BRANCH-XIII M.D. (BIOCHEMISTRY)

GUIDELINES FOR COMPETENCY BASED POST GRADUATE TRAINING PROGRAMME FOR M.D. BIOCHEMISTRY

Preamble:-

The purpose of this program is to standardize Biochemistry teaching at post-graduate level through out the country so that it will benefit in achieving uniformity in undergraduate teaching of the subject as well. Accordingly the training in M.D. Biochemistry should be distinctive from that in M.Sc., Ph.D., (Biochemistry), where the approach to the subject is primarily experimental.

Programme Objectives:-

A candidate upon successfully qualifying in the M.D. (Biochemistry) examinations should be able to:

1) Be a competent biochemist.
2) Work as a teacher in medical faculty both at undergraduate & post graduate level.
3) Supervise modern laboratory techniques & procedures in clinical Biochemistry in the hospital.
4) Purpose her / his interest to undergo further specialization.
5) Carry out & conduct various research problems both at basic and applied level.
6) Guide thesis at both post graduate and doctoral level.
7) Suggest, evaluate, interpret biochemical investigation in a given clinical situation and apply knowledge in clinical problems.

SPECIFIC LEARNING OBJECTIVES

1) Describe the concept of Biochemistry regarding biomolecules- carbohydrates, proteins, lipids, nucleic acids, enzymes, minerals.
2) Discuss the intermediary metabolism of the above biomolecules & their regulation.
3) Discuss the impairments in metabolism of the above, including inborn errors of metabolism.
4) Describe the role of nutrition in health & disease.
5) Apply theoretical knowledge to interpretation of biochemical parameters in health and disease.
6) Develop skills in performing biochemical techniques like electrophoresis, colorimetry, spectrophotometry, flame photometry & interpreting the data obtained. Optional – ELISA, RIA, techniques in molecular genetics.

Postgraduate Training

Based on the available facilities, department can prepare a list of postgraduate experiments pertaining to basic and applied biochemistry. Active learning should from the mainstay of postgraduate training. There should be lectures for postgraduates (at least 20 per year).

Postgraduate Examinations

The Postgraduate examinations shall be in 3 parts.

1. Thesis, to be submitted by each candidate at least 6 months before the date of commencement of the theory examination.
2. Theory: There shall be four theory papers- as given separately.

3. Practicals and Viva / Oral.

Practical will have 2 components namely – exercise and viva voce.

A. Practical comprising of 3 exercises.
B. Viva-voce or the oral session including a pedagogy of at least 15 minutes duration.

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COURSE CONTENT

REVISED SYLLABUS FOR M.D. – BIOCHEMISTRY

PHYSICAL AND ORGANIC ASPECTS OF BIOCHEMISTRY, INSTRUMENTATION BIOCHEMICAL TECHNIQUES, BIOSTASTICS

1) Physical Chemistry:

Water as universal biological solvent.

P^H.

Buffers.

Colloidal state and Gibbs – Donnan equilibrium.

Van der waals forces.

Surface tension.

Osmosis, diffusion and viscosity.

Law of mass action.

Hydrogen bonding, hydrophobic interactions and ionic bridges.

Determination of molecular weights.

2) Chemistry of Carbohydrates:

Structure, physical and chemical properties and biological role of :

Glucose, fructose, galactose, mannose, ribose, xylose, xylulose,

Lactose, maltose, sucrose.

Decxy and amino sugars.

Uronic acids and sugar alcohols.

Dextrin, starch, glycogen, cellulose, insulin.

Glycosaminoglycans and glycoproteins.

3) Chemistry of Proteins:

Structure, physical and chemical properties and biological function Of:

Amino acids present in proteins, including selenocysteine

Amino acids not found in proteins.

Modified amino acids.

Dissociation constant(pK_a).

Amino acids as buffers, amino acid titration, zwitterions and

Isoelectric point.

Cross-links, hydrogen bonds, disulphide bonds, non-covalent and

Ionic bonds in peptides and proteins.

X-ray diffraction studies.

Covalent structure of proteins.

Primary, secondary, tertiary and quaternary structure of proteins and

Elucidation of these Mass spectrometry.

Tandem mass spectrometers.

4) Protein structure and function:

Relationship of function to the three dimensional structure of myoglobin, hemoglobin, collagen and elastin.

Enzymes and peptide hormones.

Immunoglobulins.

