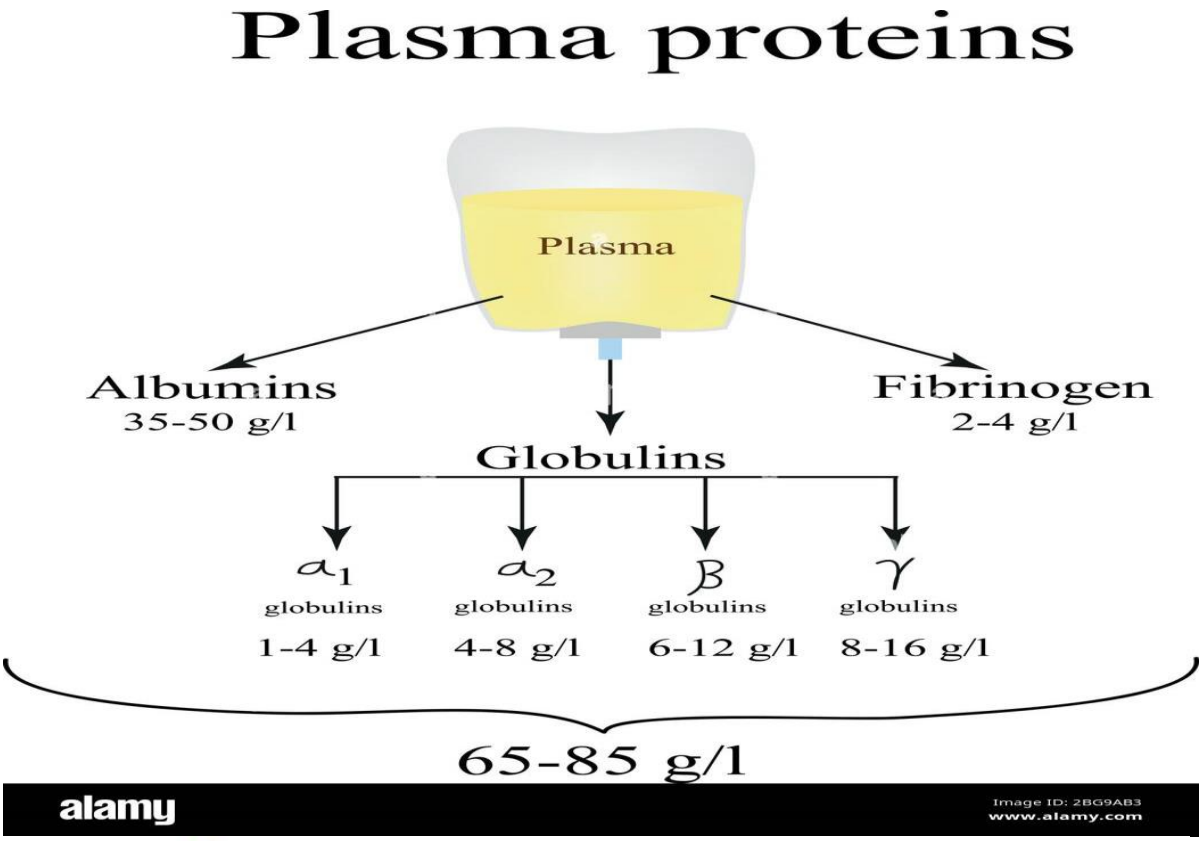
Clinical Case:

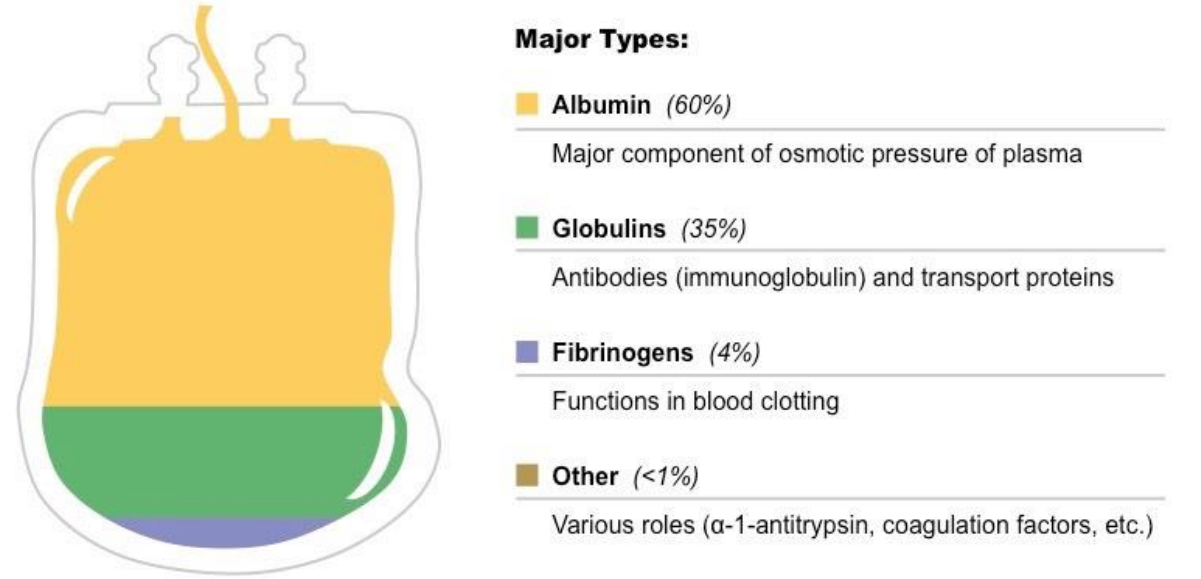
A 3-day-old newborn presents with yellow skin, high UCB, and normal liver enzymes. Diagnosis? Physiological Jaundice (Delayed UDP-Glucuronyltransferase Activation).

