

Syllabus for Ph.D Entrance Test in Clinical Biochemistry, University of Kashmir

Unit I: Biomolecules and Bioenergetics

First and second law of thermodynamic, concept of free energy, standard free energy change of a chemical reaction, Thermodynamics of high-energy phosphate compounds - ATP and other high energy phosphate compounds. ATP cycle, structural basis of free energy change during hydrolysis of ATP, Nernst equation and Redox-potentials. Carbohydrate structure, classification, properties, chemical reactions, Carbohydrate Metabolism- basic concepts, Glycolysis, Krebs cycle, Pentose phosphate pathway, Gluconeogenesis, Glycogenesis, Glycogenolysis, Regulation of carbohydrate metabolism, Disorders of galactose, lactose metabolism, Glycogen storage diseases. Amino acids: Structure, classification, properties and functions, peptides and polypeptides. Proteins: primary, secondary, tertiary and quaternary structure, protein folding, Protein stabilizing interactions, Reverse turns and Ramachandran plot. Amino acid metabolism: Biosynthesis and degradation of important amino acids and their regulation; Transamination and oxidative deamination, urea cycle. Hypo and hyper-albuminemia; hypo- and hyperglobulinemias, Alpha-1-antitrypsin deficiency, phenylketonuria, tyrosinemia.

Unit II: Biomolecules: Nucleic acids and Lipids

Classification, structure, properties, and functions of fatty acids, triacylglycerols, and phospholipids. Lipid metabolism: Biosynthesis and degradation of odd and even chain carbon fatty acids. Ketone bodies: formation and utilization. Biosynthesis and degradation of cholesterol. Lipoproteins and apolipoproteins. Disorders of lipids- Gaucher's disease, Tay-Sachs disease, Niemann-Pick disease. Structure, properties of purines and pyrimidine bases, nucleoside and nucleotides. Conformation of Nucleic acids (A, B, Z-DNA), Nucleic Acid metabolism: Biosynthesis, Regulation and degradation of purines and pyrimidines, Uric acid overproduction and under excretion; pathology and differential diagnosis of gout, Enzyme disorders of purine metabolism (Lesch-Nyhan syndrome and Orotic aciduria).

Unit III: Clinical Enzymology

Classification and nomenclature, prosthetic groups, cofactors, Mechanism of enzyme action and properties of enzymes as catalysts. Enzyme kinetics (equilibrium and steady state theory, rate equation and determination of K_m and V_{max}), specific activity, turn over number and catalytic centre activity, Enzyme regulation: Principles and mechanism of catalysis, Factors affecting rate of enzyme catalysed reactions, Enzyme inhibition: reversible and irreversible inhibition, Allosteric enzymes: Models of allostery, types and kinetics; Isoenzymes and isozymes. Factors affecting enzyme levels in blood. Principle, assay, and clinical significance of transaminases, creatine kinase, lactate dehydrogenase, phosphatases, isocitrate dehydrogenase, amylase, lipase, choline esterase, glutamate dehydrogenase, glucose-6-phosphate dehydrogenase.

Unit IV: Cell and Cancer Biology

Cell structure and function, Prokaryotic and Eukaryotic cell. Membrane Structure & transport. Cell cycle & its regulations. Cell cycle arrest, role of cyclically activated protein kinases. Cell Communication: General principles of cell communication, signal transduction via cell surface receptors (GPCR's, receptor tyrosine kinases, growth factor receptors). Cytosolic & Nuclear receptor pathways – steroid receptors, Vit D receptor's, Glucocorticoid receptor's, Hormone receptor elements. Cancer: Causes and types of cancer, signal transduction pathways involved in cancer, Proto-oncogenes, tumor suppressor genes, oncogenes and their role in growth and spread of cancer, molecular basis of cancer therapy, molecular markers. Programmed cell death and its regulation.

Unit V: Clinical Microbiology

Introduction to microbial systems, importance of microbiology in human health and environment, Microbial growth, growth curve, measurement and factors affecting the microbial growth. Classification of microorganisms- criteria for classification Normal human microflora, Virulence and pathogenesis. Toxin: Types and their mode of action. Pure culture techniques. Infectious diseases- overview, Medically important microbes,

Microbial diseases - sources, route of transmission. Pathogenesis - adhesion, invasion, host cell damage, release of pathogens. Microbial virulence and virulence factors - Signs and symptoms of microbial diseases. Treatment, prevention and control of microbial infections. Microbes as pathological agents in man - Staphylococcal, Salmonellosis food poisoning. DNA viruses- Herpes virus, Adeno virus, Hepatitis B virus. RNA viruses - Retrovirus, MERS, SARS-COV-2, HIV, Herpes virus. Antibiotic resistance: mechanism of drug resistance, origin & transmission of drug resistance in microbes.