Peptide sequencing and peptide synthesis.

5) Chemistry of lipids:

Structure, physical and chemical properties of:

Saturated and unsaturated fatty acids.

Polyunsaturated fatty acids.

Eicosanoids.

Triacylglycerol.

Sterols.

Phospholipids.

Glycolipids.

Sphingolipids.

Lipoproteins.

Membranes and fluid mosaic model.

6) Chemistry of purines and pyrimidines:

Nucleotides and their derivatives.

Polynucleotides.

Synthetic nucleotides.

7) Principles of laboratory analyses and safety:

Units of measurement.

International system of units in laboratory medicine.

Conversion from conventional units to SI units.

IFCC and IUPAC system recommendations.

Reference materials.

Reagent grade water production.

Testing for water purity.

8) Instrumentation and techniques:

Centrifugation.

Ultracentrifugation.

Radioactivity, properties of radionuclides and measurement of radioactivity.

Techniques that are radioisotopes

Autoradiography.

Geiger counter.

Scintillation counting.

Radio-immuno assay(RIA).

Radio-receptor assay.

Immuno-radiometric assay (IRMA).

Stable isotopes and mass spectrometry.

Spectrophotometry.

Reflectance photometry.

Flame emission photometry.

Atomic absorption spectrophotometry.

Flurometry.

Phosphorescence, chemiluminescence and bioluminescence.

Nephelometry.

Turbidimetry.

Direct vision spectroscope.

Electrochemistry- chemical sensors, potentiometry, ion selective electrodes, optical chemical sensors, enzyme electrodes and enzyme Immobilization.

Osmometry.

Electrophoresis (zone) – paper, agar gel, PAGE, SDS PAGE, iso-electric focusing.

Chromatography – column, paper, TLC, GLC, HPLC, gel filtration, ion exchange and their applications.

Principles of immunochemistry.

Immunoelectrophoresis.

Blotting techniques.

ELISA.

Automation in clinical chemistry.

9) Laboratory Management:

Common hazards in the laboratory.

Management of biological, chemistry and radioactive wastes.

Computer applications in clinical chemistry.

Setting up a clinical laboratory and a 24 hours emergency laboratory Service.

10) Sample Collection:

Anticoagulants and preservatives for blood.

Timed urine collections and urine preservatives.

11) Quality assurance:

Use of reference values.

Quality assurance in clinical laboratories.

12) Basic principles of biostatistics as applied to health sciences:

Concepts of probability.

Mean.

Standard deviation.

Coefficient of variation.

Correlation coefficient.

Tests of significance.

Selecting an analytical method.

Evaluation of an analytical method.

Evaluation of a diagnostic test.

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CELL PHYSIOLOGY, MOLECULAR BIOLOGY AND HUMAN GENETICS

1) Cell Physiology:

An overview of cellular structure and function.

Prokaryotic and eukaryotic cells.

Structure of eukaryotic cells – sub cellular organelles, cytosol, endoplasmic reticulum, nucleus, nucleolus, mitochondria, lysosomes, ribosomes, Golgi apparatus, peroxisomes, plasma membranes and their functions.

Receptor-mediated endocytosis.

Properties of biological membranes – motility, permeability, concept of semi-permeable membranes, electrochemical gradient and pumps, artificial membranes and liposomes.

Transport across membranes – active, facilitated and passive.

Transport mechanisms – ion channels including gated channels, carrier proteins, glucose transporters (GLUT), active transporters, symporters and antiporters.

Non-membrane organelles – cytoskeleton, microfilaments, microtubules and microvilli.

Evolution of organic molecules, endosymbiosis hypothesis, evolution of cells.

Sub-cellular fractionation – density gradient centrifugation, differential centrifugation, markers for each organelle and fraction.

Cell interactions and adhesion – types of junctions: tight junctions and gap junctions.

Surface glycoproteins and cell surface labeling – ABO blood groups, major histo-compatibility complex (MHC).

Adhesion molecules – cadherins, selectins, integrins (beta 1 and beta 2 integrins).

Cell cycle – concept of cell cycle, regulation of cell cycle, regulations – cyclins and their regulators, extra cellular regulators of cell cycle.

Cell division – mitosis and meiosis.

Cells as experimental models – E.coli, yeas, Drosophila melanogaster, viruses.

Programmed cell death.

2) Human genetics:

Structure of DNA and RNA.

