BIOCHEMISTRY

Goals and objectives given below are as per the Medical Council of India Regulations on Graduate Medical Education, 1997.

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.

SPECIFIC LEARNING OBJECTIVES

a.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 subcellular 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 fluid 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 defence and their application in medicine;
(10) outline the biochemical basis of environmental health hazards, biochemical basis of cancer and carcinogenesis;
(11) explain the principles of various conventional and specialized laboratory investigations and instrumentation analysis and interpretation of a given data;
(12) suggest experiments to support theoretical concepts and clinical diagnosis.

b. SKILLS:

At the end of the course, the student should be able to :
(1) make use of conventional techniques/instruments to perform biochemical analysis relevant to clinical screening and diagnosis;
(2) analyze and interpret investigative data;
(3) demonstrate the skills of solving scientific and clinical problems and decision making;

c.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.

TEACHING HOURS:

Theory classes: Total: 115 hours

Serial no.	*Topic*	*Number of hours*
1.	Cell	2 hours
2.	Enzymes	5 hours
3	Chemistry and metabolism of carbohydrates	15 hours
4	Chemistry and metabolism of lipids	15 hours
5	Chemistry and metabolism of proteins	15 hours

6	Vitamins	10 hours
7	Nucleotide chemistry and metabolism	6 hours
8.	Integrated metabolism	3 hours
9	Bioenergetics	3 hours
10	Homeostatic mechanisms in the body (pH, water and electrolyte balance)	4 hours
11	Immunology	2 hours
12	Minerals	5 hours
13	Haem metabolism	6 hours
14	Function tests	4 hours
15	Molecular biology	12 hours
16.	Metabolism of xenobiotics	2 hours
17.	Oxidative stress	1 hour
18.	Nutrition	3 hours
19.	Importance of and ethical issues in laboratory medicine	2 hours
	Total	115 hours

TEACHING METHODOLOGY

Lectures, tutorials, small group discussions, integrated teaching modules, use of charts (paper-based clinical scenarios) for case discussions, practical exercises and demonstrations

THEORY SYLLABUS FOR FIRST YEAR M.B.B.S.

Note: The syllabus has been prepared keeping in mind the requirements of a doctor at the end of the MBBS course. It is also to emphasize that the teaching of Biochemistry needs to continue throughout the clinical phase of training of the MBBS students, when they will be in a better position to make correlations between derangements in biochemical processes and disease conditions. The content of the syllabus has been divided into 3 categories: "must know", "desirable to know" and "nice to know".

Total number of hours recommended: 112

	TOPIC	MUST KNOW	DESIRABLE TO KNOW	NICE TO KNOW	TEACHING HOURS RECOMMENDED
1.	**CELL**				**2 hours**
	Cell and cellular organelles	Basics of structure of a eukaryotic cell. Overview of cellular organelles and their functions (mitochondria, nucleus, ribosomes, proteasomes, lysosomes, endoplasmic reticulum and golgi apparatus)	Functions of peroxisomes. Markers of sub- cellular organelles		
2.	**ENZYMES**				**5 hours**
	Nomenclature and classification	Systematic and recommended nomenclature.	IUBMB classification of enzymes - main classes of enzymes only (names, definition, general reaction catalysed and one example for each class)		
	Properties of enzymes	Mechanism of action of an enzyme with regard to its effect on activation energy of a reaction. Concept of active site in enzymes. Specificity of enzymes: reaction and substrate specificity, with an example for each. Cofactors - metals and coenzymes (definition, examples of coenzymes) and	Lock and key and induced fit models of enzyme-substrate binding		

		examples of enzymes that require them			
	Factors that influence enzyme activity	Effect of pH (concept of optimal pH with examples). Effect of temperature (concept of optimal temperature). Effect of substrate concentration (Michaelis-Menten equation [no derivation of equation required], concept of K_m and V_{max}). Effects of enzyme and product concentration.			
	Inhibition of enzymes	Types of enzyme inhibition - competitive, non-competitive, suicide inhibition. Effects of competitive and non-competitive inhibition on Km and Vmax of the enzyme. Examples of commonly used drugs that act by competitive inhibition of enzymes. Examples of non-competitive enzyme inhibition – organophosphorus/cyanide poisoning			
	Isoenzymes	Definition and examples Clinical significance of elevated plasma levels of isoenzymes of creatine kinase (CK)	Isoenzymes of lactate dehydrogenase (LDH) and ALP		