Unit VI: Molecular Biology

Organization of DNA in Prokaryotes & Eukaryotes. Heterochromatin, Euchromatin, Transposons. Extra chromosomal DNA. Plasmid DNA in prokaryotes. Mitochondrial DNA. Human Genome features. DNA replication: Initiation, elongation & termination of Replication in prokaryotes & in eukaryotes. Regulation of replication, Fidelity of replication, DNA damage & repair Structure of gene in eukaryotes & prokaryotes. Operons (Lac & Trp Operons), Structure & function of RNA types (mRNA, rRNA & tRNA). Transcription & its regulation in eukaryotes & prokaryotes. RNA processing. editing, capping, splicing & polyadenylation. Regulation of gene expression at the level of transcription. Translation (Protein synthesis) and its regulation: Initiation, elongation and termination in prokaryotes & eukaryotes. Genetic code. Aminoacylation of tRNA. Post- translational modification of proteins, Control of gene expression at translation level. Replication, Transcription & Translation inhibitors.

Unit VII: Clinical Immunology

Innate and adaptive Immunity, Cells of immune system (Phagocytic cells, B & T lymphocytes, NK cells and dendritic cells). Humoral and cell mediated immune response. Antigenicity and Immunogenicity. Complement System, Major Histocompatibility Complexes. Antigen processing & presentation. Basic structure of immunoglobulins, Immunoglobulin classes (IgM, IgD, IgG, IgE, IgA), Antigen-antibody interactions. Organization, re-arrangement and expression of antibody genes. Generation of antibody diversity. Class switching, clonal deletion, Allelic exclusion. Affinity & Avidity, Affinity maturation. Autoimmunity & autoimmune diseases.

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Hypersensitivity reactions. Interferons & anti-viral immunity. Organ transplantation & graft rejection, role of cell mediated response, transplantation antigens. Immunosuppressant therapies.

Unit VIII: Biochemical and Molecular Biology Techniques

Basic principle, instrumentation and applications of UV/Visible and Fluorescence spectroscopy, Mass Spectrometry: Types and principle, applications. Protein Identification using Mass Spectrometry. Basic principle of chromatography; Separation techniques for proteins: Ion exchange chromatography, dialysis, molecular sieving, affinity chromatography. Basic principle and applications of HPLC; Centrifugation: Basic Principle, Techniques- Preparative, analytical and ultracentrifuges, Electrophoresis, Microscopy, Flow cytometry, PCR, RT-PCR and their types.

Unit IX: Advanced endocrinology and associated disorders

General characters and classification of hormones; Hypothalamus & pituitary gland; Structure, function and biochemistry of the hormones secreted by pituitary gland. Thyroid gland: Structure, biosynthesis, secretion, transport metabolism, and function. Hypo- & hyperthyroidism. Regulation of thyroid hormone synthesis antithyroid agents. Parathyroid gland: Structure, function and biochemistry of the parathyroid hormones. Disorders of parathyroid gland. Pancreatic Hormones - synthesis and mechanism of action of insulin and glucagon: effect of on carbohydrate and lipid metabolism, Insulin signaling system, insulin deficiency. Adrenal medulla- Epinephrine and nor-epinephrine, their biosynthesis, metabolism of Epinephrine and nor-epinephrine, biological actions of Epinephrine and nor-epinephrine and their regulation. Adrenal cortex- synthesis of adrenal cortical steroids, biological actions and transport of cortical steroids. Mechanism of action of adrenal steroid hormones.

Unit X: Basics of Clinical Biochemistry

Clinical Significance and Principle of various laboratory tests -Lipid Profile (TG, Cholesterol, HDL, and LDL), Blood Glucose (Fasting, Post prandial, and GTT), Kidney Function Test (Urea, Creatinine, Uric Acid), Liver Function Test (AST, ALT). Thyroid

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function test (TSH, T3, T4) PTH, Calcitonin, Cortisol, Testosterone, hCG screen (pregnancy test), quantitative hCG, Insulin tolerance test, Bilirubin - total, conjugated (direct). Hepatitis A, B and C serology. Calculi. Iron - serum, iron binding capacity, iron saturation, transferrin, Ferritin. Lipids: cholesterol, Triglycerides, HDL-cholesterol, LDL-cholesterol, Apolipoprotein A B and E. Lipoprotein A. Automation in Clinical Biochemistry, Laboratory information systems, Types of Automation, Individual steps in the analytical processes, Reagent handling and storage, reagent delivery, Chemical reaction phase, Development of standards for laboratory automation. Other areas of automation; urine analyzers, hematology cell counters and Automatic Biochemistry analyser.