Histones, chromatins, nucleosides and chromosomes.

Different types of DNA.

Agents that cause DNA damage – ionizing radiation, ultraviolet light, mutagens, (chemical and viral).

Different types of RNA – messenger, ribosomal, transfer, heterogeneous nuclear RNA, Snurps.

DNA replication – prokaryotic and eukaryotic.

Transcription – prokaryotic and eukaryotic.

Post-transcriptional modifications.

Antibiotics and transcription.

Regulation of transcription.

Genetic code.

Mitochondrial and plasmid DNA.

Translation – eukaryotic and prokaryotic.

Post-translational modifications.

Factors affecting protein synthesis.

Regulation of protein synthesis and gene expression, helix turn helix motif, zinc finger motif and leucine zipper motif.

Signal peptides, protein targeting and chaperones.

Disorders of post-translational modifications.

Constitutive, inducible and repressible enzymes.

Viral genetics – DNA and RNA viruses.

HIV and drugs in the treatment of HIV.

3) Molecular genetics and biotechnology:

Isolation of nucleic acids.

DNA digestion with restriction enzymes.

DNA electrophoresis.

Restriction maps.

Southern analysis: hybridization and blotting.

Polymerase chain reaction (PCR): principle, procedure, and visualization of products.

Reverse transcriptase PCR (RT-PCR).

DNA sequence analysis.

Automated DNA sequencing.

Cloning and vectors – definition, characteristics of different vectors and basic cloning techniques.

Gene libraries.

cDNA libraries.

The human genome project – sequencing of the genome and physical mapping.

Genetic maps.

Restriction fragment length polymorphisms and their applications.

DNA diagnostics – methods of identifying genes in human disease.

Fluorescent in-situ hybridization(FISH).

Genetic therapy.

Repeat DNA and mobile DNA elements.

Reporter genes.

Transgenic animals.

The human proteome.

4) Molecular basis of carcinogenesis:

Carcinogenic agents – radiation, chemicals and viruses.

Oncogenes and tumor suppressor genes.

Genetic cancer syndromes – familial breast cancer, familial adenomatous polyposis coli and retinoblastoma.

Inherited conditions that predispose to development of cancer (e.g., ataxia telangiectasia, xeroderma pigmentosum, Fanconi syndrome).

Mechanisms of action of cytotoxic drugs.

Basics of Cytogenetics.

5) Population genetics:

Risk assessment and genetic counseling.

Medical ethics in counseling.

6) Bioinformatics:

Basic of bioinformatics – proteomics, drug designing (pharmacogenomics), protein data bases and micro arrays.

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INTERMEDIARY METABOLISM, MACRO AND MICRO NUTRIENTS AND INBORN ERRORS OF METABOLISM

1) Enzymes:

Biomedical importance.

Nomenclature.

Classification.

General properties.

Coenzymes and cofactors.

Mechanism of action.

Action of serine proteases.

Kinetics of enzyme action.

Km value and its significance.

Inhibitors of enzymes, naturally occurring enzyme inhibitors.

Regulation of enzyme activity.

Enzymes in clinical medicine.

Isoenzymes and isoforms of enzymes.

Metalloenzymes and metal activated enzymes.

Isolation and purification of enzymes from natural sources.

The use of enzymes as laboratory tools (for diagnostic and research applications).

2) Vitamins:

Structure, sources, recommended dietary allowances (RDA), biochemical role, metabolism in the body and deficiency manifestations of water soluble and fat-soluble vitamins.

Megavitamin therapy.

Hypervitaminosis.

Antivitamins and vitamin analogues.

Use of vitamins in therapy.

3) Bioenergetics and biological oxidation:

The role of ATP and other high-energy phosphates.

Biologic oxidation.

The respiratory chain.

Oxidative phosphorylation – theories, inhibitors, uncouplers.

Mitochondrial diseases.

4) Carbohydrates:

An overview of metabolism.

Methods of studying intermediary metabolism.

Carbohydrates of physiological significance.

Digestion and absorption of carbohydrates.

Various pathways of metabolism of glucose.

Generation of ATP by substrate – level phosphorylation.

Pathways of metabolism of fructose and galactose.

Regulation of the major metabolic pathways of carbohydrates.

Inborn errors that occur in the metabolic pathways of carbohydrate metabolism.

Regulation of blood glucose levels.

Metabolism of Glycosaminoglycans and glycoproteins; associated disorders.