	Diagnostic and therapeutic enzymes (clinically useful enzymes)	Aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), lactate dehydrogenase (LDH), creatine kinase (CK) and amylase as markers of various disease conditions. Plasma markers of myocardial infarction and liver damage. Examples of enzymes used in treatment and indications for their use.	Clinical utility of 5-nucleotidase and gamma-glutamyl transferase		
	Regulation of enzyme activity		Overview of mechanisms involved in regulating the activity of enzymes: allosteric activation and inhibition, covalent modifications (phosphorylation and dephosphorylation), induction and repression; concept of feedback inhibition Process of regulation of glycogen metabolism may be used as an example to explain the mechanisms of enzyme regulation, as listed above.		
3	**CHEMISTRY AND METABOLISM OF CARBOHYDRATES**				**15 hours**
	Chemistry of carbohydrates	Overview of classification of carbohydrates, with physiologically important examples and functions of each of these. Benedict's test for reducing sugars. Components of physiologically important disaccharides and polysaccharides.	Concept of deoxy and amino sugars and their functions. Heteropolysaccharides (heparin, hyaluronic acid, chondrointinsulphate, heparansulphate, dermatan sulphate) and their importance in the body.		

		Homopolysaccharides – starch, glycogen and cellulose			
	Digestion of carbohydrates	Examples of common dietary carbohydrates and the foods that they are present in. Enzymes involved in digestion of carbohydrates. Sources, sites and actions of the enzymes that digest carbohydrates. End products of digestion and their absorption. Rationale for the composition and use of oral rehydration solution (ORS) in the treatment of dehydration. Lactose intolerance. Importance of dietary fibre.			
	Glucose transporters	Types, functions, tissue specificity and physiological relevance			
	Glycolysis	Definition, importance, cellular site and pathway involved (with emphasis on the importance of the pathway, sites of utilization and generation of energy and irreversible reactions involved). Importance of aerobic and anaerobic forms of glycolysis. Energetics. Concept of substrate level phosphorylation. Overview of regulation of glycolysis.			

		Rapaport- Leubering shunt and its physiological importance. Concept of lactic acidosis and common causes and conditions in which it occurs. Importance of inhibition of enolase by fluoride in blood samples collected for glucose estimation.			
	Citric acid cycle/ Krebs' cycle / tricarboxylic acid (TCA) cycle	Pyruvate dehydrogenase as a link between glycolysis and Krebs' cycle (no details of reaction mechanism required). Definition, importance, cellular site, pathway (including intermediates and enzymes involved, but excluding details of reactions involved). Concept of anaplerosis, amphibolic nature of Krebs' cycle. Energetics.		Overview of regulation of pathway (no details required).	
	Pentose phosphate pathway (PPP)	Importance of pathway - ribose for nucleic acid synthesis and NADPH for synthesis of various lipids, maintenance of reduced form of iron in haemoglobin, reduced glutathione and its importance in maintaining red cell membrane integrity. Clinical relevance of the deficiency of glucose-6-phosphate dehydrogenase (G6PDH).	Definition, cellular site and overview of pathway, showing starting material and products (intermediates not required).		

	Glycogenesis	Physiological importance of glycogen in the body (including role of glycogen in the liver and in the muscle). Overview of pathway of synthesis (starting material, action of glycogen synthase and branching enzyme and the end product).	Glycogen storage disorders		
	Glycogenolysis	Physiological importance of glycogen breakdown in the body. Overview of pathway of breakdown in the liver and muscle (starting material, action of glycogen phosphorylase and debranching enzyme and products obtained).	Role of insulin and glucagon in reciprocal regulation of glycogenesis and glycogenolysis (details of reactions involved in regulation not required). Examples of glycogen storage diseases (Von Gierke's disease and McArdle's disease) may be used to illustrate functions of glycogen in the liver and muscle and the reasons for different manifestations of the diseases.		
	Gluconeogenesis	Definition, substrates used, physiological importance, sites in the body and in cell where the pathway occurs. Overview of pathway with key intermediates and enzymes. Importance of Cori's cycle and glucose-alanine cycle.	Concept of reciprocal regulation of glycolysis and gluconeogenesis (no details required). Role of insulin and glucagon in regulation.		
	Uronic acid pathway			Overview of pathway showing starting material (glucose) and product	