 SAQ:

Describe the steps of bilirubin metabolism and its excretion.

Plasma Proteins





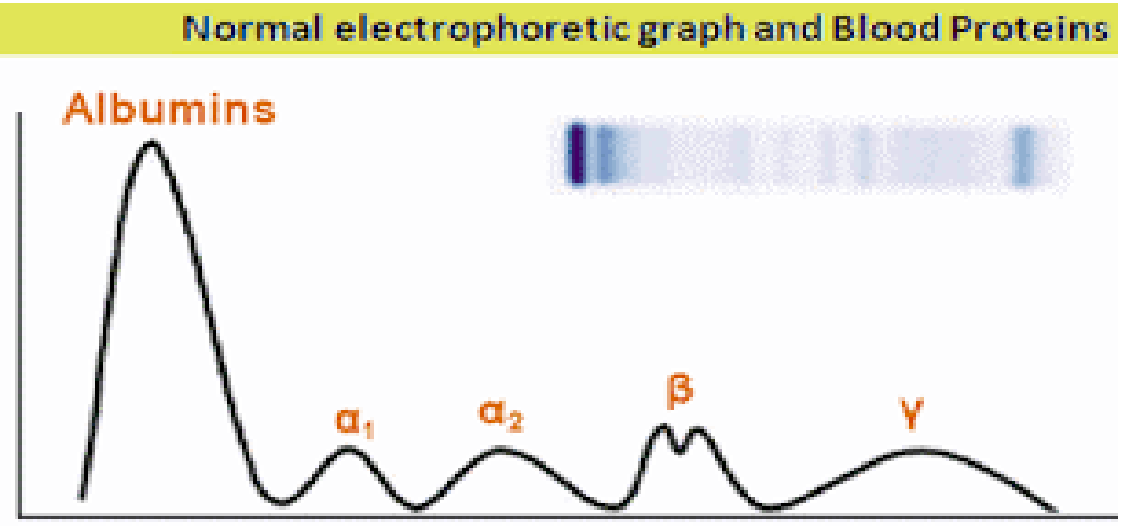
Biochemical Basis: Plasma proteins are synthesized mainly in the liver and are essential for transport, immune defense, and coagulation.

Classification of Plasma Proteins

 Albumin (60%)

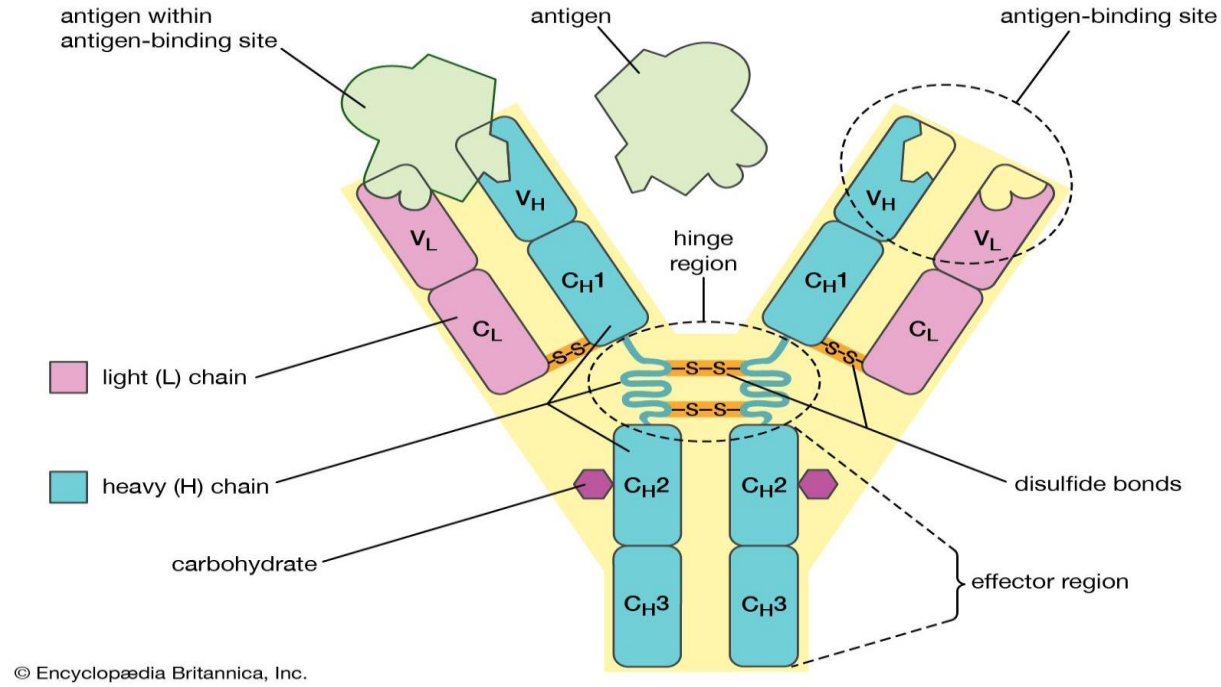
- Maintains oncotic pressure.
- Transports hormones, fatty acids, and drugs.
- Clinical Relevance: Hypoalbuminemia → Edema (Nephrotic Syndrome).

