CYRILLIC COLLEGE

COURSE TITLE	**INTRODUCTION TO BIOCHEMISTRY**
COUSRE CODE	**BCH 101**
DURATION	**45 HRS**
UNIT	**3.0**

GOAL: This course is designed to introduce the student to the essential areas of Clinical Biochemistry

GENERAL OBJECTIVES: On completion of this course, the student should be able to

1.0 Understanding Introduction to Medical Biochemistry

2.0 Understanding Enzymes

3.0 Understanding Carbohydrates

4.0 Understanding Integrative Metabolism and Bioenergetics

5.0 Understanding Lipids

6.0 Understanding Amino Acids

7.0 Understanding Vitamins and Coenzymes

8.0 Understanding Mineral Metabolism

9.0 Understanding Hormones

10.0 Understanding Molecular Genetics

1.1 Definition of Biochemistry and Clinical Biochemistry

Biochemistry: Biochemistry is the branch of science that explores the chemical processes and substances occurring within living organisms. It combines principles from both biology and chemistry to study the structure, composition, and function of biomolecules like proteins, lipids, carbohydrates, nucleic acids, and enzymes. Biochemistry plays a crucial role in understanding cellular processes, genetic information flow, metabolism, and molecular signaling.

Clinical Biochemistry (Medical Biochemistry): Clinical Biochemistry, also known as Medical Biochemistry, is a specialized branch of biochemistry that focuses on the analysis of bodily fluids (such as blood, urine, and cerebrospinal fluid) to diagnose, monitor, and manage diseases. It applies biochemical knowledge to understand disease mechanisms, identify biomarkers, and guide treatment strategies. Clinical biochemists work in laboratories to conduct tests that help detect abnormalities in metabolism, organ function, and nutrient levels.

1.2 Importance of Clinical/Medical Biochemistry

1. **Diagnosis of Diseases:**
    - Clinical biochemistry is fundamental in diagnosing various diseases, such as diabetes (through glucose testing), kidney disorders (via creatinine and urea levels), liver diseases (by analyzing liver enzymes), and thyroid disorders (through hormone levels).
    - It helps in the early detection of diseases, allowing timely intervention and treatment.
2. **Monitoring Disease Progression and Treatment:**
    - Biochemical tests help monitor the progression of chronic diseases like diabetes, heart disease, and cancer.
    - It aids in assessing the effectiveness of treatments by tracking changes in relevant biochemical markers, such as HbA1c in diabetes or cholesterol levels in cardiovascular disease.
3. **Screening and Preventive Health Care:**

- Routine biochemical screenings can identify risk factors for diseases before symptoms appear. For example, lipid profiles help identify the risk of cardiovascular diseases.
- Prenatal screenings can detect congenital disorders, ensuring early management.

4. **Guiding Therapeutic Decisions:**
   - Biochemical analysis helps customize treatment plans. For example, electrolyte levels guide fluid therapy, and hormone assays influence endocrine disorder management.
   - Therapeutic drug monitoring ensures medications are within therapeutic ranges, minimizing side effects and toxicity.
5. **Understanding Disease Mechanisms:**
   - Clinical biochemistry provides insight into the biochemical pathways affected by diseases, aiding in the development of new therapeutic targets and drugs.
   - It bridges the gap between basic biochemical research and clinical applications.
6. **Emergency Medicine:**
   - Rapid biochemical testing is essential in emergency settings. For example, measuring blood gases and lactate levels helps manage critical conditions like sepsis or respiratory failure.
7. **Research and Development:**
   - Clinical biochemistry contributes to medical research by identifying new biomarkers for diseases and evaluating the biochemical effects of new drugs.
8. **Public Health and Epidemiology:**
   - Large-scale biochemical studies help in understanding disease patterns in populations, informing public health policies and preventive strategies.

2.1 Definition of Enzymes

Enzymes are biological catalysts, typically proteins (though some are RNA-based, called ribozymes), that accelerate chemical reactions in living organisms without being consumed in the process. They lower the activation energy required for reactions to occur, making metabolic processes efficient and regulated under physiological conditions.

2.2 The Nature of Enzymes

1. **Proteinaceous Structure:**
    - Most enzymes are globular proteins composed of long chains of amino acids folded into specific three-dimensional shapes necessary for their catalytic activity.
2. **Active Site:**
    - Enzymes have specific regions called *active sites* where substrates (the reactants) bind. The active site's shape is complementary to the substrate, allowing specificity.
3. **Specificity:**
    - Enzymes are highly specific, meaning they catalyze only particular reactions or work on specific substrates. This specificity is due to the unique structure of their active sites.
4. **Cofactors and Coenzymes:**
    - Some enzymes require non-protein molecules to function:
        - **Cofactors:** Inorganic ions like Mg^{2+}, Zn^{2+}, or Fe^{2+}.
        - **Coenzymes:** Organic molecules like vitamins (e.g., NAD^{+}, FAD).
5. **Sensitivity to Environmental Conditions:**
    - Enzyme activity is influenced by factors like temperature, pH, and substrate concentration.

2.3 Properties of Enzymes

1. **Catalytic Efficiency:**
    - Enzymes significantly speed up reactions, often by factors of millions, compared to non-catalyzed reactions.
2. **Specificity:**
    - Enzymes are specific to substrates and reactions. This can be:
        - **Absolute specificity** (only one substrate),
        - **Group specificity** (a group of related substrates),
        - **Stereospecificity** (only one optical isomer of a substrate).
3. **Reversibility:**
    - Many enzyme-catalyzed reactions are reversible, depending on the concentration of substrates and products.
4. **Temperature and pH Sensitivity:**
    - Enzymes have optimal temperature and pH ranges. Extreme conditions can denature enzymes, altering their structure and function.
5. **Saturation and Michaelis-Menten Kinetics:**
    - At low substrate concentrations, enzyme activity increases with substrate concentration. However, at high substrate levels, enzymes become saturated, and activity levels off (Vmax).
6. **Inhibition:**
    - Enzymes can be inhibited by specific molecules:
        - **Competitive inhibitors** compete with the substrate for the active site.
        - **Non-competitive inhibitors** bind elsewhere on the enzyme, altering its function.
7. **Regulation:**
    - Enzyme activity can be regulated through feedback mechanisms, allosteric sites, covalent modifications (like phosphorylation), or by the availability of cofactors.

2.4 Classification of Enzymes

Enzymes are classified into **six major classes** based on the type of reaction they catalyze, according to the International Union of Biochemistry and Molecular Biology (IUBMB):

1. **Oxidoreductases:**
    - Catalyze oxidation-reduction reactions (transfer of electrons).
    - Example: *Dehydrogenases*, *oxidases*.
2. **Transferases:**
    - Transfer functional groups (e.g., methyl, phosphate) from one molecule to another.
    - Example: *Kinases* (transfer phosphate groups), *transaminases*.
3. **Hydrolases:**
    - Catalyze hydrolysis reactions (breaking bonds with water).
    - Example: *Proteases* (break down proteins), *lipases* (break down fats).
4. **Lyases:**
    - Remove groups from substrates without hydrolysis or oxidation, often forming double bonds.
    - Example: *Decarboxylases*, *aldolases*.
5. **Isomerases:**
    - Catalyze the rearrangement of atoms within a molecule (isomerization).
    - Example: *Racemases*, *epimerases*.
6. **Ligases (Synthetases):**
    - Catalyze the joining of two molecules, often with the hydrolysis of ATP.
    - Example: *DNA ligase, synthetases*.