Unit XI: Advanced Clinical Biochemistry

Cardiac Markers; CK-2 (CKMB), troponins, myoglobin, Creatinine kinase. Prostate specific antigen (PSA); alpha-fetoprotein (AFP); chorionic gonadotropin (CG). Proteins; Serum total, albumin, Urinary microalbumin, C-reactive protein. Immunoglobulin IgE, allergen specific IgE, Hemoglobins. Antibodies: anti-ds-DNA; anti-nuclear antibodies by immunofluorescence, specific anti-nuclear antibodies (SS-A, SS-B, Sm, RNP); anti-thyroglobulin, TSH receptor antibody, Islet-cell antibodies. Urine analysis (including microscopy). Obesity: Genetic basis of familial obesity, effects of neuropeptides and leptin in nutrient partitioning. Obesity related derangements in metabolic regulation. Mechanism and methods of birth control and possible biochemical consequences thereof. Biochemical marker's in infertility disorders. Quality Assurance & Management: Fundamentals of total quality management, elements of quality assurance program. External quality assessment- Identifying the source of analytical errors. Fundamentals of Lab Safety. Establishment and use of reference values: Concept of reference values, Selection of reference individuals, Specimen collection, Analytical procedures and quality control. Methods for determining the reference values and presentation of an observed value in relation to reference value.

Unit XII: Fluid electrolyte imbalance and drug metabolism

Regulation of water and electrolyte balance; Role of Na⁺ and K⁺, Hyper-natremia, hypo-natremia; (SIADH), hypo-kalemia, hyper-kalemia. Acid-Base balance; regulation by kidney and hormones. Diffusion of gases through respiratory membranes, role of transferrin, oxygen, CO, CO₂ in respiration. Chronic respiratory failure, Tests of kidney function and their Clinical co-relations: tests of glomerular functions, measurement of GFR, Clearance tests (creatinine and inulin clearance), Plasma creatinine, urea, β_2 -microglobulin. Drug Metabolism: Concept of drug metabolism, major organs participating in drug metabolism. Phase-I reactions and its significance, types of phase-I reactions, CYP-P450 oxidase system. Phase-II (Conjugation) reactions and significance. Factors affecting drug metabolism. Introduction to Pharmacokinetics. Pharmacodynamics, Drug excretion.

Unit XIII: Gastrointestinal and Hepatobiliary disorders

Mechanism of gastric secretion - HCl production, Gastrointestinal hormones, Clinical features and laboratory findings in diseases of the stomach: peptic ulcer, neoplastic disease. Assessment of pancreatic function. Pancreatic enzymes; Secretin and CCK-PZ tests. Assessment of intestinal function; Small bowel malabsorption tests; Xylose, Lactose and other disaccharides). Clinical features and laboratory findings in: Malabsorption, Malabsorption, Malabsorption syndromes (A); gluten intolerance, inflammatory bowel disease, Crohn's disease. Biochemical indices of hepatobiliary disorders, Liver function assesment and diseases of hepatobiliary system - acute liver diseases: viral hepatitis, Toxic hepatitis (hepatotoxic drugs); chronic liver diseases - liver cirrhosis.

Unit XIV: Neuro muscular and Cardiovascular system

Nerve impulse transmission: Structure of neuron, mechanism of nerve impulse conduction along axon, Action Potential; Threshold action potential. Neurotransmitters; Excitatory and Inhibitory neurotransmitters, Presynaptic and post-synaptic events of neuromuscular junctions, Structure of nervous system; CNS, peripheral nervous system. Disorders of neurotransmission: cholinergic systems (Myasthenia gravis); Huntington's disease, Multiple sclerosis. Anatomy and

physiology of heart, cardiac cycle (cardiac output, venous return and their regulation). Examination of cardiovascular system, Myocardial Infarction - troponin, myoglobin and other markers; congestive heart failure, Atherosclerosis, Shock and Hypertension.

Unit XV: Molecular Diagnostics

rDNA technology: Genomic and cDNA libraries, DNA manipulation enzymes, isolation of specific genes. Gene cloning, Cloning Vectors: Definition and Properties Plasmid vectors: pBR and pUC series Bacteriophage lambda and M13 based vectors Cosmids, BACs, YACs. Experimental research: Early experimentation, experimental groups, control groups, variables, method of controlling variables, designing and validation of experiments. Data collection, limitations and sources of error. Types of data Analysis: Descriptive, Inferential and Computer data analysis. Role of molecular diagnostics in present diagnostic era, Benefits of molecular diagnostics over serological diagnostic tests, Ethical issues related to molecular diagnostics, Basic techniques used in molecular diagnostics, Molecular diagnostics of HIV, SARS-COV-2, Tuberculosis, cholera and pathogenic *E. Coli*.

XVI: Biostatistics and Bioinformatics

Principles and practice of statistical methods in biological research, samples and populations, Basic statistics-average, statistics of dispersion, coefficient of variation, confidence limits, Probability distribution, normal, binomial and Poisson distribution. Mean variants, standard deviations and standard error, correlation and regression, test of statistical significance, and analysis of variance and covariance. Bioinformatics: Introduction and applications of Bioinformatics, Bioinformatics resources. Biological Databases: Overview to Biological Databases, Nucleotide Databases (GenBank), Protein sequence databases (Uniprot, Swiss prot), Protein structure databases (PDB). Sequence analysis: Sequence similarity search, BLAST, FASTA, CLUSTAL. Genomics: Introduction to Genomics, Comparative Genomic Databases.

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