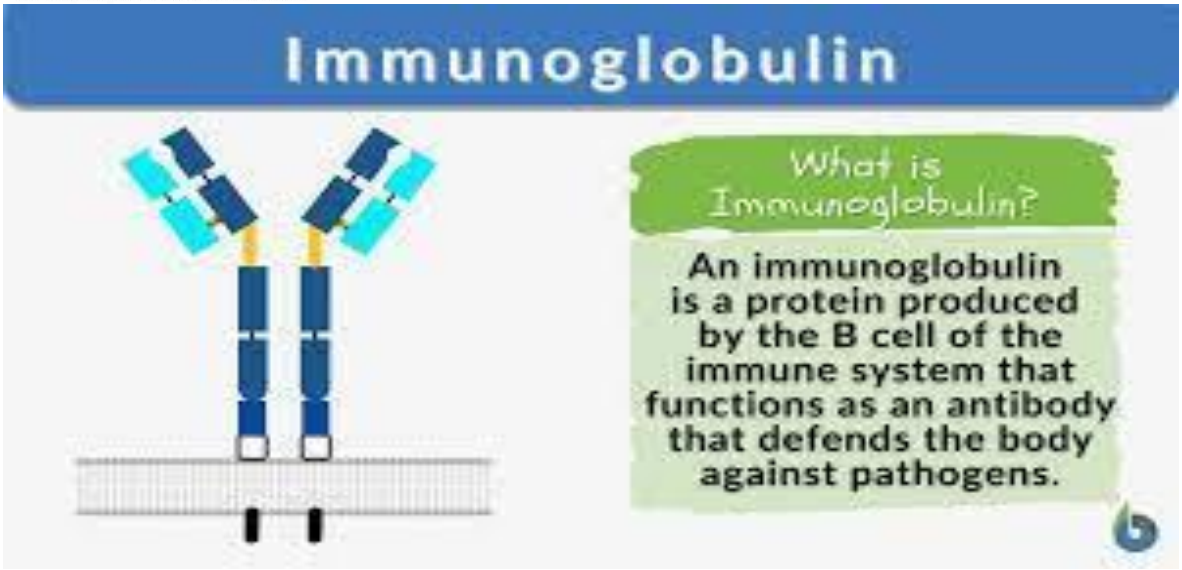
□ Globulins (Immunoglobulins, Transport Proteins)



- α1-Globulins (Antitrypsin, Thyroxine-binding globulin).
- α2-Globulins (Haptoglobin, Ceruloplasmin).
- β-Globulins (Transferrin, LDL).
- γ-Globulins (Immunoglobulins – IgG, IgA, IgM, IgE, IgD).
    - □ Fibrinogen & Coagulation Factors
        - Involved in blood clotting (Fibrinogen → Fibrin by Thrombin).

Immunoglobulins (Antibodies)





- IgG – Most abundant, crosses placenta (passive immunity).
- IgA – Found in mucosal secretions (breast milk, saliva).
- IgM – First antibody produced in infections.
- IgE – Involved in allergic reactions, mast cell degranulation.
- IgD – Unclear function, B-cell receptor.

Clinical Relevance:

- Multiple Myeloma: Excess Ig production → Monoclonal M spike on electrophoresis.
- Nephrotic Syndrome: Albumin loss → Generalized edema.

Clinical Case:

A 50-year-old male presents with recurrent infections and low IgG levels. Diagnosis? Common Variable Immunodeficiency (CVID).

 THINK TANK:

Why do patients with IgA deficiency have recurrent respiratory infections?

