

Paper II: Technical Subject

1. Principles of Human Biochemistry

1.1 **Basics:** Acid-Base, pH, Henderson Hasselbachequation, pH measurements, Buffer solutions, biological membrane and transport system, Gibbs Donnan equilibrium

1.2 **Biomolecules**

1.2.1 Carbohydrates: Introduction, biochemical importance, classification, structure, isomerism, properties, detection of carbohydrates

1.2.2 Lipids: Introduction, biochemical importance, classification, properties of lipid; Fatty Acids, lipoproteins, triglycerides, phospholipids, glycolipids and steroids; Prostaglandins and their biological significance

1.2.3 Proteins: Classification, structure and properties of amino acid; Structure, classification, properties and techniques of separation for proteins

1.2.4 Nucleic Acids: Nucleosides, nucleotides, nucleoproteins and nucleic acids; Structure, properties, types and functions of DNA and RNA

1.3 **Enzymes:** Definitions, classification, nomenclature, catalysis, mechanism of enzyme action, factors affecting the enzyme activity, units of activity, diagnostic/clinical enzymology.

1.4 **Micronutrients**

1.4.1 Vitamins: Biochemical importance and roles in metabolism, deficiency manifestations, effects of hypervitaminosis, toxicity of fat soluble vitamins and water soluble vitamins

1.4.2 Minerals: Biochemical roles, roles in metabolism and disease, bulk and trace elements, mineral deficiencies and toxicity

1.4.3 Nutritional Value of Food: BMR, Respiratory Quotient and its significance; Energy calculation, balanced diet, plan diet in health and disease, biological value of proteins, protein energy malnutrition, malabsorption, parental nutrition, Modification and supplementation of dietary requirements in health and disease.

1.5 **Metabolism:** Concepts, Biochemical Roles, Importance and Related Disorders

1.5.1 Carbohydrates: Glycolysis, Krebs' cycle, gluconeogenesis, glycogen metabolism, HMP pathway and metabolism of fructose, galactose, amino sugars and lactose synthesis; Biological oxidation and Bioenergetics including the Electron Transport Chain and Oxidative Phosphorylation.

1.5.2 Lipids: Fatty acid oxidation, biosynthesis of fatty acids, cholesterol and triacylglycerol, lipoprotein metabolism (composition, metabolism, function and significance of chylomicron, VLDL, LDL and HDL), apolipoproteins and their role in lipoprotein metabolism, dyslipidemia, atherosclerosis, obesity.

1.5.3 Proteins: Transamination, deamination, urea cycle, ammonia transport and its toxicity and individual amino acids metabolism.

1.5.4 Nucleic Acids: Synthesis and degradation of purine and pyrimidine; Replication, Transcription and post transcriptional modification,

Translation and post translational modifications, types of mutation and its repair mechanisms, gene regulation, operon hypothesis.

- 1.6 **Inborn Errors of Metabolism (Congenital disorders):** Carbohydrate disorders, Amino acids metabolism disorders, Lipids and Lipoprotein metabolism disorders, Purine, Pyrimidine and Nucleic Acids disorders, laboratory findings, and their management
- 1.7 **Integration of Metabolism:** Feed and fast cycle, metabolic interrelationships of tissues (Liver, Brain, Skeletal muscles, Adipose tissue, Placenta), metabolism in obesity, starvation, exercise, pregnancy, stress, injury, liver disease, renal disease and acid-base disorder

2. Cell Biology

- 2.1 An overview of cellular structure and function
- 2.2 Prokaryotic and eukaryotic cells
- 2.3 Structure of eukaryotic cells-sub cellular organelles, cytosol, endoplasmic reticulum, nucleus, nucleolus, mitochondria, lysosomes, ribosomes, Golgi apparatus, peroxisomes, plasma membranes and their functions
- 2.4 Receptor-mediated endocytosis
- 2.5 Properties of biological membranes -motility, permeability, concept of semi permeable membranes, electrochemical gradient, pumps, and liposomes
- 2.6 Transport across membranes- active, facilitated and passive. Transport mechanisms-ion channels including gated channels, carrier proteins, glucose transporters (GLUT), active transporter, symporters and antiporters
- 2.7 Non-membrane organelles-cytoskeleton, microfilaments, microtubules and microvilli
- 2.8 Cell interactions and adhesion- types of junctions: tight junctions and gap junctions
- 2.9 Adhesion molecules-cadherins, selectins, integrins (beta 1 and beta 2 integrins)
- 2.10 Cell cycle, regulation of cell cycle, apoptosis, biochemistry of aging
- 2.11 Stem cells and their differentiation
- 2.12 Cell as experimental models- *E.coli*, yeast, *Drosophila melanogaster*, viruses
- 2.13 Programmed cell death

