BIOCHEMISTRY

Biochemistry includes Molecular Biology.

1. GOAL

The broad goal of the teaching of undergraduate students in Biochemistry is to make them understand the scientific basis of the life processes at the molecular level and to orient them towards the application of the knowledge acquired in solving clinical problems.

2. OBJECTIVES

2.1. Knowledge

At the end of the course, the student should be able to

1. Describe the molecular and functional organization of a cell and list its sub-cellular components;
2. Delineate structure, function and inter-relationships of biomolecules and consequences of deviation from normal;
3. Summarize the fundamental aspects of enzymology and clinical application wherein regulation of enzymatic activity is altered;
4. Describe digestion and assimilation of nutrients and consequences of malnutrition;
5. Integrate the various aspects of metabolism and their regulatory pathways;
6. Explain the biochemical basis of inherited disorders with their associated sequelae;
7. Describe mechanisms involved in maintenance of body fluids and pH homeostasis;
8. Outline the molecular mechanisms of gene expression and regulation-the principles of genetic engineering and their application in medicine;
9. Summarize the molecular concepts of body defense and their application in medicine;
10. Outline the biochemical basis of environmental health hazards, biochemical basis of cancer and carcinogenesis;
11. Familiarize with the principles of various conventional and specialized laboratory investigations and instrumentation analysis and interpretation of a given data;
12. The ability to suggest experiments to support theoretical concepts and clinical diagnosis.

2.2. Skills

At the end of the course, the student should be able to:

2.2.1. Make use of conventional techniques/instruments to perform Biochemical analysis relevant to clinical screening and diagnosis;

2.2.2. Analyze and interpret investigative data;

2.2.3. Demonstrate the skills of solving scientific and clinical problems and decision making;

2.3. Integration

The knowledge acquired in Biochemistry should help the students to integrate molecular events with structure and function of the human body in health and disease.

3. SYLLABUS

3.1. Theory

3.1.1. Cell

Subcellular components - Molecular and functional organization - Plasma membrane, cytoplasm, Nucleus and subcellular components like Mitochondria, Endoplasmic reticulum, lysosomes, peroxisomes, cytoskeleton, Golgi apparatus etc.

3.1.2. Biomolecules

Introduction - Chemistry of Carbohydrates: Monosaccharides, disaccharides, homo and hetero Polysaccharides - Chemistry of Lipids: Classification, fatty acids, Eicosanoids and derivatives- Triglyceride, Phospholipids, Sphingolipids, Cholesterol, and lipoprotein - Chemistry of protein: Classification of amino acids; peptides, peptide hormones (e.g.) Insulin, glucagon, parathyroid hormone, and few pituitary hormones; Plasma proteins; classification, method of Separation and Electrophoretic pattern of plasma protein in health and disease; Protein structure and function; Special Proteins; Structural Proteins - Bases: Purines & Pyrimidines, Nucleotides, Nucleic acids: DNA & RNA Structure, Nucleic acid analogues of medical importance - Structure of Haemoglobin, Myoglobin; structural relationship with the function (Outline); Abnormal haemoglobin; Congenital and acquired - Vitamins and Minerals (in brief / details in Nutrition)

3.1.3. Enzymes

Fundamental aspects of enzymology - definition, classification, mechanism of action, factors affecting enzyme activity - Enzyme regulation - Coenzymes - Isozymes - enzymes of clinical importance.

3.1.4. Nutrition

Digestion and assimilation of Nutrients - Carbohydrates, proteins, lipids, vitamins and minerals - Nutritional requirements; RDA, SDA, Balanced diet and limiting amino acid - Vegetarianism - Consequences of malnutrition: Marasmus, Kwashiorkor, over nutrition.

3.1.5. Metabolism and Regulatory Pathways

1. Introduction to metabolism

Emphasize the purpose of metabolism like energy production, inter- conversion and synthesis of important bio-molecules etc. - High energy compounds - Biological oxidation - enzymes involved - Oxidative phosphorylation - theories - shuttles.