Disorders of carbohydrate metabolism – diabetes mellitus, lactose intolerance, galactosemia, disorders of fructose metabolism.

Metabolism of alcohol.

5) Lipids:

Lipids of physiological significance.

Digestion and absorption of lipids.

Importance of bile.

Assembly of chylomicrons and their metabolism.

Oxidation of fatty acids.

Biosynthesis of fatty acids.

Metabolism of Triacylglycerol.

Metabolism in adipose tissue (including brown adipose tissue).

Metabolism of ketone bodies and associated disorders.

Metabolism of cholesterol and associated disorders.

Compounds derived from cholesterol.

Metabolism of apoproteins and lipoproteins and associated disorders.

Functions and metabolism of Eicosanoids.

Metabolism of phospholipids.

Lipid storage disorders.

Obesity.

Metabolic adaptations in starvation and obesity.

Metabolic syndrome.

6) Proteins:

Digestion and absorption of proteins.

General reactions of catabolism of amino acids.

Urea cycle and associated disorders.

Hyperammonemia.

Catabolism of carbon skeleton of amino acids.

Biosynthesis of nonessential amino acids.

Degradation of individual amino acids.

Specialized products formed from amino acids.

Inborn errors of amino acid metabolism.

7) Integration of metabolism:

The provision of metabolic fuels.

Convergent points of acety1 Co A and glucose 6-phosphate.

8) Metabolism in specialized tissues:

Erythrocytes.

Liver.

Muscle.

Central nervous system.

Adipose tissue.

Lens.

Kidney.

9) Nucleic acids:

Metabolism of purines.

Disorders associated with abnormalities in the metabolism of purines.

Metabolism of pyrimidines.

Disorders associated with abnormalities in the metabolism of pyrimidines.

Nucleotide analogues in chemotherapy.

10) Haem:

Functions.

Biosynthesis.

Disorders associated with defects in biosynthesis.

Degradation of bilirubin.

Disorders associated with abnormalities in the metabolism of bilirubin.

Laboratory diagnosis in these disorders.

Abnormal haemoglobins and haemoglobinopathies.

11) Biochemical and molecular aspects of processes in the body:

Muscle contraction.

Nerve conduction.

Coagulation of blood.

12) Metabolism of minerals:

Sodium.

Potassium.

Calcium.

Phosphorus.

Magnesium.

Copper.

Zinc.

Iron.

Chromium.

Selenium.

Cobalt.

Manganese.

Other trace minerals.

Inborn errors of mineral metabolism.

13) Metabolism of xenobiotics and detoxification.

14) Free radicals and anti-oxidants.

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CLINICAL BIOCHEMISTRY, HUMAN NUTRITION, ENDOCRINOLOGY, IMMUNOLOGY AND RECENT ADVANCES IN BIOCHEMISTRY

The following topics are to be covered with special emphasis on the laboratory investigations relevant to the conditions:

1) Carbohydrates:

Diabetes mellitus including gestational diabetes mellitus.

Laboratory diagnosis and monitoring of diabetes mellitus.

Diabetic ketoacidosis.

Other metabolic complications of diabetes mellitus.

Monitoring of treatment.

Hycated proteins.

Urinary albumin excretion.

Hypoglycemia.

Inborn errors of carbohydrate metabolism – disorders of galactose, fructose lactose and pentose metabolism.

Glycogen storage disorders.

2) Lipids:

Disorders of lipoprotein metabolism.
Laboratory diagnosis of these disorders.
Association with atherosclerosis and the consequences.
Biochemical derangements in metabolic syndrome.

3) Proteins:

Plasma proteins in health and disease.
Proteins in other body fluids (urine, cerebrospinal fluid, amniotic fluid, Saliva and faeces).

4) Amino acids:

Aminoacidurias and their laboratory diagnosis.
Disorders of amino acid metabolism and their laboratory diagnosis.

5) Clinical enzymology:

Enzymes of liver, cardiac and skeletal muscle.
Laboratory diagnosis of myocardial infarction.
Pancreatic enzymes.

6) Tomour markers:

7) Fluid and electrolyte homeostasis:

Maintenance of fluid and dectrolyte balance.

Associated disorders and laboratory diagnosis.

8) Hydrogen ion homeostasis:

Maintenance of p^H

Associated disorders and laboratory diagnosis.