Clinical Relevance of Leukocytes, Plasma Proteins & Immunoglobulin Disorders

Leukocytes (WBCs) and plasma proteins play a crucial role in immune defense, inflammation, and homeostasis. Alterations in their levels can indicate infection, malignancy, immune disorders, or nutritional deficiencies.

1. Significance of Altered Levels of Leukocytes (WBCs)

Biochemical Basis: Leukocytes (WBCs) include neutrophils, lymphocytes, monocytes, eosinophils, and basophils. Their normal count ranges from 4,000 – 11,000 cells/µL. An increase or decrease in WBCs can indicate infection, inflammation, or hematological malignancies.

- Leukocytosis (↑ WBC Count > 11,000/µL)
- Neutrophilia (↑ Neutrophils) → Bacterial infections, inflammation, stress.
- Lymphocytosis (↑ Lymphocytes) → Viral infections, leukemia, tuberculosis.
- Monocytosis (↑ Monocytes) → Chronic infections (TB), autoimmune diseases.
- Eosinophilia (↑ Eosinophils) → Parasitic infections, allergies, asthma.
- Basophilia (↑ Basophils) → Chronic myeloid leukemia (CML), allergies.
- Leukopenia (↓ WBC Count < 4,000/µL)
- Neutropenia → Chemotherapy, viral infections, bone marrow failure.
- Lymphopenia → HIV/AIDS, corticosteroid use, malnutrition.

Clinical Case 1: A 30-year-old male presents with fever, sore throat, and fatigue. Blood tests show WBC count of 15,000/µL with increased lymphocytes. Diagnosis? Viral infection (likely Mononucleosis due to EBV).

Clinical Case 2: A 50-year-old woman undergoing chemotherapy develops fever and mouth ulcers. Her blood test shows WBC count of 2,000/µL with neutropenia. Diagnosis? Chemotherapy-induced neutropenia, making her prone to infections.

 THINK TANK:

Why does CML cause basophilia?

How does HIV lead to lymphopenia?

 MCQ:

Which type of leukocytosis is seen in parasitic infections?

A) Neutrophilia

B) Monocytosis

C) Eosinophilia

D) Lymphocytosis

(Answer: C) Eosinophilia

Clinical Disorders Associated with Plasma Proteins & Immunoglobulins

Plasma proteins, including albumin, globulins, and clotting factors, maintain oncotic pressure, immune defense, and transport functions. Their abnormalities can result in edema, malnutrition, and plasma cell disorders like multiple myeloma.

A. Edema

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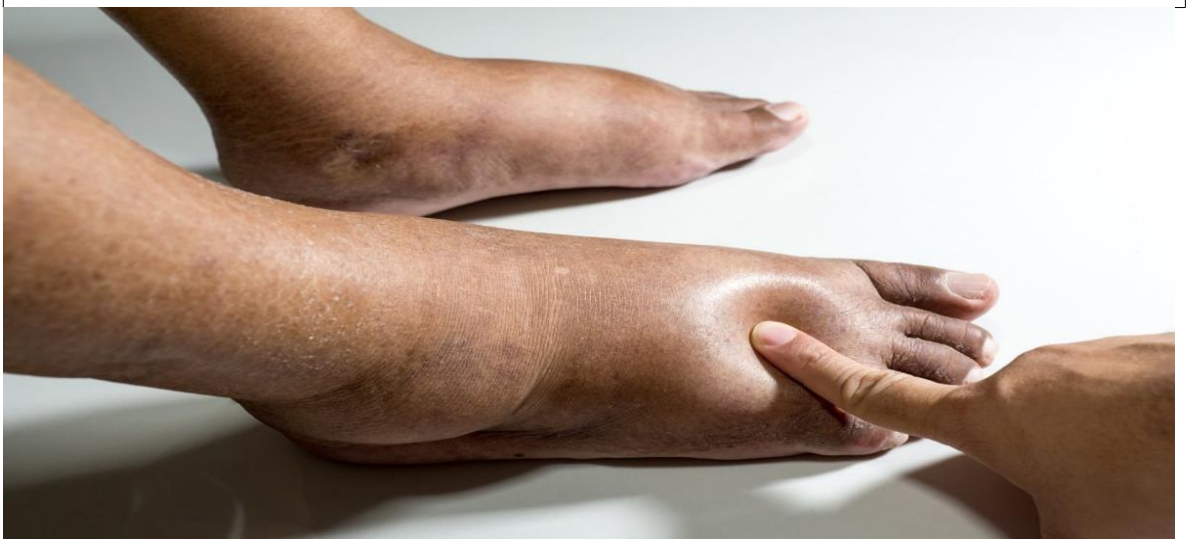


Biochemical Basis: Edema is the abnormal accumulation of fluid in interstitial spaces due to:

- 1. ↓ Plasma Oncotic Pressure (↓ Albumin) – Seen in liver disease, nephrotic syndrome, malnutrition.
- 2. ↑ Capillary Permeability – Inflammation, burns.