2.5 Mechanism of Enzyme Action

The mechanism of enzyme action describes how enzymes facilitate chemical reactions. It involves the following key steps:

1. **Substrate Binding:**
    - The substrate binds to the enzyme's active site, forming an *enzyme-substrate complex (ES)*.
    - Binding can follow two models:
        - **Lock and Key Model:** The substrate fits precisely into the enzyme's active site.
        - **Induced Fit Model:** The enzyme undergoes a conformational change to better accommodate the substrate.
2. **Formation of the Enzyme-Substrate Complex:**
    - The enzyme stabilizes the transition state, lowering the activation energy required for the reaction.
3. **Catalysis:**
    - The enzyme facilitates the conversion of the substrate into the product through various mechanisms like:
        - Acid-base catalysis,
        - Covalent catalysis,
        - Metal ion catalysis.
4. **Product Formation and Release:**
    - The chemical reaction results in the formation of the product, which has a lower affinity for the enzyme and is released from the active site.
5. **Enzyme Recovery:**
    - After releasing the product, the enzyme returns to its original state, ready to catalyze another reaction cycle.

3.1 Definition of Carbohydrates in Chemical Terms

Carbohydrates are organic compounds composed of carbon (C), hydrogen (H), and oxygen (O) atoms, typically in a ratio of **1:2:1** (general formula: **$(CH_2O)_n$**). They are polyhydroxy aldehydes or ketones, or compounds that yield such structures upon hydrolysis. Carbohydrates are vital as energy sources, structural components, and signaling molecules in living organisms.

3.2 Classification of Carbohydrates into Three Major Groups

Carbohydrates are classified based on the number of sugar units:

1. **Monosaccharides (Simple Sugars):**
    - Single sugar units that cannot be hydrolyzed into simpler sugars.
    - **Examples:** Glucose, Fructose, Galactose.
2. **Disaccharides (Double Sugars):**
    - Composed of two monosaccharide units linked by a glycosidic bond.
    - **Examples:** Sucrose (Glucose + Fructose), Lactose (Glucose + Galactose), Maltose (Glucose + Glucose).
3. **Polysaccharides (Complex Carbohydrates):**
    - Long chains of monosaccharide units linked together.
    - **Examples:** Starch (plant energy storage), Glycogen (animal energy storage), Cellulose (plant structural component).

3.3 Monosaccharides of Biological Importance and Their Properties

1. **Glucose:**
    - **Structure:** Aldohexose (6-carbon sugar with an aldehyde group).
    - **Importance:** Primary energy source for cells; regulated by insulin and glucagon.
    - **Properties:** Soluble in water, sweet-tasting, reducing sugar.
2. **Fructose:**
    - **Structure:** Ketohexose (6-carbon sugar with a ketone group).
    - **Importance:** Found in fruits and honey; part of sucrose.
    - **Properties:** Sweetest natural sugar, water-soluble, reducing sugar.
3. **Galactose:**
    - **Structure:** Aldohexose.

- **Importance:** Part of lactose (milk sugar); important in glycoproteins and glycolipids.
- **Properties:** Less sweet than glucose, water-soluble, reducing sugar.

4. **Ribose and Deoxyribose:**
    - **Structure:** Aldopentoses (5-carbon sugars); deoxyribose lacks one oxygen atom compared to ribose.
    - **Importance:** Ribose is a component of RNA; deoxyribose is found in DNA.
    - **Properties:** Water-soluble, structural role in nucleic acids.

General Properties of Monosaccharides:

- Sweet taste (especially glucose and fructose).
- Water-soluble due to multiple hydroxyl groups.
- Exhibit optical isomerism (D- and L- forms).
- Reducing sugars (except ketoses like fructose under some conditions).

3.4 Disaccharides of Biological Importance and Their Properties

1. **Sucrose:**
    - **Composition:** Glucose + Fructose (linked by α-1,2 glycosidic bond).
    - **Importance:** Common table sugar, major transport form of carbohydrates in plants.
    - **Properties:** Non-reducing sugar (no free anomeric carbon), highly soluble, sweet.
2. **Lactose:**
    - **Composition:** Glucose + Galactose (linked by β-1,4 glycosidic bond).
    - **Importance:** Milk sugar, important in infant nutrition.
    - **Properties:** Reducing sugar, less sweet than sucrose, lactose intolerance results from lactase deficiency.
3. **Maltose:**
    - **Composition:** Glucose + Glucose (linked by α-1,4 glycosidic bond).
    - **Importance:** Product of starch digestion, found in malted foods.

- **Properties:** Reducing sugar, less sweet, water-soluble.

3.5 Polysaccharides of Biological Importance and Their Properties

1. **Starch:**
   - **Composition:** Mixture of amylose (linear) and amylopectin (branched) chains of glucose.
   - **Importance:** Primary energy storage in plants.
   - **Properties:** Insoluble in cold water, forms a gel-like paste when heated, non-reducing.
2. **Glycogen:**
   - **Composition:** Highly branched polymer of glucose (similar to amylopectin but more branched).
   - **Importance:** Main energy storage in animals, especially in liver and muscle.
   - **Properties:** Soluble in water, rapidly mobilized for energy, non-reducing.
3. **Cellulose:**
   - **Composition:** Linear chains of glucose linked by β-1,4 glycosidic bonds.
   - **Importance:** Structural component in plant cell walls.
   - **Properties:** Insoluble in water, indigestible by humans (due to lack of cellulase), forms dietary fiber.
4. **Chitin:**
   - **Composition:** Polymer of N-acetylglucosamine.
   - **Importance:** Structural component in fungal cell walls and exoskeletons of arthropods.
   - **Properties:** Tough, flexible, and water-insoluble.

3.6 Chemistry and Functions of Glycoproteins

Chemistry of Glycoproteins:

- **Glycoproteins** are proteins that have carbohydrate chains covalently attached to their polypeptide backbone.
- The carbohydrate portion can be simple sugars or complex oligosaccharides.
- Carbohydrate chains are attached via **N-glycosidic bonds** (to the nitrogen in asparagine) or **O-glycosidic bonds** (to the oxygen in serine or threonine).

Functions of Glycoproteins:

1. **Cell-Cell Recognition and Communication:** Found on cell membranes as receptors (e.g., in immune response).
2. **Structural Roles:** Components of connective tissues (e.g., collagen).
3. **Hormones and Enzymes:** Some hormones like **erythropoietin** are glycoproteins.
4. **Immune Response:** Antibodies (immunoglobulins) are glycoproteins.
5. **Blood Group Determinants:** ABO blood groups are defined by glycoproteins on red blood cells.

3.7 Metabolism of Glucose in the Body

1. **Glycolysis:**
    - Breakdown of glucose into pyruvate, generating **ATP** and **NADH**.
    - Occurs in the cytoplasm and is anaerobic (doesn't require oxygen).
2. **Gluconeogenesis:**
    - Synthesis of glucose from non-carbohydrate precursors (e.g., amino acids, lactate) primarily in the liver.
3. **Glycogenesis:**
    - Conversion of glucose into glycogen for storage, mainly in liver and muscle tissues.
4. **Glycogenolysis:**
    - Breakdown of glycogen back into glucose when energy is needed.
5. **Pentose Phosphate Pathway (PPP):**

- Produces NADPH (for biosynthetic reactions) and ribose-5-phosphate (for nucleotide synthesis).

6. **Aerobic Respiration:**
    - In the presence of oxygen, pyruvate enters the mitochondria and is converted to acetyl-CoA, entering the citric acid cycle for further ATP production.