3. Molecular Biology and Genetics

- 3.1 DNA Replication:Replication process, DNA Repair, Recombination between homologous DNA sequences, DNA Rearrangements
- 3.2 Transcription:Prokaryotic and Eukaryotic transcription, Regulation of transcription in Eukaryotes, RNA processing and turnover
- 3.3 Translation: Prokaryotic and Eukaryotic Protein synthesis, Regulation of translation, Protein folding, Post-translational modification, Protein degradation.
- 3.4 Regulation of gene expression, Mutation, Stem Cell and differentiation, Apoptosis

- 3.5 Cancer genetics: Carcinogenic Agent- Radiation, chemicals and viruses, Oncogenes, Tumor suppressor genes, Genetic cancer syndromes- familial breast cancer, familial adenomatous polyposis coli and retinoblastoma Inherited conditions and predispose to development of cancer (e.g., Ataxia-telangiecatasia, Xerodermapigmentosum, Fanconi syndrome), Mechanisms of action of cytotoxic drugs, application of molecular biology to cancer prevention and treatment.
 - 3.6 Recombinant DNA technology: A knowledge of Recombinant DNA, vector, cloning, restriction enzyme, blotting techniques, miRNA and their application in medicine.
 - 3.7 Polymerase Chain Reaction: Introduction, Primer and its designing, Phases of reactions (denaturation, annealing and annexing), Open array, digital PCR and their application.
 - 3.8 Genetic mapping and Physical mapping, DNA Sequencing, Human genome project, cDNA Library and Gene Bank, Gene Therapy.
 - 3.9 Genetic Testing: Restriction fragment length polymorphism (RFLPs), Its application in mutation detection and DNA fingerprinting, Analysis of Gene Expression: Microarray, Western blot
 - 3.10 Introduction to Medical Genetics and its brief history, Mendelian Inheritance, Non-Mendelian Inheritance, Single gene diseases and Multifactorial Inheritance, Autosomal, Sex linked and Mitochondrial Inheritance, Chromosome and Cytogenetics, Biochemical disorders of carbohydrate, lipid, amino and purine and pyrimidine metabolism seen in the local hospital, Population genetics, Genetic Counselling, Medical ethics.
 - 3.11 Inherited Disorders and their evaluation from a biochemical perspective: A comprehensive overview of Autosomal and Sex Linked genetic disorders and the biochemical tests used in diagnosis and monitoring of these conditions
- 4. Bioinformatics and computational Biology:** Genomics, proteomics and bioinformatics, computer aided drug design and discovery, genome guided personalized medicine, Basic Local Alignment Search Tool (BLAST) for protein and nucleic acid, protein data base.
- 5. Immunology:**
- 5.1 Concept, mechanisms and role of innate and acquired immunity, humoral and cell mediated immunity, antigen and antibodies, antibody diversity, class switching, MHC.
 - 5.2 Recognition of antigens: Primary interaction, antigen processing and presentation
Immune response: Lymphocyte maturation, activation of T and B lymphocytes, cytokines, regulation of immune response, immunodeficiency, tumor immunity, transplantation, immunosuppression and immunopotentiality including vaccination