- 3. ↑ Hydrostatic Pressure – Heart failure, venous obstruction.
- 4. Lymphatic Obstruction – Cancer, filariasis (elephantiasis).

Clinical Case: A 5-year-old child with a distended abdomen and swollen legs presents with low albumin levels and a history of malnutrition. Diagnosis? Kwashiorkor (Protein Deficiency → Hypoalbuminemia → Edema).

 THINK TANK:

Why do patients with liver cirrhosis develop ascites (fluid accumulation in the abdomen)?

 MCQ:

Which of the following is the primary cause of edema in nephrotic syndrome?

A) ↑ Capillary permeability

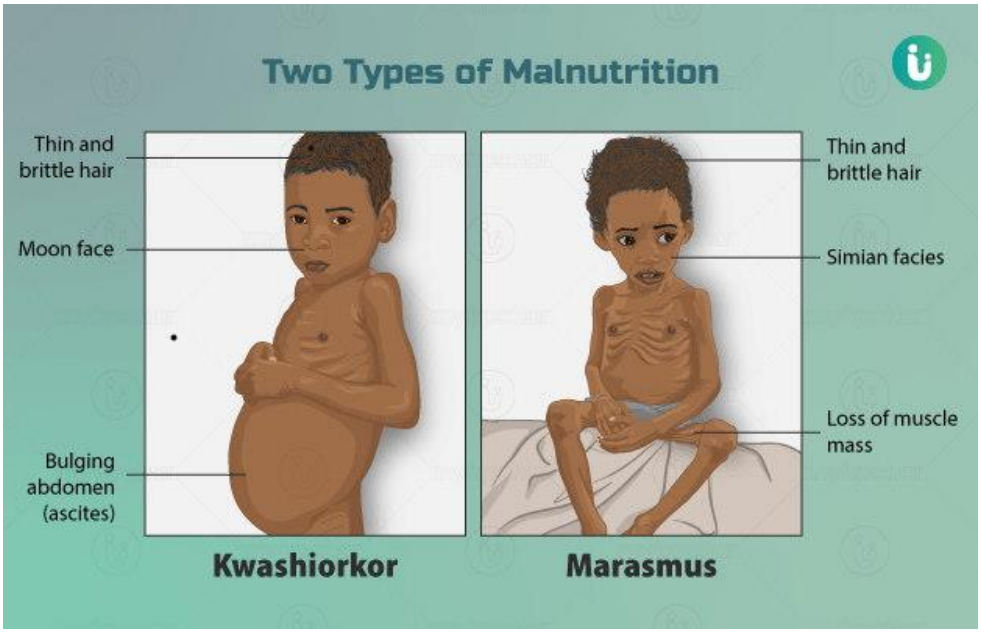
B) ↓ Plasma oncotic pressure

C) Lymphatic obstruction

D) Sodium retention

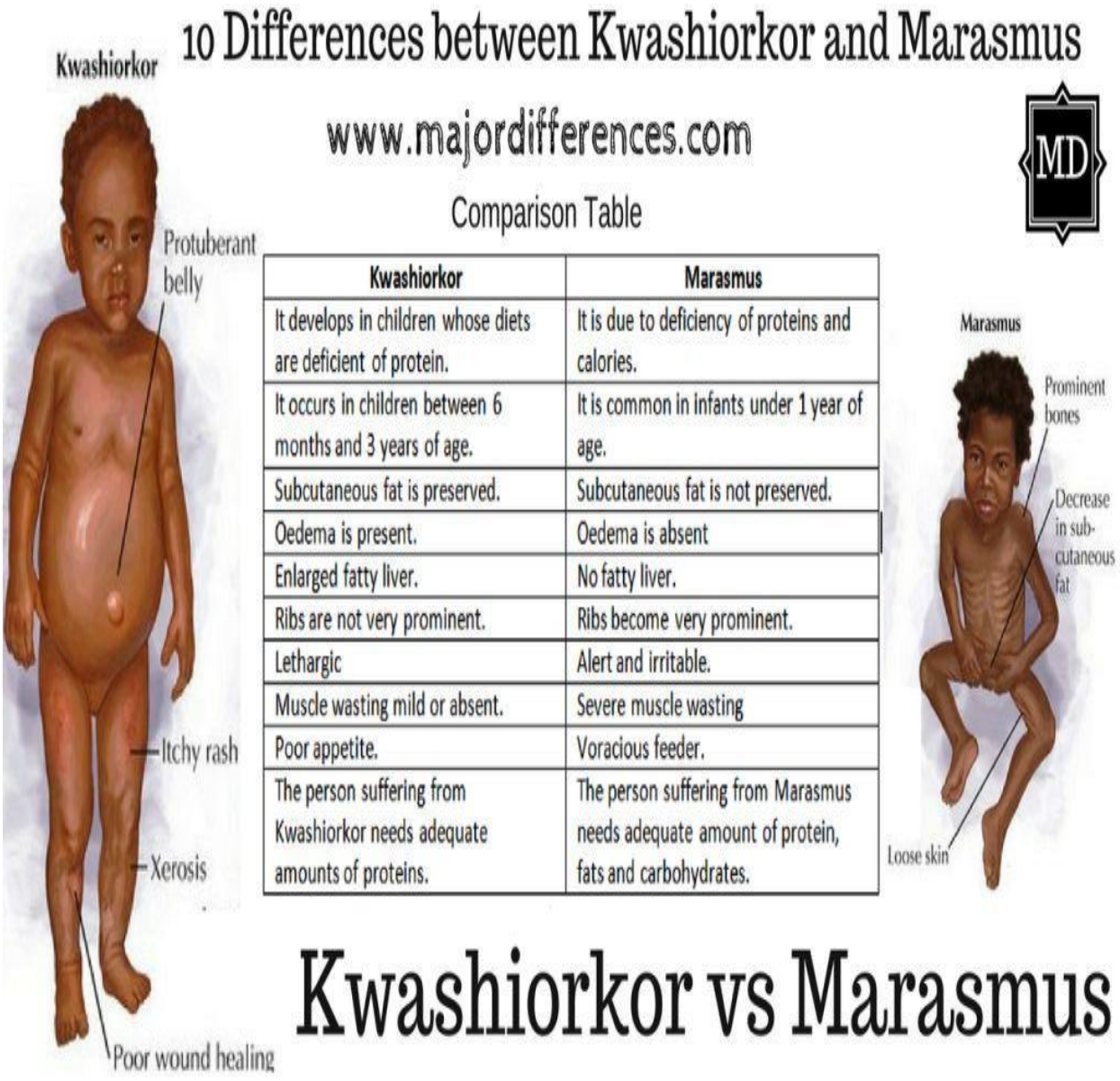
(Answer: B) ↓ Plasma oncotic pressure due to albumin loss.

B. Malnutrition (Protein Deficiency Disorders)



Biochemical Basis

- 1. Kwashiorkor (Severe Protein Deficiency)
  - Features: Edema, fatty liver, flaky paint dermatitis, apathy.
  - Pathophysiology: ↓ Albumin → ↓ Plasma oncotic pressure → Edema.
- 2. Marasmus (Severe Calorie & Protein Deficiency)
  - Features: Severe muscle wasting, no edema.
  - Pathophysiology: Total energy depletion (protein + fat loss).



Kwashiorkor	Marasmus
It develops in children whose diets are deficient of protein.	It is due to deficiency of proteins and calories.
It occurs in children between 6 months and 3 years of age.	It is common in infants under 1 year of age.
Subcutaneous fat is preserved.	Subcutaneous fat is not preserved.
Oedema is present.	Oedema is absent
Enlarged fatty liver.	No fatty liver.
Ribs are not very prominent.	Ribs become very prominent.
Lethargic	Alert and irritable.
Muscle wasting mild or absent.	Severe muscle wasting
Poor appetite.	Voracious feeder.
The person suffering from Kwashiorkor needs adequate amounts of proteins.	The person suffering from Marasmus needs adequate amount of protein, fats and carbohydrates.

Clinical Case:

A 2-year-old child from a refugee camp presents with swollen feet, irritability, and skin changes. Labs show low albumin and total protein. Diagnosis? Kwashiorkor.

 THINK TANK:

Why does Kwashiorkor cause a fatty liver but Marasmus does not?

 MCQ:

Which condition is characterized by muscle wasting without edema?