2. Metabolic pathways, regulation and metabolic errors

2.1. Carbohydrates

Glycolysis - HMP Pathway - Gluconeogenesis - Uronic acid pathway - glycogen metabolism - fructose and galactose metabolism and TCA cycle -Regulation of blood glucose - Diabetes Mellitus - hypoglycaemia - Hyper glycaemia. Inborn errors of carbohydrate metabolism - Clinically important investigations pertaining to carbohydrate metabolism - reduction test of urine, differential diagnosis for glycosuria including chromatography - Blood sugar values, GTT, glycosylated haemoglobin, fructosamine

2.2. Lipid metabolism

Synthesis of fatty acid - Fatty acid oxidation - energetics of oxidation, Ketone bodies, metabolism of unsaturated fatty acids - prostaglandins - prostacycline - Thromboxanes -Triacylglycerol-phospholipids - Sphingolipids - Cholesterol and its derivatives. Apoproteins - Lipoprotein Metabolism - Fatty liver, Lipotropic factors, inborn errors - Clinically important investigations pertaining to lipids and lipoproteins.

2.3. Protein metabolism

Dynamic state of body proteins - Inter organ transport of amino acids - body amino acid pool - Ammonia production - Transport of ammonia - its disposal - Urea cycle - Metabolism of individual amino acids - Biologically important compounds obtained from amino acids including Gamma amino butyric acid and Polyamines, Neurotransmitters - Clinically important investigations pertaining to protein metabolism - Total protein - albumin - globulin - A.G. ratio - Serum protein electrophoresis - Blood urea - BUN - Serum creatinine - urea and creatinine clearances - Amino acid chromatography for screening inborn errors

2.4. Integration of Metabolism

Main control sites of metabolic pathways and key enzymes - Metabolic adaptation during fed state and starvation - Metabolism in Principal organs like liver, RBC, adipose tissue, muscle, kidney, heart and brain.

2.5. Nucleic acid Metabolism

Purine and Pyrimidine synthesis and Degradation - Salvage pathways - Abnormalities of Nucleotide metabolism - inborn errors

2.6. Metabolism of Haemoglobin, Porphyrias and Bilirubinaemia Porphyrias, Abnormal Hemoglobin and Jaundice and investigations pertaining to these disorders

3.1.6. Gene Expression and Regulation

Principles of Genetic Engineering and their applications in Medicine - Basics of Genetics - Chromosomal structure - arrangement of coding sequence and genetic code - Biosynthesis of Proteins with Post translational modification - Cell Cycle: DNA Replication and its repair; RNA Synthesis and Processing; Mutation - Gene Expression and Regulation: Operon concept, genetic switches; Gene rearrangement; gene amplification; Gene protein Interaction - Genetic engineering techniques and their applications in medicine: Restriction enzymes, Vectors, genome library; DNA probes; Blot transfer techniques; Recombinant DNA technology, PCR; Polymerase Chain Reaction; Clinical application of genetic engineering; RFLP, DNA sequencing, Gene therapy, Human Genome Project, Cloning etc.

3.1.7. Inborn Errors

1. Biochemical basis of inherited disorders with their associated sequelae Introduction to various types of inheritance and types of mutation defect in relation to various inherited disorders.

2. Carbohydrates

Glycogen storage diseases, Galactosemia, G6PD deficiency - Lactose Intolerence, Fructose intolerance, Fructosuria, Pentosuria,

3. Lipids

Disorders of FA Oxidation, Sphingolipidoses, dyslipoproteinaemias

4. Proteins

Urea cycle disorders, inborn errors associated with each amino acid: Porphyrias, hyperbilirubinemia (congenital and acquired); Hyperuricaemia, Gout, Orotic Aciduria, Lesch Nyhan Syndrome; Neonatal screening and prenatal diagnosis of inborn errors

3.1.8. Homoeostasis

Mechanisms involved in the maintenance of body fluids and pH homeostasis.

Metabolism of water and electrolytes, Homeostasis of pH - buffer system, Role of Kidney and

Lungs - Acid base disorders

Blood gas analysis and its interpretation and correlation to acid base disorders.

3.1.9. Immunity

Molecular concept of body defense and application in medicine

Immunoglobulin structure, type, synthesis and function - Antigen binding - monoclonal antibodies - Hyper and Hypogammaglobulinaemia - Immunodeficiency and AIDS - Biochemical methods of assessing the Immunoglobulin - RIA, ELISA.