				(glucuronic acid). Importance of glucuronic acid in conjugation of bilirubin and drugs and synthesis of heteropolysaccharides. Essential pentosuria	
	Metabolism of galactose	Dietary sources of galactose. Overview of pathway by which galactose is metabolized (showing the sites of 3 main enzymes involved). Eventual fate of galactose in the body. Galactosemia (definition, causes, biochemical basis of clinical manifestations and rationale of treatment).			
	Metabolism of fructose	Dietary sources of fructose. Overview of pathway by which fructose is metabolized (showing entry into glycolysis and formation of triacylglycerol). Importance of fructose in seminal fluid.		Disorders of fructose metabolism	
	Minor pathways of carbohydrate metabolism	Polyol pathway and its importance in pathogenesis of complications of diabetes mellitus.			

	Regulation of blood glucose levels	Factors maintaining blood glucose levels - role of dietary carbohydrates, role of hormones (insulin, glucagon, glucocorticoids and catecholamines) and roles of liver and kidney.			
	Diabetes mellitus	Types and pathogenesis of diabetes mellitus. Concept of insulin resistance. Metabolic derangements and clinical features. Diagnostic criteria (ADA criteria). Concept of impaired fasting glucose and impaired glucose tolerance. Gestational diabetes – definition and diagnosis Acute and chronic complications of diabetes mellitus. Pathogenesis of diabetic ketoacidosis.		Pathogene-sis of chronic complicati-ons of diabetes mellitus.	
	Laboratory investigations in diabetes mellitus	Blood glucose estimations (fasting and post-prandial). Glycated haemoglobin (HbA1c). Urinalysis for detection of glucose, ketone bodies and proteins in urine. Detection and importance of microalbuminuria. Role of glucose tolerance test in diagnosis of diabetes mellitus.			

		Indications for and interpretation of results of glucose tolerance test (OGTT), including use in gestational diabetes mellitus (GDM). Serum lipid profile in diabetics.			
	Hypoglycemia	Definition, importance, causes, clinical manifestations.			
4	**CHEMISTRY AND METABOLISM OF LIPIDS**				**15 hours**
	General featuresof lipids	Definition of a lipid. Properties with regard to solubility and hydrophobicity. Important functions of lipids in the human body. Concept of importance of lipids in causation of disease (atherosclerosis with subsequent myocardial infarction and stroke; obesity, cholelithiasis, etc).			
	Classification of lipids	Major types of lipids in the body (classification into simple, complex and precursor or derived lipids). Relevant examples of each type and the importance of each type in the body.			
	Fatty acids	Concept of system of nomenclature (concept of systematicnames and symbols), with C and n numbering of fatty acids. Classification system based on chain length, degree of saturation (saturated and mono- and polyunsaturated fatty			

		acids), and nutritional requirement. Concept of saturated fatty acids in animal fat and unsaturated fatty acids in plant fats. Names of essential fatty acids and their functions. Importance of ω3 and ω6 fatty acids (dietary sources and their health benefits).			
	Simple lipids (fats)	Concept of importance of saturated and unsaturated fats in one's diet (including hydrogenation of oils). Basic concept of cis and trans forms of fatty acids and the health hazards of trans fats. Basic concept of mono, di- and triacylglycerols and where they are found in the body.			
	Derived lipids – steroids	Functions of cholesterol Health hazards associated with high blood levels of cholesterol.			
	Complex lipids	Lipoproteins - definition, general structure, types, components of each type, function of each type, role of apoproteins, importance in health and disease.	Phospholipids (definition, types, components, amphipathic nature, functions, clinically relevant examples) Importance of each type of phospholipid: phosphatidylcholine (including importance of surfactant in health and disease, concept of lecithin/sphingomye-lin [L/S] ratio),	Glycolipids - definition, types, components, functions, examples. Basic concepts of cerebrosides and gangliosides and importance of each type in the body. Basic concept	

			phosphatidylinositol and sphingomyelin Liposomes (definition, structure and importance)	of abnormalities in lipids in demyelinating diseases and sphingolipido-sis	
	Miscellaneous	Micelles (definition, structure and importance). Biological membranes (structure and importance).	Basic concepts of transport mechanisms across membranes		
	Metabolism of lipids				
	Digestion of lipids	Names of main lipids present in the diet. Enzymes responsible for digestion of lipids and their sources and sites of action. Role of bile in lipid digestion and absorption. End-products of lipid digestion. Process of absorption of lipids. Steatorrhoea. Salient features of formation, metabolism and physiological importance of chylomicrons.			
	Fate of fatty acids				
	Fatty acid oxidation	Importance of oxidation of fatty acids in the body. Types of oxidation of fatty acids. Beta-oxidation of even chain fatty acids (site, activation of a fatty acid, the role of carnitine, steps	End-products of beta- oxidation of odd chain fatty acids. Alpha oxidation of fatty acids.	Conditions where fatty acid oxidation is impaired.	