9) Renal function:

Disorders of renal function, including acute and chronic renal failure.

Laboratory assessment of renal function.

10) Laboratory assessment of gastrointestinal function:

Gastric function tests.

Pancreatic function tests.

Intestinal function tests.

Investigation of jaundice.

Investigation of Hepatobiliary function.

11) Endocrinology:

Signal transduction due to neurotransmitters, hormones, growth factors, cytokines and rhodopsin.

Mechanisms of hormone action by interaction with intracellular and membrane – associated receptors.

Structure, functions, synthesis and regulation, metabolism, actions, associated disorders and laboratory assessment of various hormones

produced by the hypothalamus, pituitary gland, thyroid gland, parathyroid gland, adrenal gland, pancreas, gastrointestinal tract and gonads.

Endocrine functions of kidney, heart, lungs and adipose tissue.

Placental hormones.

Biochemistry of conception, reproduction and contraception.

12) Mineral and bone metabolism:

Laboratory assessment of rickets, osteomalacia, osteoporosis.

Markers for osteoblasts and osteoclasts.

Hyper and hypocalcernia.

Disorders of magnesium.

13) Disorders of porphyrin metabolism:

Laboratory assessment of porphyries.

Laboratory assessment of jaundice.

14) Cerebrospinal and other body fluids:

Analysis in health and disease.

15) Principles of hemo and peritoneal dialysis:

16) Immunology:

Types of immunity.

Immunoglobulins – classification, functions, generation of antibody diversity (immunogenetics), multiple mycelia and other associated

disorders, polyclonal and monoclonal antibodies and their applications.

17) Miscellaneous:

Neonatal screening for in-born errors in metabolism.

Prenatal diagnosis.

Fetal monitoring including fetal lung maturity.

Paediatric biochemistry.

Biochemistry in the elderly.

Lysosomal storage disorders.

Disorders of connective tissue.

18) Human Nutrition:

General nutritional requirements.

Energy requirements.

Macronutrients and their roles.

Biological value of proteins.

Specific dynamic actions.

Balanced diet.

Dietary fibre.

Dietary supplements.

Fortification of foods.

Food additives.

Food fads.

Vegetarianism.

Nutritional support.

Disorders of nutrition (protein malnutrition and protein energy malnutrition).

Biochemical assessment of nutritional status.

Laboratory diagnosis of nutritional disorders.

National Nutrition Programme.

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LIST OF PRACTICALS

1) Reactions of carbohydrates, lipids, proteins and amino acids.
2) Chromatographic separation of sugars, amino acids and lipids.
3) Estimation of nitrogen in a protein.
4) Estimation of calcium and phosphorus in milk.
5) Haemoglobin and its derivatives.
6) Preparation and estimation of glycogen and casein from biological samples.
7) Determination of enzyme activity and kinetic properties of acid phosphates and catalase.
8) Agarose gel electrophoresis.
9) Polyacrylamide gel electrophoresis (PAGE).
10) Experiments of milk.
11) Glucose estimation in plasma / serum.
12) Glucose tolerance test.
13) Estimation of cholesterol, Triacylglycerol and lipoproteins in plasma.
14) Estimation of calcium, electrolytes, p^H and blood gas.
15) Estimation of urea acid, creatinine, ammonia in blood and urine.

16) Clearance studies.
17) Estimation of bilirubin, ALT, AST, GGT, cholinesterase, prothrombin time.
18) Estimation of copper, ceruloplasmin, lithium, iron, iron binding capacity, magnesium in serum.
19) T3 and T4 assays and TSH measurement.
20) Urinalysis for normal and abnormal constituents.
21) Estimation of 17-ketosteroids and vanilly1 mandelic acid (VMA) in urine.
22) Analysis of gastric juice.
23) Analysis of renal and biliary calculi.
24) Estimation of LDH, phosphates, amylase and creative kinase in serum.
25) Separation of serum LDH Isoenzymes by Polyacrylamide gel electrophoresis.
26) Separation of serum alkaline phosphates Isoenzymes.
27) Estimation of ethanol in blood and urine.
28) CSF analysis for biochemical parameters.
29) Analysis of ascetic, pleural and other fluids.
30) Estimation of serum proteins.
31) Electrophoresis of serum proteins and lipoproteins.
32) Estimation of glycated Haemoglobin.
33) Estimation of urine proteins.
34) Detection of Bence-Jones protein in urine.

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