#### **CURRICULUM MD**

#### **BIOCHIMESTRY**

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## **Programme Objectives**

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

- I. Be a competent Biochemist,
- II. Work as a teacher in medical faculty both at undergraduate & postgraduate level.,
- III. Supervise modern laboratory techniques & procedures in clinical Biochemistry in the hospital.,
- IV. Pursue her/his interest to undergo further specialization.,
- V. Carry out & conduct various research problems both at basic and applied level.,
- VI. Guide thesis at both post Graduate and Doctoral level.,
- VII. Suggest, evaluate, interpret Biochemical investigation in a given clinical situation and apply knowledge in clinical problems.,

# **Specific Learning Objectives**

- **I.** Understand the concept of Biochemistry regarding Biomolecules-Carbohydrates, proteins, lipids, Nucleic acids, Enzymes, Minerals.
- **II.** Have knowledge of intermediary metabolism of the above & regulation of individual metabolism.
- **III.** Possess the knowledge of the impairment of metabolism including inborn errors of metabolism.
- **IV.** Understand the role of nutrition in health& disease.
- **V.** Apply biochemical knowledge in normal & diseased states.
- **VI.** Have knowledge regarding the analysis of biological fluids for its chemical constituents& correlating the same in health& disease.
- **VII.** Develop skills of performing biochemical, & interpreting the data. Optional-ELISA, RIA, Molecular Biology techniques.

### **Postgraduate Training**

Duration of course - Three years Eligibility - M.B.B.S

Selection - Through Delhi PG entrance and all India test

#### **Training Programme**

Based on the available facilities, department can prepare a list of postgraduate experiments pertaining to basic and applied biochemistry. Active learning should form the mainstay of postgraduate training there should be lectures for postgraduates (at least 20 per year). Along with seminars, symposia, group-discussions, journal clubs. The postgraduate students should regularly take the ward rounds of various clinical departments and lean cases of interest for discussion with the Biochemistry faculty. They should render special investigative services in their respective area of specialization. Each college should have a medical education unit to generate teaching resource material for UG and evolving of problem solving modules.

## **Course Content**

#### THEORY:

- 1. There should be 4 theory papers with the following broad subdivision of topics-
- **Paper I** Biomolecules /Cell biology, Principles of Biophysics and Physical chemistry, Biostatistics /Research methodology and Biochemical techniques.
- **Paper II** –Enzymes, Bioenergetics, Biolog1cal oxidation, Intermediary metabolism plus regulation, Inborn errors of metabolism, Nutrition and Endocrinology.
- **Paper III** Molecular biology and Immunology.
- **Paper IV** Molecular medicine (Biochemistry of different body systems/organs in health and disease), Clinical Biochemistry and Recent advances.
- 2. Under the above main division of topics, the subtopics already mentioned in the circulated guidelines are not mentioned. Only those subtopics which have not received adequate mention or importance in these are being highlighted below, and these must be included in the final curriculum -

#### Paper I-

### Cell Biology -

Structure of the cell and different sub cellular organelles, Structure of cell membrane Movement of substances across cell membranes, Interaction between cells and environment, Glycoprotein's and proteogycans, Extracellular matrix, Integrins, Cell-cell interaction-selectins, Cadherins, Tight junctions ,Gap junctions, Intracellular traffic and sorting of proteins-endoplasmic reticulum, Golgi complex, Vesicle transport, Endocytic pathway, Protein targeting to cell surface, Nucleus, Lysosomes, Mitochondria, peroxisomes, Cytoskeleton and cell motility, Cell cycle, Muscle contraction, Hemoglobin and Myoglobin,

Biostatistics/research methodology-

Types of study design, Calculation of adequate sample size, Students 't' test, Paired 't' test, Chi square test, Fisher's exact test, Nonparametric tests of significance, One way and two way analysis of variance, Multivariate analysis, Survival analysis-logrank test, Relative risk calculation-Odd's ratio, commonly used statistical software's.

Biochemical Techniques-

Centrifugation-ultracentrifugation, Optical techniques-spectrophotometery, reflectance photometry, flame photometry, atomic absorption spectrophotometery, fluorometery, phosphorescence, chemiluminescence, turbidimetery and nephelometry, Electrochemistry- chemical sensors and biosensors, Electrophoresis, Chromatography, Immunochemical techniques-immunoassays, Spectroscopic techniques-circular dichroism, electron spin resonance, nuclear magnetic resonance, Mass spectrometry and tandem mass spectrometry, Nanotechnology and microfabrication, Techniques to study in vivo metabolism-NMR, SPECT, PET scans, Radioisotope techniques.