3.1.10. Environmental Hazards and Cancer

Biochemical basis of Environmental Hazards - occupational hazards (lead, organophosphorus compounds etc.) Hazards due to modern industrialization (H2S) and traffic pollution (CO), Xenobiotics - Biochemical basis of cancer and carcinogenesis - Tumor markers

3.1.11. Laboratory Investigation

Principles of Various conventional and specialized Laboratory investigations and Instrumentation analysis and interpretation of data - Principles of conventional and specialised Lab investigation including instrumentation analysis - Conventional: manual colorimetric methods for biochemical parameters (dealt with in practical classes) - Spectrophotometer - Flame photometer - Spectroscopy, pH meter, Centrifuge

1. **Specialized**

Automated techniques Semi and random auto analyzer - ELISA - RIA - Fluorimetry - Blood Gas Analyzer, Semi and fully automated analyzers

2. **Interpretation of data**

Normal range of biochemical parameters - Causes for deviation from normal.

3.1.12. Clinical Chemistry

Experiments to support theoretical concept and clinical diagnosis: Biochemical tests to determine the functional ability of an organ; Liver function test; Renal function test; Pancreatic function test - Investigations pertaining to hormones: Mode of action of hormone and its function; Thyroid function tests; Parathyroid function tests; Adrenal function tests - Biochemical tests to confirm the clinical diagnosis of a disease and their interpretation: Jaundice (hemolytic, hepatic and obstructive); Cirrhosis liver - Acute Renal failure, Chronic Renal failure, Nephrotic syndrome - Myocardial infarction - Diabetes mellitus (Type I and Type II) (mild, moderate and severe); Renal glycosuria; Alimentary glycosuria - Rickets - Hypo and hyperparathyroidism; Hypo and hyper thyroidism; Pancreatitis - Metabolic acidosis, alkalosis; Both uncompensated and compensated - Respiratory acidosis, alkalosis; Both uncompensated and compensated

3.2. PRACTICAL

3.2.1. Quantitative Estimation

Blood Sugar - Urea - Creatinine - Total Proteins and Albumin - Uric Acid - Demonstration by semi / fully automated analyzers; Bilirubin - One Enzyme - ALP/ AST - Demonstration ; Estimation of electrolytes by using ion selective electrode (ISE) / Flame Photometer - Demonstration of Arterial blood gas analyzer

3.2.2. Qualitative Analysis

Carbohydrates: General reactions of carbohydrates; Monosac-charides; Glucose, Fructose - Disaccharides; Maltose, Lactose, Sucrose - Identification of unknown carbohydrates - Proteins:

General reactions of albumin, Casein - Identification of unknown proteins - Non Protein Nitrogenous substances (NPN): Urea, Uric acid, Creatinine; Identification of unknown NPN - Scheme for identification of an unknown - Substances of Biochemical importance - Normal and Abnormal Urine

3.2.3. Clinical Chemistry Exercise

3.2.3.1. Spotters

The student must identify the spotter and write one most important use of the spotter

1. Identification of instruments & specify their principle -pH paper, pH Meter, Colorimeter, Centrifuge. Urinometer, Electrophoresis apparatus
2. OSAZONES: Identification of Glucosazone / Fructosazone, Lactosazone, Maltosazone
3. Electrophoresis pattern - normal pattern & abnormal patterns -Nephrotic syndrome, Cirrhosis of liver, Multiple myeloma
4. Chromatography paper & pattern and apparatus
5. Structure of tRNA, Cholesterol, glucose, fructose
6. Identification of reactions - Hay's test, Molisch test, Colour reactions of proteins, Rothera's test, Aldehyde reaction etc.
7. Identification of pictures of diseases like Rickets, Xerophthalmia, Bitot's spots, Kwashiorkor, PEM etc.
8. Identification of dietary nutrients & discuss - egg, milk, rice, potato

3.2.3.2. Charts

1. Suggest investigations for a case of: Jaundice - Diabetes mellitus, Type I & II,DKA - Acute renal failure - Proteinuria -Nephrotic syndrome - Rickets - Myocardial infarction - Acidosis; Metabolic and Respiratory - Alkalosis; Metabolic and Respiratory - Glycosuria - Aminoaciduria - Hyper and Hypo parathyroidism - Hyper and hypothyroidism

2. Calculate: Calculate Albumin - Globulin ratio with total protein and albumin values - Calculate minute volume from 24 hours urine volume - Calculate creatinine clearance with the required parameters given.

3. Interpret: Electrophoresis patterns; normal, cirrhosis liver, Nephrotic syndrome, Multiple myeloma - Normal GTT and Diabetes Mellitus, glycosurias - Acute pancreatitis - Myocardial infarction - Acute renal failure and nephrotic syndrome - Acidosis, alkalosis -Hypo and hyper thyroidsm - Hypo and hyper parathyroidism - Rickets -Jaundice