A) Kwashiorkor

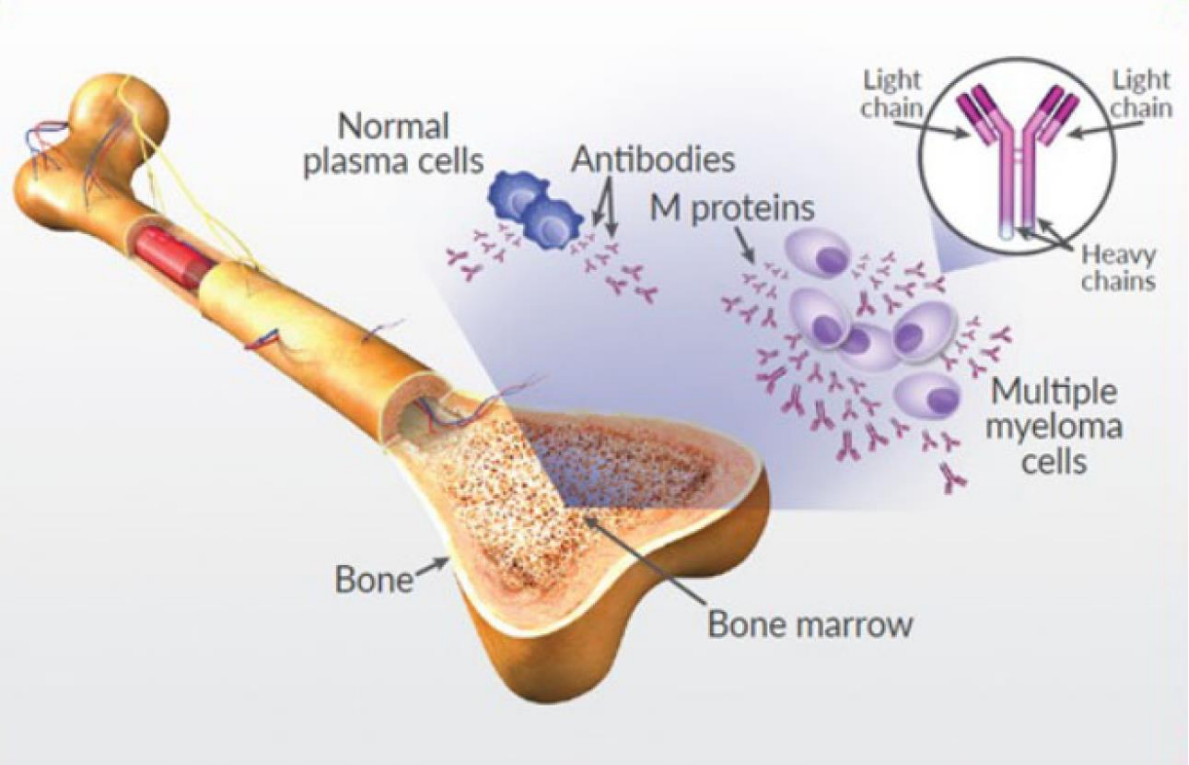
B) Marasmus

C) Nephrotic Syndrome

D) Liver Cirrhosis

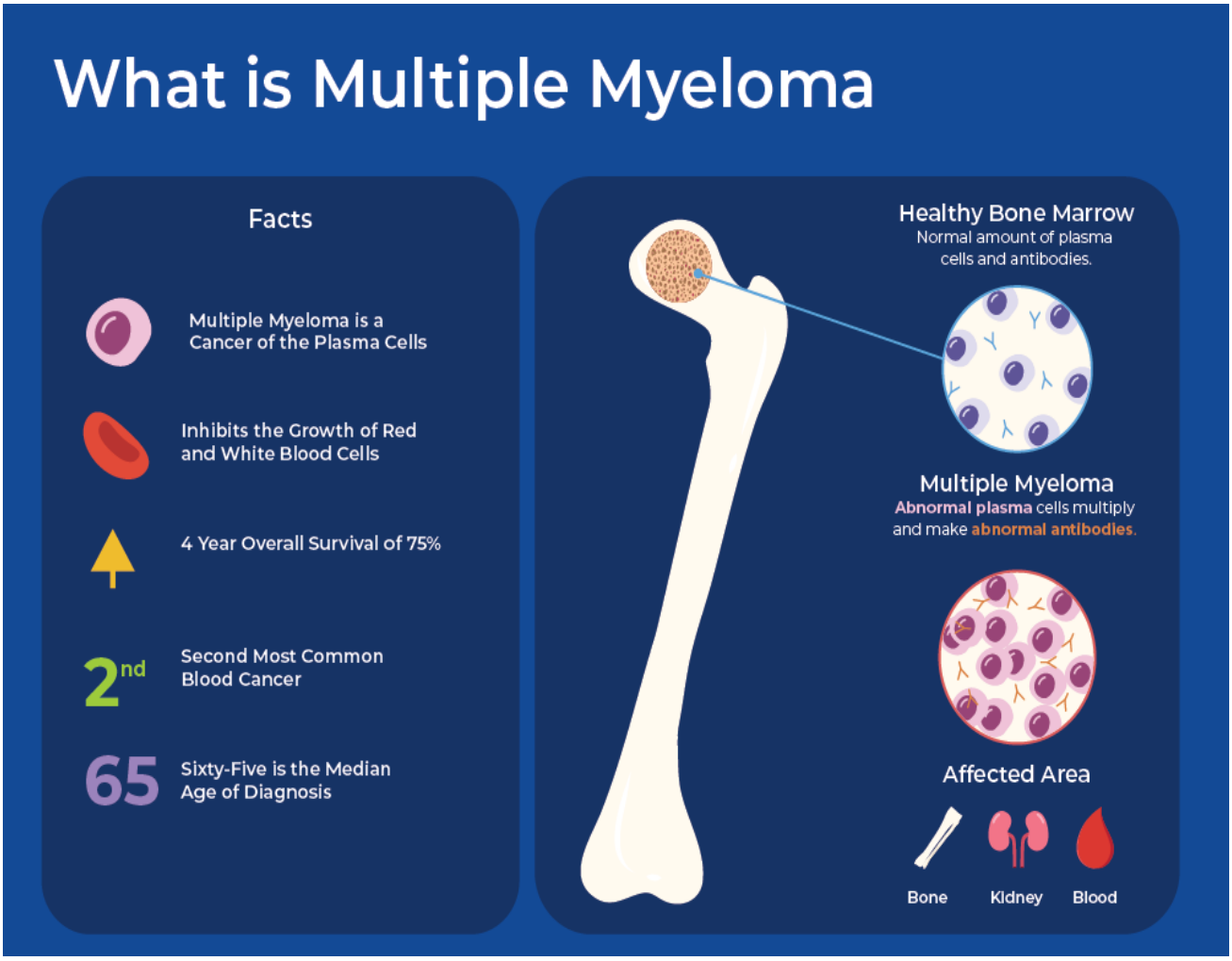
(Answer: B) Marasmus

C. Multiple Myeloma (Plasma Cell Dyscrasia)



Biochemical Basis: Multiple Myeloma is a cancer of plasma cells leading to excessive production of abnormal monoclonal immunoglobulins (IgG, IgA). This causes hyperviscosity, bone damage, renal failure.

- Pathophysiology:
    - 1. Bone Pain & Fractures – Due to osteoclast activation (↑ IL-6, RANKL).
    - 2. Hypercalcemia – From bone resorption.
    - 3. Kidney Damage (Myeloma Kidney) – Due to Bence-Jones proteinuria (light chains).
    - 4. Infections – Due to immune suppression.
- Diagnostic Markers:
    - M Spike on Serum Protein Electrophoresis (Monoclonal IgG/IgA).
    - Bence-Jones Proteins in Urine.
    - Punched-out bone lesions on X-ray.



Clinical Case:A 65-year-old male presents with bone pain, recurrent infections, and fatigue. Labs show anemia, hypercalcemia, and an M spike on electrophoresis. Diagnosis? Multiple Myeloma.

 THINK TANK:

Why does Multiple Myeloma cause hypercalcemia and renal damage?

 MCQ:

Which finding is most characteristic of Multiple Myeloma?

A) Low Ig levels

B) Bence-Jones Proteinuria

C) Hypocalcemia

D) Increased Albumin

(Answer: B) Bence-Jones Proteinuria

Quick Recap Mnemonics:

✓Leukocytosis Causes: "NLMEB" → Neutrophilia (Bacteria), Lymphocytosis (Virus), Monocytosis (TB), Eosinophilia (Parasites), Basophilia (CML).

✓Multiple Myeloma Symptoms: CRAB → Calcium ↑, Renal failure, Anemia, Bone lesions.

✓Kwashiorkor vs. Marasmus: "Kwashiorkor = Edema, Marasmus = Muscle Wasting".

EXTRA RESOUCRCES FOR STUDY

Video Lectures:

1. Osmosis Biochemistry Playlist: Osmosis offers concise and informative videos covering various biochemistry topics suitable for medical students.