3.8 Mechanism of Cellular ATP Formation and Utilization

ATP Formation:

1. **Substrate-Level Phosphorylation:**
    - Direct transfer of a phosphate group to ADP from a phosphorylated intermediate (e.g., during glycolysis).
2. **Oxidative Phosphorylation:**
    - Occurs in the mitochondria during electron transport chain (ETC).
    - Electrons from NADH and $FADH_2$ pass through the ETC, creating a proton gradient across the mitochondrial membrane.
    - Protons flow back into the mitochondrial matrix through **ATP synthase**, driving ATP synthesis.
3. **Photophosphorylation (in plants):**
    - ATP production in chloroplasts using light energy during photosynthesis.

ATP Utilization:

1. **Energy Currency:**
    - ATP provides energy for cellular processes like muscle contraction, active transport, biosynthesis, and signal transduction.
2. **Phosphorylation Reactions:**
    - ATP donates phosphate groups to activate or deactivate enzymes and other proteins.
3. **Signal Transduction:**

- ATP is a precursor for cyclic AMP (cAMP), a second messenger in many signaling pathways.

5.1 Definition of Lipids in Chemical Terms

Lipids are a diverse group of hydrophobic or amphipathic organic compounds primarily composed of carbon (C), hydrogen (H), and oxygen (O), with some containing phosphorus, nitrogen, or sulfur. Unlike carbohydrates, lipids do not follow a specific ratio of these elements. They are insoluble in water but soluble in non-polar solvents like ether, chloroform, and benzene. Chemically, lipids include fatty acids and their derivatives, as well as substances related biosynthetically or functionally to these compounds.

5.2 General Functions of Lipids

1. **Energy Storage:**
   - Lipids, particularly triglycerides, provide a dense source of energy, yielding **9 kcal/g** upon oxidation, more than twice that of carbohydrates and proteins.
2. **Structural Components:**
   - Lipids are essential in cell membranes (phospholipids, cholesterol) and organelles, providing structural integrity and fluidity.
3. **Insulation and Protection:**
   - Fat deposits act as thermal insulators, especially in animals in cold environments. Lipids also cushion vital organs, offering mechanical protection.
4. **Signaling Molecules:**
   - Steroid hormones, eicosanoids (like prostaglandins), and lipid-soluble vitamins (A, D, E, K) are involved in cellular signaling pathways.
5. **Vitamin Absorption:**
   - Lipids facilitate the absorption of fat-soluble vitamins (A, D, E, K) in the intestine.

6. **Waterproofing:**
    - Waxes in plants and animals prevent water loss (e.g., cuticles in plants, sebum in human skin).
7. **Metabolic Regulation:**
    - Lipids like cholesterol are precursors to bile acids and hormones, regulating metabolism and digestion.

5.3 Classification and Types of Lipids

Lipids are classified into **simple**, **compound**, and **derived lipids** based on their structure and function:

1. **Simple Lipids:**
    - **Definition:** Esters of fatty acids with various alcohols.
    - **Types:**
        - **Fats and Oils (Triglycerides):** Glycerol esterified with three fatty acids. Solid at room temperature (fats) or liquid (oils).
        - **Waxes:** Esters of long-chain fatty acids with long-chain alcohols. Found in plant cuticles and animal skin.
2. **Compound (Complex) Lipids:**
    - **Definition:** Lipids containing fatty acids, alcohols, and additional functional groups.
    - **Types:**
        - **Phospholipids:** Contain phosphate groups (e.g., phosphatidylcholine in membranes).
        - **Glycolipids:** Contain carbohydrate groups; important in cell recognition (e.g., cerebrosides).
        - **Lipoproteins:** Complexes of lipids with proteins; transport lipids in the bloodstream.
3. **Derived Lipids:**
    - **Definition:** Substances derived from simple and compound lipids by hydrolysis.
    - **Types:**

        - **Steroids:** Include cholesterol, steroid hormones (e.g., testosterone, estrogen).
        - **Fatty Acids:** Saturated (no double bonds) and unsaturated (one or more double bonds).
        - **Eicosanoids:** Derived from arachidonic acid; include prostaglandins, thromboxanes.
4. **Miscellaneous Lipids:**
    - Includes fat-soluble vitamins (A, D, E, K), pigments like carotenoids, and synthetic lipids.

5.4 Digestion and Absorption of Lipids

1. Digestion:

- **Mouth:**
    - Minimal digestion via *lingual lipase* in infants.
- **Stomach:**
    - *Gastric lipase* starts breaking down triglycerides into diglycerides and free fatty acids, particularly in infants.
- **Small Intestine (Primary Site):**
    - **Emulsification:** Bile salts from the liver emulsify large fat droplets into smaller micelles, increasing surface area for enzyme action.
    - **Enzymatic Action:**
        - *Pancreatic lipase* breaks triglycerides into monoglycerides and free fatty acids.
        - *Phospholipase A2* digests phospholipids.
        - *Cholesterol esterase* hydrolyzes cholesterol esters into free cholesterol and fatty acids.

2. Absorption:

- **Micelle Formation:**
    - Digested lipids form micelles with bile salts, facilitating transport to the intestinal epithelium.

- **Intestinal Absorption:**
    - Fatty acids and monoglycerides diffuse into enterocytes (intestinal cells).
- **Re-esterification and Chylomicron Formation:**
    - Inside enterocytes, fatty acids are re-esterified into triglycerides and packaged into *chylomicrons* (lipoproteins) for transport via the lymphatic system into the bloodstream.

5.5 Metabolism of Lipids

1. **Lipolysis (Breakdown of Lipids):**
    - **Triglycerides** are broken down into glycerol and free fatty acids by *hormone-sensitive lipase* in adipose tissue.
    - **Glycerol** enters glycolysis or gluconeogenesis.
    - **Fatty acids** undergo **β-oxidation** in mitochondria, producing acetyl-CoA, NADH, and $FADH_2$ for energy production via the citric acid cycle and electron transport chain.
2. **Lipogenesis (Synthesis of Lipids):**
    - Occurs in the liver and adipose tissue when energy is abundant.
    - **Acetyl-CoA** is converted to fatty acids through a series of enzymatic reactions, then esterified to form triglycerides for storage.
3. **Ketogenesis:**
    - In conditions of carbohydrate deprivation (e.g., fasting, diabetes), the liver converts acetyl-CoA into **ketone bodies** (acetoacetate, β-hydroxybutyrate, acetone) as alternative energy sources for the brain and muscles.
4. **Cholesterol Metabolism:**
    - Synthesized from acetyl-CoA in the liver.
    - Used in the formation of cell membranes, bile acids, steroid hormones, and vitamin D.

5.6 Lipid-Related Disorders

1. **Hyperlipidemia (High Blood Lipids):**

- Elevated levels of cholesterol or triglycerides, increasing the risk of **atherosclerosis** and cardiovascular diseases.

2. **Atherosclerosis:**
   - Accumulation of cholesterol-rich plaques in arterial walls, leading to reduced blood flow and risk of heart attack or stroke.
3. **Obesity:**
   - Excessive accumulation of body fat, often associated with metabolic syndrome, type 2 diabetes, and cardiovascular diseases.
4. **Fatty Liver Disease (Hepatic Steatosis):**
   - Accumulation of fat in liver cells; can be alcoholic or non-alcoholic (NAFLD).
5. **Lipid Storage Diseases:**
   - Genetic disorders like **Tay-Sachs disease** and **Gaucher disease**, characterized by the abnormal accumulation of lipids in cells due to enzyme deficiencies.
6. **Essential Fatty Acid Deficiency:**
   - Deficiency in omega-3 and omega-6 fatty acids leads to skin disorders, impaired growth, and neurological issues.