6. Organ System Function

- 6.1 **Cardio - Vascular System:** Characteristics features of heart muscles and its metabolism, ischaemic heart disease, atherosclerosis, pre-disposing factors leading to ischemia and infarction, myocardial infarction, cardiac markers (enzymatic and non-enzymatic), iron containing haem and non-haem proteins and their functions, intestinal absorption, distribution kinetics in the body, process of haem biosynthesis and catabolism, iron deficiency anaemia and acute intermittent porphyria, diagnostic tests for iron deficiency states, classification of porphyria, causes, diagnosis and management of porphyria
- 6.2 **Respiratory System and Acid Base Balance:** Physiological buffer system, oxygen content, oxygen saturation, pKa, acid base balance, acidemia, alkalemia, compensated and no compensated, Neonatal Respiratory Distress Syndrome and its biochemical basis and management, function of haemoglobin and properties of dissociation curve of oxyhaemoglobin, different forms of carbon dioxide existence in blood and mechanism of transport, interrelationship among Hb, O₂, CO₂, H⁺ and 2-3 DPG, Carbonmonoxide poisoning, Anion gap and its significance and ABG analysis and interpretation.
- 6.3 **Gastrointestinal and Hepatobiliary System:** Gastrointestinal composition and biochemical methods of investigation of gastric secretion; Tests of carbohydrate and fat absorption, Gastric function tests and clinical significance; Investigation of malabsorption and diarrhea; Characteristic features and metabolism of liver, role of liver in metabolism of carbohydrates, lipids, proteins and foreign toxic substances, types of jaundices and their biochemical features, bilirubin metabolism, acute and chronic liver disease, cirrhosis of liver, alcoholic liver disease, cholestatic liver disease, infiltration of liver, Liver function tests and interpretations in different liver disease; Chemical composition and biochemical basis of formation of gall stones and their analysis; Exocrine functions of pancreas, acute and chronic pancreatitis, pancreatic function tests and clinical significance, biochemical tests for steatorrhea.
- 6.4 **Renal System and Electrolyte Balance:** Role of kidneys in acid base balance, characteristic features and metabolism of kidney cells, interrelationship between water, sodium and extra-cellular fluid and osmolality, role of aldosterone and natriuretic peptide hormones in maintaining ECF osmolality, renal handling of sodium and potassium, Renal function tests and interpretations, glomerular function tests, tubular functions tests, clearance tests, Glomerular filtration rate, urine azotemia, uremia, hyper and hypo conditions of electrolytes (Na⁺, K⁺, Cl⁻ etc.) osmolality and renal concentration tests, renal failure and its consequences, nephrotic syndrome, glomerulonephritis, Fanconi syndrome, its basis and

biochemical findings, chemical composition and biochemical basis of formation of renal stones and their analysis.

- 6.5 **Endocrine and Metabolic System:** Introduction and biomedical importance of hormones, mechanism of action of hormones, Bio-signaling and signal transduction mechanisms, hypothalamic releasing factors and their functions; Pituitary hormones, their functions, hyper and hypo conditions (diabetes insipidus its basis and management) biochemical basis; Biosynthesis, secretion, transportation, regulation and functions of thyroid hormone of thyroiditis, hypothyroidism, hyperthyroidism and goiter; Synthesis and biochemical functions adrenal gland hormone; Causes, molecular basis and biochemical investigation of Addison's disease, Cushing's syndrome and Cohn's disease; Synthesis, biochemical functions and disorders of parathyroid hormone, mode of action and biological functions of insulin, glucagon and somatostatin, diabetes mellitus and its type, gestational diabetes, biochemical investigations and interpretations, biochemical basis of complications of diabetes, composition of lens- biochemical changes during cataractogenesis.
- 6.6 **Reproductive System and Infertility:** Male and female reproductive hormones, gonadal hypo and hyper function, infertility, amenorrhea, hirsutism, fetoplacental disorders, genetic defects, placental hormones, biochemistry of conception, reproduction and contraception.
- 6.7 **Neurological System :** Clinical features, laboratory diagnosis of disorders of the nervous system, disturbances of neuro-anatomic systems, inherited disorders with neurological systems e.g. acute intermittent porphyria, metachromatic leucodystrophy [shilder's disease], mucopolysaccharide storage diseases, disorders of neurotransmission : Alzheimer's disease, Myasthenia gravis, dopaminergic systems, Parkinson's disease, Schizophrenia, depression, mania, epilepsy, Huntington's disease, Multiple sclerosis, meningitis, biochemical changes in cerebrospinal fluid.
- 6.8 **Musculoskeletal System :** General knowledge of pathophysiology of broad spectrum of disorders affecting the joints, diffuse connective tissue disease, malignant hyperthermia, fuels of muscle, molecular basis of muscle contraction, role of troponin and calcium in muscle contraction , fuels used by red and white muscles, metabolism in marathon runners and sprinters, hormones involved in calcium and phosphate homeostasis, conditions related with hypo and hypercalcemia and along with their biochemical basis.