### Paper II-

Enzymes: General properties, classification and nomenclature, kinetic model, Km value, factors influencing enzymes action, specificity, mechanism of enzymes action, enzymes kinetics, regulation of enzyme action, isolation, isoenzymes

Biological oxidation and reduction, bioenergetics.

Digestion and absorption of food and other nutrients

Detoxification/ xenobiotics

Chemical anatomy of human body

Role of oxido-reductases

Cytochrome P450 system

Free radicals formation, scavenging oxygen free radicals. Antioxidants. Role in diseases.

Respiratory chain and oxidative phosphorylation, components of respiratory chain control, site specific inhibitors, uncouplers.

High energy phosphate compounds

Vitamins: Structure, sources, daily requirements, physiological role and deficiency manifestation of vitamins, hypo and hyper vitamins and vitamins

Mechanism of action of coenzymes

Mineral metabolism and role of micro and macronutrients

Intermediary Metabolism

Methods of studying intermediary metabolism

Intermediary metabolism of carbohydrates, lipids, proteins, and aminoacids, nucleic acid in human system

Muscular contraction, nerve conduction, coagulation of food

Metabolism in specialized tissues like erythrocytes, lens nervous tissues etc.

Metabolism interrelationships and metabolism in starvation.

Inborn errors of metabolism:

Inborn errors of carbohydrates, lipids amino acids, protein nuclein acids, mineral metabolism.

Human Nutrition: Principal food components, general nutritional requirements, energy requirements, biological value of proteins, specific dynamic action, balanced diet, diet formulation in health and disease, mixed diet, nutritional supplements, food toxins and additives, parental nutrition, disorders of nutrition, obesity, protein and protein energy, malnutrition dietary fibers, under-nutrition, laboratory diagnosis of nutrition disorders, national nutritional programme.

Nutrition -should be inclusive of vitamins, minerals and trace elements.

## Paper III-

Molecular Biology-metabolism of nucleotides/nucleic acids, regulation of gene expression, protein targeting, recombinant DNA and other molecular biology techniques, Human genome project, functional genomics, proteomics, Bioinformatics.

Principles of human genetics- Transmission of genetic disease-mutations and their functional consequences, alleles, genotypes, haplotypes, phenotypes, genetic linkage, identification of disease causing gene, chromosomal disorders, monogenic Mandelian disorders, mitochondrial disorders, nucleotide repeat expansion disorders, polygenic disease and complex genetic traits, imprinting disorders, methods of mutation detection, gene therapy.

Stem cells in clinical medicine.

Immunology-Overview-innate and acquired immunity, cells and organs of the immune system-T and B cells, macrophages, dendritic cells, NK cells, granulocytes, antigens, epitopes and haptens, immunoglobulins classes, isotypes, allotypes, idiotypes, monoclonal antibodies, organization and expression of immunoglobulin genes, immunoglobulin gene rearrangement, class switching, antigen-antibody interaction-

immunochemical techniques, MHC, antigen processing and presentation, T cell and B cell receptor, toll like receptors, cell maturation/activation/differentiation, B cell generation /activation/ differentiation, cytokines, complement system, cell mediated immunity, T regulatory cells, Hypersensitivity, immune response to infections, vaccinesnewer approaches, immunodeficiency, autoimmunity, transplantation immunology, cancer and immune system, immunodiagnostics and immunotherapy.

### Paper IV –

Molecular medicine (Biochemistry of different body systems/organs in health and disease)-

- 1. Fluid and electrolyte balance and Acid-Base balance-regulation and disturbances.
- **2. Hematopoietic disorders**-Iron deficiency and other hypoproliferative anaemias-iron metabolism, laboratory tests of iron status, iron therapy, anemia of chronic disease, anaemia of renal disease

Hemoglobinopathies- sickle cell anaemia, methaemoglobinemias, thalassemia syndromes Megaloblastic anaemias

RBC membrane and metabolism,. Hemolytic anaemias-inherited defects in RBC membrane and enzymes-G6PD deficiency, immunologic causes of hemolysis.

ABO blood group system-biochemical basis, transfusion biology.

Plasma cell disorders-multiple myeloma, MGUS.

- **3. Hemostasis and thrombosis**: Biochemical mechanisms, related laboratory tests, antiplatelet /anticoagulant / fibrinolytic therapy.
- **4.** Cardiovascular system-Atherosclerosis- pathogenesis, risk factors, its prevention and treatment

Heart-Heart failure, acute coronary syndrome, cardiac biomarkers, cardiomyopathyetiology.

Hypertension-essential and secondary, genetics, laboratory evaluation, approach to therapy.