5.7 Lipoproteins

Lipoproteins are complexes of lipids and proteins that transport hydrophobic lipids through the aqueous environment of the bloodstream. They vary in density and function:

1. **Chylomicrons:**
   - **Composition:** High in triglycerides, low in protein.
   - **Function:** Transport dietary lipids from the intestines to peripheral tissues.
2. **Very Low-Density Lipoproteins (VLDL):**
   - **Composition:** High in triglycerides, moderate cholesterol.
   - **Function:** Transport triglycerides from the liver to tissues.
3. **Low-Density Lipoproteins (LDL):**
   - **Composition:** High in cholesterol.
   - **Function:** Deliver cholesterol to peripheral tissues.

- **Clinical Importance:** Known as "bad cholesterol" due to its role in atherosclerosis.

4. **High-Density Lipoproteins (HDL):**
    - **Composition:** High in protein, low in lipids.
    - **Function:** Collect excess cholesterol from tissues and return it to the liver for excretion (reverse cholesterol transport).
    - **Clinical Importance:** Known as "good cholesterol" for its protective role against cardiovascular disease.
5. **Intermediate-Density Lipoproteins (IDL):**
    - Transitional form between VLDL and LDL.

Structure of Lipoproteins:

- **Core:** Hydrophobic lipids (triglycerides and cholesterol esters).
- **Surface:** Amphipathic phospholipids, free cholesterol, and apolipoproteins (proteins that help stabilize the lipoprotein and direct it to specific receptors).

6.1 Definition of Amino Acids

Amino acids are organic compounds that serve as the building blocks of proteins. Chemically, they consist of a central carbon atom (**α-carbon**) bonded to four distinct groups:

1. A hydrogen atom (**H**),
2. An amino group (**$–NH_2$**),
3. A carboxyl group (**–COOH**),
4. A distinctive side chain (**R-group**) that determines the identity and properties of the amino acid.

The general formula is **NH_2–CHR–COOH**. At physiological pH (~7.4), amino acids exist as **zwitterions**, meaning they have both positive (on the amino group) and negative (on the carboxyl group) charges.

6.2 Classification of Amino Acids

Amino acids can be classified based on various criteria:

1. **Based on Side Chain Properties (Polarity and Charge):**
    - **Nonpolar (Hydrophobic) Amino Acids:** Glycine, Alanine, Valine, Leucine, Isoleucine, Methionine, Proline, Phenylalanine, Tryptophan.
    - **Polar Uncharged Amino Acids:** Serine, Threonine, Cysteine, Tyrosine, Asparagine, Glutamine.
    - **Polar Charged Amino Acids:**
        - **Acidic (Negatively Charged):** Aspartic acid, Glutamic acid.
        - **Basic (Positively Charged):** Lysine, Arginine, Histidine.
2. **Based on Nutritional Requirement:**
    - **Essential Amino Acids (must be obtained from diet):** Histidine, Isoleucine, Leucine, Lysine, Methionine, Phenylalanine, Threonine, Tryptophan, Valine.
    - **Non-Essential Amino Acids (synthesized in the body):** Alanine, Asparagine, Aspartic acid, Glutamic acid, Serine.
    - **Conditionally Essential Amino Acids (required in specific conditions like illness):** Arginine, Cysteine, Glutamine, Tyrosine, Glycine, Proline.
3. **Based on Metabolic Fate:**
    - **Glucogenic Amino Acids:** Converted into glucose through gluconeogenesis (e.g., Alanine, Glutamine).
    - **Ketogenic Amino Acids:** Converted into ketone bodies (e.g., Leucine, Lysine).
    - **Both Glucogenic and Ketogenic:** Isoleucine, Phenylalanine, Threonine, Tryptophan, Tyrosine.
4. **Based on Structure:**
    - **Aliphatic:** Glycine, Alanine, Valine.
    - **Aromatic:** Phenylalanine, Tyrosine, Tryptophan.
    - **Sulfur-containing:** Cysteine, Methionine.
    - **Hydroxyl-containing:** Serine, Threonine.

6.3 Peptide Bonds

A **peptide bond** is a covalent bond that links two amino acids together in a protein. It forms between the **carboxyl group (–COOH)** of one amino acid and the **amino group ($–NH_2$)** of another, releasing a molecule of water in a condensation (dehydration synthesis) reaction.

Peptide bond formation:

- **Reaction:**
  Amino acid 1 –COOH + Amino acid 2 $–NH_2$ → Peptide bond + H_2O

The resulting bond has partial double-bond character, restricting rotation and making the peptide bond planar.

6.4 Physiology of Peptide Bonds

1. **Structural Stability:**
   - The partial double-bond character of the peptide bond results in rigidity and planarity, which contributes to the structural stability of proteins.
2. **Polypeptide Formation:**
   - Multiple amino acids linked by peptide bonds form **polypeptides** or **proteins**. The sequence of amino acids in a polypeptide is called the **primary structure** of a protein.
3. **Directional Nature:**
   - Peptides have two ends:
     - **N-terminus:** The end with a free amino group.
     - **C-terminus:** The end with a free carboxyl group.
   - Peptide synthesis and reading occur from the N-terminus to the C-terminus.
4. **Protein Folding:**
   - While peptide bonds are rigid, the bonds adjacent to the α-carbon are flexible, allowing proteins to fold into complex 3D structures critical for their function.
5. **Hydrolysis:**

- Peptide bonds can be broken down by hydrolysis, catalyzed by **proteolytic enzymes** like **pepsin**, **trypsin**, and **chymotrypsin** during digestion.

6.5 Definition of Proteins

Proteins are large, complex macromolecules composed of one or more long chains of amino acids linked by peptide bonds. They have diverse structures and functions, playing vital roles in nearly all biological processes.

- Proteins typically consist of **50 or more amino acids**, while shorter chains are referred to as **peptides**.

6.6 Functions of Proteins

1. **Structural Support:**
   - Proteins like **collagen** (in connective tissues), **keratin** (in hair, nails), and **elastin** provide structural integrity.
2. **Enzymatic Activity:**
   - Many proteins function as **enzymes** (e.g., amylase, pepsin), catalyzing biochemical reactions in the body.
3. **Transport and Storage:**
   - Proteins like **hemoglobin** transport oxygen, while **ferritin** stores iron.
4. **Hormonal Regulation:**
   - Some hormones are proteins or peptides (e.g., **insulin**, **glucagon**), regulating physiological processes like metabolism and growth.
5. **Immune Response:**
   - **Antibodies (immunoglobulins)** are proteins that recognize and neutralize foreign substances.
6. **Movement:**
   - **Actin** and **myosin** are proteins involved in muscle contraction.

7. **Cell Communication:**
    - Receptor proteins on cell membranes mediate signaling (e.g., **insulin receptor**).
8. **Buffering:**
    - Proteins help maintain acid-base balance by acting as buffers (e.g., hemoglobin in blood).
9. **Energy Source:**
    - In times of energy shortage, proteins can be broken down to provide energy (4 kcal/g).