2. Khan Academy Biochemistry Playlist: Khan Academy provides comprehensive tutorials on fundamental biochemistry concepts, including molecular structures and metabolic pathways.

3. Armando Hasudungan's Biochemistry Videos: Armando uses hand-drawn illustrations to explain complex biochemistry topics, making them easier to understand.

4. Interactive Biochemistry Animations by Wiley: These animations offer visual representations of biochemical processes, enhancing comprehension of dynamic mechanisms.

5. Harvard University's Biochemistry Lectures: Access in-depth lectures from Harvard University covering various aspects of biochemistry, from basic principles to advanced topics.

6. Med School Simplified is a YouTube channel dedicated to providing high-quality medical education content tailored for MBBS students

7. Ninja Nerd provides detailed and engaging biochemistry lectures with clear explanations and visuals, covering topics like metabolism, enzyme kinetics, and biochemical pathways.

8. Armando Hasudungan creates hand-drawn educational videos that simplify complex biochemical processes, making topics like carbohydrate metabolism and lipid digestion easy to understand.

9. Dr. Najeeb's Lectures provide in-depth, visually enriched medical tutorials covering biochemistry and other subjects with detailed explanations, making complex concepts easy to understand.

Standard Textbooks:

1. Lippincott Illustrated Reviews: Biochemistry – A well-illustrated and student-friendly book with conceptual clarity and clinical correlations.

2. Harper's Illustrated Biochemistry – Comprehensive and detailed, ideal for understanding biochemical pathways and clinical applications.

Review Books & Exam Preparation:

6. Rapid Review Biochemistry (by Goljan) – Concise and high-yield for exam preparation.

7. Biochemistry for the Medical Sciences (by Michael Lieberman & Rick Ricer) – A great summary book with key concept.