**5. Respiratory system-**Gaseous exchange in lungs-physiological features and disturbances, arterial blood gases.

Pathogenesis of asthma, cystic fibrosis, emphysema, α1AT deficiency.

- **6. Kidney**-Kidney function tests, Pathophysiology, biochemistry ,laboratory findings and management in acute renal failure, chronic renal disease and failure/uremia, Estimation of GFR, Glomerular diseases-pathogenesis and mechanisms of glomerular injury, Nephrotic syndrome, Diabetic nephropathy, Tubular disorders, Renal tubular acidosis, Proteinuria, Nephrolithasis, Renal replacement therapy, Kidney transplant.
- **7. Gastrointestinal system-**Alimentary tract-gastric physiology, pathophysiology of peptic ulcer disease, role of H.pylori ,gastric function tests, Zollinger Ellison syndrome, nutrient digestion and absorption, evaluation of malabsorption, celiac sprue, inflammatory bowel disease, steatorrhea, lactose intolerance, protein losing enteropathy, investigation of maldigestion / malabsorption, GIT regulatory peptides , Neuroendocrine tumors.

Liver- liver function tests, hyperbilirubinemias, viral hepatitis, serologic /virologic markers, alcoholic liver disease, fatty liver, chronic liver disease, cirrhosis and its complications, pathogenesis of ascites, hepatic encephalopathy, metabolic diseases affecting liver, Reye's syndrome, diseases of gall bladder/bile ducts-pathogenesis of gallstones.

Pancreas-acute and chronic pancreatitis, cystic fibrosis, pancreatic function tests.

- 8.Disorders of Immune system, connective tissue and joints-Immune tolerance mechanisms of immune mediated damage to host tissues, primary immune deficiency diseases-laboratory evaluation, allergies/anaphylaxis: pathophysiology -lipid mediators, autoimmunity-immunopathogenetic mechanisms, SLEetiology/pathogenesis/laboratory tests for autoantibodies, Rheumatoid arthritisgenetics, pathogenesis, lab findings, vasculitic syndromes-pathophysiology,lab findings, sarcoidosis, amylodosis. osteoarthritis-pathophysiology ,gout,pseudogout,Rheumatic fever- immunological aspects,Scleroderma,synovial fluid analysis...
- 9.**Bone and mineral metabolism**-bone structure and metabolism,calcium,phosphate and magnesium metabolism,regulation and abnormalities,vitamin D,calcitonin,PTH,PTHrP,osteoporosis-pathophysiology,markers of bone turnover.
- **10.Nervous system and Neurologic disorders**-Neurotransmitters and their receptors, ion channels and channelopathies, memory and learning-signaling pathways, neurotrophic

factors, excitotoxicity and apoptosis, protein aggregation and neurodegeneration, genetic disorders of CNS, pathophysiology of ischemic stroke, Alzheimer's disease, Parkinson'disease, Huntington'disease, Inherited ataxias, Amyotrophic lateral sclerosis and other motor neuron diseases, Multiple sclerosis. Prions and Prion diseases,

Guillain-Barre syndrome-immunopathogenesis, Myasthenia gravis-pathophysiology, Hereditary myopathies-Duchenne muscular dystrophy, Inherited disorders of muscle energy metabolism, mitochondrial myopathies. Biochemistry of olfaction taste, vision and touch.

### **11. Psuchiatric disorders**-Anxiety, depression ,schizophrenia-pathophysiology.

Neuropsychiatric drugs-biochemical basis of mode of action, biochemical basis of drug addiction and abuse, CSF analysis.

**12.Cancer**-Cancer genetics, clonal origin and multistep nature, oncogenes, tumour suppressor genes, familial cancer syndromes, chromosomal instabilityin solid tumours, viruses in human cancer, epigenetic regulation in cancer, gene expression profiling in cancer, cancer cell biology, cell cycle abnormalities, telomerase, apoptosis, metastasis-molecular basis and therapeutic strategies, tumour angiogenesis-molecular events and antiangiogenic therapy, biological basis of cancer chemotherapy, multidrug resistance, molecularly targeted cancer therapy, cancer immunotherapy.

Environmental Biochemistry-xenobiotic metabolism

Clinical Biochemistry-Investigative aspects-principles of laboratory analysis and safety, specimen collection and processing, automation, point of care testing, evidence based laboratory medicine, selection and analytical evaluation of methods, clinical evaluation of methods-sensitivity and specificity, ROC curves, establishment and use of reference values, preanalytical variables, clinical laboratory informatics, Total quality management, Biomedical waste disposal.