6.7 Classification of Proteins

Proteins can be classified based on their structure, composition, and function:

1. **Based on Composition:**
    - **Simple Proteins:** Yield only amino acids upon hydrolysis (e.g., **albumin**, **globulin**).
    - **Conjugated Proteins:** Contain a non-protein group (prosthetic group) in addition to amino acids.
        - **Examples:**
            - **Glycoproteins** (protein + carbohydrate): Immunoglobulins.
            - **Lipoproteins** (protein + lipid): HDL, LDL.
            - **Metalloproteins** (protein + metal): Hemoglobin (contains iron).
            - **Phosphoproteins** (protein + phosphate): Casein (in milk).
    - **Derived Proteins:** Formed by partial hydrolysis of simple or conjugated proteins (e.g., **peptides**).
2. **Based on Shape:**
    - **Fibrous Proteins:** Long, insoluble, structural proteins (e.g., **collagen**, **keratin**).
    - **Globular Proteins:** Spherical, soluble proteins with dynamic functions (e.g., **enzymes**, **hormones**, **antibodies**).
3. **Based on Function:**
    - **Enzymatic Proteins:** Catalyze biochemical reactions (e.g., **amylase**, **lipase**).
    - **Transport Proteins:** Move substances across membranes or in the bloodstream (e.g., **hemoglobin**, **albumin**).

- **Structural Proteins:** Provide support and shape (e.g., **collagen**, **elastin**).
- **Defensive Proteins:** Involved in immune response (e.g., **antibodies**).
- **Regulatory Proteins:** Regulate physiological processes (e.g., **insulin**, **growth hormone**).
- **Motor Proteins:** Facilitate movement (e.g., **actin**, **myosin**).

6.8 Protein-Related Disorders

1. **Protein-Energy Malnutrition (PEM):**
   - **Kwashiorkor:** Caused by protein deficiency with adequate calorie intake, leading to edema, fatty liver, and growth retardation.
   - **Marasmus:** Severe deficiency of both protein and calories, resulting in muscle wasting and stunted growth.
2. **Cystic Fibrosis:**
   - A genetic disorder caused by mutations in the **CFTR protein**, leading to thick mucus buildup in lungs and digestive organs.
3. **Sickle Cell Anemia:**
   - Caused by a mutation in the **hemoglobin** gene, leading to the production of abnormal hemoglobin (HbS) and resulting in misshapen red blood cells.
4. **Phenylketonuria (PKU):**
   - A metabolic disorder caused by deficiency of **phenylalanine hydroxylase**, leading to the accumulation of phenylalanine and resulting in intellectual disabilities if untreated.
5. **Albinism:**
   - Caused by mutations affecting the **tyrosinase** enzyme involved in melanin production, leading to lack of pigmentation.
6. **Maple Syrup Urine Disease (MSUD):**
   - A disorder caused by defects in the metabolism of branched-chain amino acids, leading to their accumulation and a characteristic sweet-smelling urine.
7. **Amyloidosis:**
   - A condition characterized by the deposition of abnormal **amyloid proteins** in organs and tissues, leading to organ dysfunction.
8. **Prion Diseases:**

- Caused by misfolded prion proteins, leading to neurodegenerative diseases like **Creutzfeldt-Jakob disease**.

9. **Collagen Disorders:**
    - Genetic mutations affecting collagen synthesis, leading to disorders like **Ehlers-Danlos syndrome** (hyperflexibility) and **osteogenesis imperfecta** (brittle bones).

6.9 Digestion and Absorption of Proteins

1. Overview: Protein digestion involves breaking down dietary proteins into absorbable units like amino acids, dipeptides, and tripeptides. This process occurs in multiple stages involving the stomach, pancreas, and small intestine.

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2. Digestion of Proteins:

a. In the Stomach:

- **Denaturation by Hydrochloric Acid (HCl):**
  HCl, secreted by **parietal cells** of the stomach, denatures proteins, unfolding them to expose peptide bonds for enzymatic action.
- **Enzymatic Breakdown by Pepsin:**
  Pepsinogen (secreted by **chief cells**) is activated to **pepsin** in the presence of HCl. Pepsin is an **endopeptidase** that breaks down proteins into smaller polypeptides by cleaving peptide bonds within the chain, especially at aromatic amino acids like **phenylalanine, tryptophan**, and **tyrosine**.

b. In the Small Intestine:

- **Pancreatic Enzymes:**
    - The partially digested polypeptides enter the **duodenum**, where they are further broken down by pancreatic enzymes:

        - **Trypsin** (activated from trypsinogen by **enteropeptidase**): Cleaves at the carboxyl side of basic amino acids like **lysine** and **arginine**.
        - **Chymotrypsin**: Targets aromatic amino acids.
        - **Elastase**: Acts on small, neutral amino acids like **glycine** and **alanine**.
        - **Carboxypeptidase A & B**: Exopeptidases that cleave terminal amino acids from the carboxyl end.
- **Brush Border Enzymes:**
    - **Aminopeptidases**: Remove amino acids from the amino (N-terminal) end.
    - **Dipeptidases** and **tripeptidases**: Break down dipeptides and tripeptides into individual amino acids.

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3. Absorption of Amino Acids:

- **Location:**
  Absorption occurs primarily in the **jejunum** and **ileum** of the small intestine.
- **Mechanism of Absorption:**
    - **Active Transport:**
      Amino acids are absorbed via **sodium-dependent active transport** systems, requiring energy (ATP). Sodium-amino acid co-transporters move amino acids into the enterocytes (intestinal cells).
    - **Transport of Dipeptides and Tripeptides:**
      Small peptides are absorbed through **proton-dependent peptide transporters (PepT1)** and are then hydrolyzed into free amino acids within the enterocytes.
    - **Facilitated Diffusion:**
      Once inside the enterocyte, amino acids are transported across the **basolateral membrane** into the bloodstream via facilitated diffusion.

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4. Transport to the Liver:

- Amino acids enter the **portal circulation** and are transported to the **liver** via the **hepatic portal vein**.
- In the liver, amino acids are either:
    - Used for **protein synthesis**,
    - Converted into other **biomolecules**,
    - **Deaminated** for energy production,
    - Released into the bloodstream for use by other tissues.

6.10 Metabolism of Proteins

Protein metabolism involves the synthesis, breakdown, and transformation of proteins and amino acids for energy, growth, and repair.

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1. Protein Synthesis (Anabolism):

- **Transcription and Translation:**
    - **Transcription:** DNA is transcribed into mRNA in the nucleus.
    - **Translation:** mRNA is translated into polypeptide chains at the ribosome, using amino acids supplied from the diet or the body's amino acid pool.
- **Post-Translational Modifications:** Proteins undergo modifications like **phosphorylation**, **glycosylation**, and **acetylation** to become functional.

---

2. Protein Catabolism (Degradation):

When proteins are not needed for synthesis, they are broken down to release amino acids, which can be used for energy or converted into other compounds.

- **Proteolysis:**
  Cellular proteins are continuously broken down and recycled. This process involves **lysosomes** and the **ubiquitin-proteasome pathway**.

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3. Amino Acid Metabolism:

a. Deamination:

- **Definition:**
  The removal of the amino group (**–NH_2**) from an amino acid, producing **ammonia (**NH_3**)** and a **keto acid**.
- **Location:**
  Primarily in the **liver**.
- **Enzymes Involved:**
  - **Glutamate dehydrogenase**: Catalyzes the oxidative deamination of glutamate to produce α-ketoglutarate and ammonia.