- 6.9 **Pregnancy and Related Disorders:** Maternal serum screening, triple test, amniotic fluid and fetal blood examination, ectopic pregnancy, diabetes, pre-eclampsia.

7. Clinical Biochemistry

7.1 Basic Laboratory Principles

7.1.1 Sample collection, preservation, transport and storage

7.1.2 Handling and use of laboratory equipments (Centrifuge, Water Bath, Electronic Balance, pH Meters, Pippettes, Glassware, Dispensers, Hot Air Oven)

7.2 **Instruments:** Principles, operation protocols and applications of photometry; Concepts of colorimeter, visible and ultraviolet spectrophotometer, turbidometry, nephelometry, fluorimetry, flame Photometer, ion selective electrodes, atomic adsorption and mass spectrometry.

7.3 Separation Techniques

7.3.1 Chromatography: Principles, types, and applications in biochemistry

7.3.2 Electrophoresis: Principles, types, working techniques and application in biologic systems

7.4 Immunoassays

7.4.1 Enzyme based Assays: Principle and applications of ELISA and EIA, modified enzyme based investigative techniques and Chemiluminescent Immunoassay and Enhanced Chemiluminescent Immunoassays

7.4.2 Radioactivity and RIA: Application of radioactive substances in medicine and hazards of radioactivity and prevention; principle and applications of Radioimmuno assay

7.5 Automation Techniques in Clinical Chemistry (Autoanalyzers, Automated Immunoassays)

7.6 **Body Fluids:** Biochemical analysis of ascetic, peritoneal, pleural and synovial fluids, CSF and urine analysis

7.7 Analytical Biochemistry and Data Interpretation

7.7.1 **General Tests:** Knowledge, principle, application and predictive values for routine biochemical tests along with their evolution over time

7.7.2 **Drugs:** Knowledge, principle and application of drug levels in the diagnosis, treatment and monitoring of disease states and immunomodulation

7.7.3 **Diagnostic Tests:** Knowledge of diagnostic tests in endocrinology including Dexamethasone suppression test, Synacthen test, Ham's test, Water Deprivation test, Schumm's test, Schilling test

7.7.4 **Special Tests:** Testing principles and applications of hormone tests, iron profile, lipids, special proteins and other emerging biomarkers

7.7.5 **Other Tests and Tumor Markers:** Principle, application and techniques for tests used for collagen disorders, tumor markers in diagnosis and

monitoring of cancers, hormone profiles, metals, vitamins and enzymes in clinical syndromes

7.8 **Quality Control:** Precision, accuracy, errors of laboratory instruments; use of standardization units: SI and conventional; Process of internal quality control, external quality control; Use of statutory proficiency testing programs: primary and secondary standards; Use of Reference materials: international reference materials and reference methods; Course of action of evaluation and comparison of methods and instruments

7.9 **Role of the Clinical Biochemist in Laboratory Management**

7.9.1 **Laboratory Reporting Systems:** Ensuring that the information reaches the attending physician within a time frame, critical values, directing attention to abnormal results when necessary, providing clinical interpretation when appropriate, laboratory information system, electronic data transfer, instrument interfacing

7.9.2 **Laboratory Records:** Retention policies, workload measurement system, preparation and maintenance of proper laboratory manuals, SOPs accreditation requirements

7.9.3 **Laboratory Reagents:** Assessing the quality, stability, cost of reagents, commercial "kits", inventory, proper storage and management

7.9.4 **Instruments:** Laboratory instruments and analyzers; and their technical implications and maintenance

7.9.5 **Test Interpretation:** Effect of biological/physiological variation in biochemical tests results. Normal or reference ranges and clinically significant limits and the therapeutic and toxic level of drugs

7.9.6 **Laboratory Hazards:** Laboratory safety measures, waste disposal management

7.9.7 **Laboratory Management:** Leadership role, manpower management, planning and implementation of operation protocols

8. **Clinical Toxicology and therapeutics-** Mechanisms and symptoms of most important types of Toxic syndromes (anticholinergics, cholinergics, opioids, sedatives, sympathomimetics), Pharmacology and analysis of specific drugs and toxins.

9. **Principles of haemo and peritoneal dialysis**

10. **Biochemical monitoring of treatment of various diseases**

11. **Recent Advances:** Emerging biomarkers / Laboratory techniques and their implications