Analytes-Amino acids/peptides/proteins, plasma proteins, enzymes, clinical enzymology ,tumour markers, carbohydrates,lipids/lipoproteins/apolipoproteins,cardiovascular,risk factors,electrolytes,blood,gases,hormones,catecholamines/serotonin,vitamins,and,trace elements, hemoglobin, iron and bilirubin, porphyrins and their disorders,

Therapeutic drug monitoring.

Pituitary, adrenal and thyroid function,

Reproductive related disorders-infertility,

Pregnancy-maternal and fetal health,

Inborn errors of metabolism,

Clinical toxicology,

Molecular diagnostics.

### **PRACTICALS:**

### 1. List of suggested practicals:

Protein fractionation- Ion exchange chromatography, gel filtration chromatography

TLC for lipids, amino acids

Kinetic analysis of enzymes (Alkaline phosphatase) from a suitable source

Separation and molecular weight determination of proteins by SDS-PAGE

Western blotting

Purification of IgG by protein A-Sepharose affinity column chromatography

Estimation of proteins by Lowry and Bradford methods

Separation of LDH isoenzymes by PAGE

Serum protein electrophoresis on agarose gel and densitometric scanning.

Immunofixation

Lipoprotein electrophoresis

Paper chromatography for separation of amino acids

Separation of peripheral blood lymphocytes on Ficoll Hypaque

Subcellular fractionation by ultracentrifugation

Isolation of high molecular weight DNA from tissues/blood

Restriction enzyme digestion of DNA

Isolation of plasmid and agarose gel electrophoresis

PCR-Immunodiffusion techniques-radial immunodiffusion, ouchterlony

ELISA for hormones/tumour markers

radioactivity measurements, RIA

Clinical Biochemistry-

Estimation in blood of glucose, GTT, glycosylated Hb, urea creatinine, uric acid, ammonia, clearance tests, cholesterol, triglycerides, HDL, LDL, bilirubin, total

proteins, albumin, AST, ALT, ALP, GGT, acidphosphatase, amylase, LDH, CK total, CKMB, calcium,

Phosphorus, serum electrolytes-sodium and potassium, blood gas analysis, Apo A ,ApoB, copper, ceruloplasmin, iron,TIBC, ferritin, troponin, myoglobin.

Urine analysis, microalbuminuria.

Analysis of CSF and other body fluids.

#### 2. Demonstrations-

Chemiluminescence based immunoassays, Cell culture, HPLC, Mass spectrometry.

3. Practical examination

There will be

- 1. A spotting session which will include few short clinical cases as problem solving exercises.
- 2. Micro teaching
- 3. Thesis presentation.
- 4. Books Recommended:
  - 1. Biochemistry Ed. Lubert Stryer. W.H. Free man and Company, New York.
  - 2. Principles of Biochemistry. Ed. Lehninger, Nelson and Cox. CBS Publishers and Distributors.
  - 3. Harper's Biochemistry. Ed. R.K.Murray, D.K.Granner, P.A. Mayes and V.W.Rodwell. Appleton and Lange, Stamford, Connecticut.
  - 4. Textbook of Biochemistry with Clinical Correlations. Ed. Thomas M. Devlin, Wiley- Liss Publishers.
  - 5. Genes VIII Ed Benjamin Lewin. Oxford University Press.
  - 6. Tietz Textbook of Clinical Chemistry and molecular diagnostics Ed Burtis and Ashwood. W.B Saunders Company.
  - 7. Principles and techniques of Practical Biochemistry. Ed Keith Wilson and John Walker. Cambridge University Press.
  - 8. Biochemistry. Ed. Donald Voet and Judith G. Voet. John Wiley & Sons, Inc.
  - 9. Molecular Cell Biology, H. Lodish, A, Berk, S.L.Zipursky, P. Matsudaira, D. Baltimore, J. Darnell.
  - 10. Medical Biochemistry by Bhagwan.

## 11. KU BY's Immunology.

### Evaluation:-

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.

- **Paper I** Biomolecules /Cell biology, principles of Biophysics and Physical chemistry, Biostatistics /Research methodology and Biochemical techniques.
- **Paper II** –Enzymes, Bioenergetics ,Biolog1cal oxidation, Intermediary metabolism plus regulation, Inborn errors of metabolism, Nutrition and Endocrinology.
- **Paper III** Molecular biology and Immunology.
- **Paper IV** Molecular medicine (Biochemistry of different body systems/organs in health and disease), Clinical Biochemistry and Recent advances.
- 3 Practical

Practical will have 2 components namely – exercise and viva voice

- A Practical comprising of 3 exercises
- B Viva –Voce or the oral sessions including a component of seminar presentation of at least 15 minutes duration.