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b. Transamination:

- **Definition:**
  The transfer of an amino group from one amino acid to a keto acid, forming a new amino acid and a new keto acid.
- **Enzymes Involved:**
  Aminotransferases (or transaminases), like **alanine aminotransferase (ALT)** and **aspartate aminotransferase (AST)**.
- **Importance:**
  This process is key in amino acid biosynthesis and the disposal of nitrogen.

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4. Fate of the Amino Group:

- **Ammonia Toxicity:**
  Ammonia is toxic and must be safely disposed of.
- **Urea Cycle (Ornithine Cycle):**
  - **Definition:**
    A cycle in the **liver** that converts ammonia into **urea**, which is less toxic and can be excreted in the urine.
  - **Key Steps:**
    1. Ammonia combines with **CO_2** to form **carbamoyl phosphate**.
    2. Carbamoyl phosphate enters the urea cycle, ultimately producing **urea**.
    3. Urea is transported to the **kidneys** and excreted in the urine.

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5. Fate of the Carbon Skeleton (Keto Acid):

After deamination, the remaining carbon skeleton (**keto acid**) can enter various metabolic pathways:

- **Gluconeogenesis:**
  Some amino acids are **glucogenic** and can be converted into glucose.
- **Ketogenesis:**
  Some amino acids are **ketogenic** and can be converted into **ketone bodies**.
- **Energy Production:**
  Keto acids can enter the **citric acid cycle (TCA cycle)** to produce ATP.

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6. Special Products from Amino Acids:

- **Neurotransmitters:**
  - **Glutamate** → **GABA** (gamma-aminobutyric acid)
  - **Tryptophan** → **Serotonin**

    - **Tyrosine → Dopamine**, **Norepinephrine**, **Epinephrine**
- **Hormones:**
    - **Tyrosine → Thyroid hormones (T3, T4)**.
    - **Arginine → Nitric oxide**.
- **Porphyrins and Heme:**
    - **Glycine** is a precursor for **heme** synthesis.
- **Melanin:**
    - **Tyrosine → Melanin** (pigment in skin and hair).

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7. Disorders of Protein Metabolism:

1. **Urea Cycle Disorders:**
   Deficiencies in enzymes of the urea cycle lead to **hyperammonemia**, causing neurological symptoms.
2. **Phenylketonuria (PKU):**
   Deficiency of **phenylalanine hydroxylase** leads to accumulation of **phenylalanine**, causing intellectual disabilities.
3. **Maple Syrup Urine Disease:**
   Deficiency of enzymes that break down **branched-chain amino acids** causes sweet-smelling urine and neurological symptoms.
4. **Alkaptonuria:**
   Deficiency of **homogentisate oxidase** leads to accumulation of **homogentisic acid**, causing dark-colored urine and joint issues.
5. **Homocystinuria:**
   Defect in **methionine metabolism**, leading to elevated **homocysteine** levels, associated with cardiovascular and skeletal issues.

7.1 Define Vitamins

Definition: Vitamins are **organic compounds** required in **small amounts** for various physiological functions necessary for maintaining health, growth, and metabolism. Unlike macronutrients (carbohydrates, proteins, and fats), vitamins do **not provide energy** but act as **coenzymes**, **antioxidants**, or **hormone precursors** in vital biochemical processes.

Key Characteristics:

- **Essential Nutrients:** The body either cannot synthesize vitamins at all or produces them in insufficient quantities, making **dietary intake essential**.
- **Micronutrients:** Needed in minute amounts, but deficiencies can lead to serious health problems.
- **Diverse Functions:** Involved in **metabolism regulation**, **immune function**, **cell growth**, and **repair**.

7.2 List Fat-Soluble Vitamins and Water-Soluble Vitamins

Vitamins are classified based on their **solubility**:

A. Fat-Soluble Vitamins: These vitamins dissolve in **fats and oils** and are stored in the **liver** and **adipose tissues**. Excessive intake can lead to **toxicity** due to accumulation in the body.

1. **Vitamin A** (*Retinol, Retinal, Retinoic acid*)
2. **Vitamin D** (*Calciferol*)
3. **Vitamin E** (*Tocopherol*)
4. **Vitamin K** (*Phylloquinone, Menaquinone*)

B. Water-Soluble Vitamins: These dissolve in **water**, are not stored in significant amounts, and are excreted in **urine** if consumed in excess, making **regular intake** necessary.

1. **Vitamin B Complex:**
    - **B1** (*Thiamine*)
    - **B2** (*Riboflavin*)
    - **B3** (*Niacin/Nicotinic acid*)
    - **B5** (*Pantothenic acid*)
    - **B6** (*Pyridoxine, Pyridoxal, Pyridoxamine*)
    - **B7** (*Biotin*)
    - **B9** (*Folic acid/Folate*)
    - **B12** (*Cobalamin*)
2. **Vitamin C** (*Ascorbic acid*)

7.3 Explain the Physiology of Vitamins

Vitamins play crucial roles in various physiological processes, including enzyme function, metabolism, immune response, and cellular maintenance. Here's how they function in the body:

A. Fat-Soluble Vitamins Physiology:

1. **Vitamin A (Retinol):**
    - **Role in Vision:** Essential for forming **rhodopsin**, a pigment in the retina that is critical for **low-light** vision.
    - **Cellular Growth and Differentiation:** Regulates gene expression, promotes **epithelial tissue health**, and supports **immune function**.
    - **Antioxidant Activity:** Protects cells from oxidative damage.
2. **Vitamin D (Calciferol):**
    - **Calcium and Phosphorus Homeostasis:** Enhances absorption of **calcium** and **phosphorus** in the intestines, crucial for **bone mineralization**.
    - **Immune Function:** Modulates the **immune response** and reduces inflammation.
    - **Hormonal Role:** Functions like a hormone by binding to **vitamin D receptors** in various tissues, influencing gene expression.

3. **Vitamin E (Tocopherol):**
    - **Antioxidant Function:** Protects cell membranes from oxidative damage by neutralizing **free radicals**.
    - **Immune System Support:** Enhances the body's immune responses, especially in aging populations.
    - **Skin and Eye Health:** Maintains **skin integrity** and protects **eye cells** from oxidative damage.
4. **Vitamin K:**
    - **Blood Clotting (Coagulation):** Essential for synthesizing **clotting factors** (II, VII, IX, and X) in the liver.
    - **Bone Metabolism:** Assists in **osteocalcin** synthesis, a protein that binds calcium in bones, promoting **bone health**.

B. Water-Soluble Vitamins Physiology:

1. **Vitamin B Complex:**
    - **B1 (Thiamine):** Acts as a coenzyme in **carbohydrate metabolism** and **nerve function**. Deficiency causes **beriberi**.
    - **B2 (Riboflavin):** Part of **FAD** and **FMN** coenzymes involved in **redox reactions**.
    - **B3 (Niacin):** Precursor of **NAD+** and **NADP+**, vital for **energy metabolism**. Deficiency causes **pellagra**.
    - **B5 (Pantothenic acid):** Component of **Coenzyme A (CoA)**, crucial for **fatty acid metabolism**.
    - **B6 (Pyridoxine):** Involved in **amino acid metabolism**, **neurotransmitter synthesis**, and **hemoglobin production**.
    - **B7 (Biotin):** Coenzyme for **carboxylation reactions** in metabolism of fats, proteins, and carbohydrates.
    - **B9 (Folic acid):** Essential for **DNA synthesis** and **cell division**. Crucial during **pregnancy** to prevent **neural tube defects**.
    - **B12 (Cobalamin):** Involved in **red blood cell formation**, **DNA synthesis**, and **nerve function**. Deficiency leads to **pernicious anemia**.

2. **Vitamin C (Ascorbic Acid):**
    - **Antioxidant:** Protects against oxidative stress and regenerates other antioxidants like **vitamin E**.
    - **Collagen Synthesis:** Crucial for **wound healing** and maintaining the integrity of connective tissues.
    - **Iron Absorption:** Enhances the absorption of **non-heme iron** from plant-based foods.
    - **Immune Support:** Strengthens the immune system by stimulating **white blood cell** activity.

C. General Functions of Vitamins in Physiology:

1. **Cofactors and Coenzymes:**
   Many vitamins, especially **B-complex** vitamins, act as **coenzymes** or precursors to coenzymes that are essential for **enzyme-catalyzed reactions** in metabolism.
2. **Antioxidant Protection:**
   Vitamins like **C**, **E**, and **A** help neutralize **free radicals**, reducing oxidative stress and cellular damage.
3. **Hormonal Functions:**
   Vitamin D functions like a hormone, regulating **calcium metabolism** and influencing gene expression in various tissues.
4. **Immune System Support:**
   Vitamins such as **A**, **C**, **D**, and **E** play roles in enhancing **immune responses** and protecting against infections.
5. **Cell Growth and Repair:**
   Folic acid (B9) and **vitamin B12** are vital for **DNA synthesis**, **cell division**, and **tissue repair**.
6. **Bone Health:**
   Vitamin D aids in **calcium absorption**, while **vitamin K** contributes to **bone mineralization**.

7. **Blood Clotting:**
   Vitamin K is essential for the synthesis of **clotting factors** required in the coagulation cascade.

8.1 Physiology and Disorders Related to Minerals

Minerals are **inorganic nutrients** essential for various physiological functions, including maintaining **electrolyte balance**, **bone health**, **enzyme activity**, and **oxygen transport**. They are classified as **macrominerals** (needed in larger amounts) and **trace minerals** (required in smaller quantities).

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1. Sodium (Na^+)

Physiology:

- **Electrolyte Balance:** Sodium is the primary **extracellular cation** and plays a critical role in maintaining **osmotic pressure** and **fluid balance**.
- **Nerve Transmission and Muscle Contraction:** It is essential for generating **action potentials** in nerves and muscles.
- **Acid-Base Balance:** Involved in regulating **pH** via the **sodium-bicarbonate buffer system**.
- **Renal Regulation:** The **kidneys** regulate sodium levels through hormones like **aldosterone**.

Disorders:

- **Hyponatremia (Low Sodium):**
  - **Causes:** Excess water intake, kidney disorders, heart failure.
  - **Symptoms:** Nausea, headache, confusion, seizures, coma.
- **Hypernatremia (High Sodium):**
  - **Causes:** Dehydration, excessive sodium intake, diabetes insipidus.

- **Symptoms:** Thirst, muscle weakness, confusion, irritability.

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2. Potassium (K^+)

Physiology:

- **Primary Intracellular Cation:** Potassium is the major **intracellular ion**, essential for **cellular function**.
- **Nerve Impulse Transmission:** Regulates **membrane potential** and facilitates **nerve signal conduction**.
- **Muscle Contraction:** Critical for **cardiac** and **skeletal muscle** function.
- **Acid-Base Balance:** Participates in maintaining the **acid-base balance**.

Disorders:

- **Hypokalemia (Low Potassium):**
  - **Causes:** Diuretics, vomiting, diarrhea, hyperaldosteronism.
  - **Symptoms:** Muscle weakness, cramps, arrhythmias, fatigue.
- **Hyperkalemia (High Potassium):**
  - **Causes:** Renal failure, potassium-sparing diuretics, acidosis.
  - **Symptoms:** Muscle paralysis, cardiac arrhythmias, potentially fatal **ventricular fibrillation**.

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3. Calcium (Ca^{2+})

Physiology:

- **Bone and Teeth Formation:** 99% of calcium is stored in bones and teeth, providing **structural strength**.
- **Muscle Contraction:** Calcium ions are essential for **muscle contraction** through the **actin-myosin interaction**.

- **Nerve Function:** Facilitates **neurotransmitter release** at synapses.
- **Blood Clotting:** Acts as a cofactor in the **clotting cascade**.
- **Hormonal Regulation:** Regulated by **parathyroid hormone (PTH)**, **vitamin D**, and **calcitonin**.

Disorders:

- **Hypocalcemia (Low Calcium):**
  - **Causes:** Hypoparathyroidism, vitamin D deficiency, kidney disease.
  - **Symptoms:** Muscle spasms (**tetany**), seizures, cardiac arrhythmias.
- **Hypercalcemia (High Calcium):**
  - **Causes:** Hyperparathyroidism, malignancies, excessive vitamin D intake.
  - **Symptoms:** Weakness, kidney stones, constipation, cardiac arrhythmias.

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4. Iron (Fe)

Physiology:

- **Oxygen Transport:** Essential for **hemoglobin** and **myoglobin** synthesis, facilitating oxygen transport and storage.
- **Enzyme Function:** Part of various enzymes involved in **energy metabolism** and **DNA synthesis**.
- **Storage and Transport:** Stored in **ferritin** and transported by **transferrin**.

Disorders:

- **Iron Deficiency Anemia:**
  - **Causes:** Poor dietary intake, chronic blood loss, malabsorption.
  - **Symptoms:** Fatigue, pallor, shortness of breath, brittle nails.
- **Hemochromatosis (Iron Overload):**
  - **Causes:** Genetic disorder causing excessive iron absorption.
  - **Symptoms:** Joint pain, liver damage, diabetes, skin pigmentation.

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5. Copper (Cu)

Physiology:

- **Enzyme Cofactor:** Essential for enzymes involved in **iron metabolism**, **antioxidant defense**, and **collagen synthesis**.
- **Iron Absorption:** Necessary for the **oxidation of iron** for incorporation into hemoglobin.
- **Neurological Function:** Involved in neurotransmitter synthesis.

Disorders:

- **Menkes Disease (Copper Deficiency):**
  - **Causes:** Genetic disorder affecting copper absorption.
  - **Symptoms:** Growth retardation, intellectual disability, brittle hair.
- **Wilson's Disease (Copper Overload):**
  - **Causes:** Genetic defect leading to copper accumulation in tissues.
  - **Symptoms:** Liver disease, neurological symptoms, **Kayser-Fleischer rings** in the eyes.

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6. Magnesium (Mg^{2+})

Physiology:

- **Cofactor for Enzymes:** Involved in over **300 enzymatic reactions**, including those related to **ATP synthesis**, **protein synthesis**, and **nucleic acid metabolism**.
- **Muscle and Nerve Function:** Regulates **neuromuscular excitability** and maintains **cardiac rhythm**.
- **Bone Health:** About **60%** of magnesium is stored in bones, contributing to bone strength.

Disorders:

- **Hypomagnesemia (Low Magnesium):**
  - **Causes:** Malnutrition, alcoholism, diarrhea, diuretics.
  - **Symptoms:** Muscle cramps, seizures, cardiac arrhythmias.

- **Hypermagnesemia (High Magnesium):**
    - **Causes:** Renal failure, excessive magnesium supplementation.
    - **Symptoms:** Muscle weakness, hypotension, respiratory depression, cardiac arrest.

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7. Fluorine (Fluoride, F^-)

Physiology:

- **Bone and Dental Health:** Fluoride strengthens **tooth enamel** and prevents **dental caries** (cavities).
- **Bone Mineralization:** In small amounts, fluoride contributes to **bone density**.

Disorders:

- **Fluorosis (Excess Fluoride):**
    - **Dental Fluorosis:** Mottling and discoloration of teeth.
    - **Skeletal Fluorosis:** Bone pain, joint stiffness, and increased risk of fractures.
- **Fluoride Deficiency:**
    - Increased risk of **dental cavities** and **tooth decay**.

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8. Zinc (Zn^{2+})

Physiology:

- **Enzyme Function:** Cofactor for over **300 enzymes** involved in **DNA synthesis**, **wound healing**, **immune function**, and **growth**.
- **Immune System Support:** Essential for **T-cell** function and overall **immune response**.
- **Wound Healing and Skin Health:** Important for **collagen synthesis** and **skin repair**.

Disorders:

- **Zinc Deficiency:**
    - **Causes:** Malnutrition, malabsorption, chronic diarrhea.
    - **Symptoms:** Growth retardation, delayed wound healing, **hypogonadism**, impaired immune response, **skin lesions**.
- **Zinc Toxicity:**
    - **Causes:** Excessive supplementation.
    - **Symptoms:** Nausea, vomiting, immune suppression, copper deficiency.

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9. Selenium (Se)

Physiology:

- **Antioxidant Defense:** Component of **glutathione peroxidase**, protecting cells from **oxidative damage**.
- **Thyroid Function:** Involved in the metabolism of **thyroid hormones**.
- **Immune System:** Supports immune response and prevents cellular damage.

Disorders:

- **Selenium Deficiency:**
    - **Keshan Disease:** Cardiomyopathy associated with selenium deficiency.
    - **Symptoms:** Muscle weakness, immune dysfunction, hypothyroidism.
- **Selenium Toxicity (Selenosis):**
    - **Causes:** Excessive supplementation.
    - **Symptoms:** Hair loss, nail brittleness, gastrointestinal distress, neurological abnormalities.

9.1 Nature, Types, and General Mechanism of Action of Hormones

Nature of Hormones:

Hormones are **chemical messengers** secreted by **endocrine glands** directly into the **bloodstream**. They regulate various physiological processes such as **growth**, **metabolism**, **reproduction**, and **homeostasis**. Hormones act on specific **target organs or tissues** that have **receptors** for them.

Types of Hormones:

1. **Peptide/Protein Hormones:** Composed of amino acids (e.g., **insulin**, **glucagon**, **growth hormone**).
2. **Steroid Hormones:** Derived from cholesterol (e.g., **cortisol**, **estrogen**, **testosterone**).
3. **Amino Acid Derivatives:** Derived from single amino acids (e.g., **thyroxine** from tyrosine, **epinephrine**).
4. **Fatty Acid Derivatives:** Derived from fatty acids (e.g., **prostaglandins**).

General Mechanism of Action:

1. **Peptide Hormones:** Bind to **cell surface receptors** triggering **second messenger systems** (e.g., cAMP) to activate cellular responses.
2. **Steroid Hormones:** Pass through the **cell membrane** and bind to **intracellular receptors**, influencing **gene transcription**.
3. **Amino Acid Derivatives:** Can act via **membrane receptors** (e.g., epinephrine) or **nuclear receptors** (e.g., thyroxine).

9.2 Chemistry, Synthesis, and Metabolic Role of Various Hormones

Chemistry and Synthesis:

- **Peptide Hormones:** Synthesized as **preprohormones** in the **rough endoplasmic reticulum**, processed to **prohormones**, and then activated in the **Golgi apparatus**.

- **Steroid Hormones:** Synthesized from **cholesterol** in the **smooth endoplasmic reticulum**.
- **Amino Acid Derivatives:** Synthesized from **tyrosine** or **tryptophan** through enzymatic modifications.

Metabolic Roles:

- **Insulin:** Lowers blood glucose by promoting **glucose uptake** and **glycogen synthesis**.
- **Glucagon:** Raises blood glucose by stimulating **glycogenolysis** and **gluconeogenesis**.
- **Thyroid Hormones (T3, T4):** Increase **basal metabolic rate** and stimulate **protein synthesis**.
- **Cortisol:** Regulates **glucose metabolism**, **immune response**, and **stress response**.
- **Growth Hormone:** Stimulates **growth**, **cell reproduction**, and **regeneration**.

9.3 Diseases Associated with Abnormal Levels of Hormones

1. **Diabetes Mellitus:**
    - **Cause:** Insufficient insulin production/action.
    - **Symptoms:** Hyperglycemia, polyuria, polydipsia.
2. **Hyperthyroidism (Graves' Disease):**
    - **Cause:** Excess thyroid hormone.
    - **Symptoms:** Weight loss, heat intolerance, tachycardia.
3. **Hypothyroidism:**
    - **Cause:** Deficient thyroid hormone.
    - **Symptoms:** Fatigue, weight gain, cold intolerance.
4. **Cushing's Syndrome:**
    - **Cause:** Excess cortisol.
    - **Symptoms:** Weight gain, hypertension, moon face.
5. **Addison's Disease:**
    - **Cause:** Insufficient cortisol and aldosterone.
    - **Symptoms:** Fatigue, hypotension, hyperpigmentation.

6. **Acromegaly:**
    - **Cause:** Excess growth hormone in adults.
    - **Symptoms:** Enlarged hands/feet, facial changes.

10.1 Nature, Structure, and Metabolism of Nucleic Acids

Nature and Structure:
Nucleic acids are **biopolymers** essential for **storage**, **transmission**, and **expression** of genetic information. The two main types are **DNA (deoxyribonucleic acid)** and **RNA (ribonucleic acid)**.

- **DNA:** Double helix composed of nucleotides (adenine, thymine, cytosine, guanine).
- **RNA:** Single-stranded, with uracil replacing thymine.

Metabolism:
Involves **synthesis (replication)**, **transcription** into RNA, and **degradation** by nucleases.

10.2 Stages of the Process of Protein Synthesis

1. **DNA Replication:**
    - Process of copying DNA before cell division.
    - **Key Enzymes:** DNA polymerase, helicase, ligase.
2. **DNA Transcription:**
    - Conversion of DNA into **mRNA** in the nucleus.
    - **Enzyme:** RNA polymerase.
3. **mRNA Translation:**
    - Occurs in the **ribosome**; mRNA is decoded to synthesize proteins.
    - **Key Players:** tRNA, ribosomes, amino acids.

10.3 The Genetic Code

- The genetic code is a set of **triplet codons** in mRNA that specify particular **amino acids**.
- **Characteristics:** Universal, redundant (degenerate), and has start (AUG) and stop codons (UAA, UAG, UGA).

10.4 Disorders Related to Genetic Coding

1. **Sickle Cell Anemia:**
    - **Cause:** Mutation in the **beta-globin** gene.
    - **Effect:** Abnormal hemoglobin leads to sickle-shaped red blood cells.
2. **Cystic Fibrosis:**
    - **Cause:** Mutation in the **CFTR** gene.
    - **Effect:** Thick mucus accumulation in lungs and digestive tract.
3. **Tay-Sachs Disease:**
    - **Cause:** Mutation in the **HEXA** gene.
    - **Effect:** Accumulation of lipids in neurons, leading to neurodegeneration.
4. **Duchenne Muscular Dystrophy:**
    - **Cause:** Mutation in the **dystrophin** gene.
    - **Effect:** Progressive muscle weakness and degeneration.