		involved and energetics of the process).			
	Biosynthesis of fatty acids (lipogenesis)	Conditions under which it occurs and sites involved. Starting material and end products of fatty acid synthesis. Source of acetyl CoA. Regulatory role of acetyl CoA carboxylase. Overall reaction catalyzed by fatty acid synthase (individual enzymes and reactions not required). Importance of NADPH in the pathway and its sources. Role of the nutritional state and insulin as factors that regulate synthesis of fatty acids			
	Metabolism in the adipose tissue		Metabolism in the adipose tissue with regard to lipogenesis and lipolysis (conditions where it occurs, and products obtained) and its regulation by hormones, including enzymes involved		
	Metabolism of ketone bodies	Names of the ketone bodies and their importance. Pathway of ketogenesis and utilization of ketone bodies and sites where these occur. Factors that favour ketone body formation. Causes and clinical importance of			

		ketoacidosis.			
	Metabolism of cholesterol	Functions of cholesterol. Sources of cholesterol in the body (dietary and endogenous). Importance of HMG CoA reductase in the regulation of biosynthesis of cholesterol. Importance of maintaining normal cholesterol levels in blood and ways to reduce blood cholesterol levels (including mechanism of action of statins and other lipid lowering agents). Bile acids (names, source and functions). Enterohepatic circulation of bile acids.	Cellular site of biosynthesis of cholesterol. Basic overview of biosynthesis of cholesterol (showing starting material, HMG CoA [HMG CoA synthase], mevalonate [action of HMG CoA reductase] and formation ofcholesterol, without showing any other intermediates). Overview of synthesis (including regulatory enzyme).	Role of lipids in formation of gall stones.	
	Metabolism of lipoproteins	Association of high levels of LDL with atherosclerosis. Anti-atherogenic effect of HDL	Brief overview of metabolism of VLDL, LDL and HDL (including reference values). Lipoprotein (a) Dyslipidemias – causes (with emphasis on secondary causes of dyslipidemia and familial hypercholesterol-emia) and consequences. Risk factors for atherosclerosis and coronary artery disease; prevention of coronary artery disease.		

			Overview of metabolic syndrome.		
	Eicosanoids	Names and functions of various eicosanoids. Role of aspirin as an anti-platelet agent.	Mechanism of action of NSAIDs and their effect as anti-inflammatory agents	Therapeutic uses of prostaglandins.	
	Phospholipids	Clinical relevance of lecithin-sphingomyelin (L/S) ratio in amniotic fluid	Biochemical defect and clinical features of Niemann-Pick's, Tay- Sach's and Gaucher's disease.	Sites of action of various phospholipases . Sphingolipido-sis other than the examples specified.	
	Miscellaneous	Role of liver in lipid metabolism. Fatty liver (causes, including role of lipotropic factors, and consequences).			
5	**CHEMISTRY AND METABOLISM OF PROTEINS**				**15 hours**
	Amino acids	Classification based on nutritional requirement and metabolic fates. Peptide bond formation by amino acids. Reaction with ninhydrin as a general reaction for all amino acids (details of reaction not required).	Classification of amino acids based on side chain		
	Peptides and proteins	Structural organization of proteins - primary, secondary, tertiary and quaternary structures. Denaturation of proteins – definition, agents causing denaturation and consequences (loss of biological activity of protein). Overview of structure-function relationship of haemoglobin, myoglobin and collagen.	Oxygen dissociation curve of haemoglobin; Bohr effect.		

		Hemoglobinopathies: sickle cell anaemia and thalassemia			
	Digestion and absorption	Mechanism of activation of enzymes involved in the digestion of proteins in the stomach and small intestine (conversion of zymogens to active proteases) – proteolytic enzymes of the gastric and pancreatic secretions. Role of gastric acid in protein digestion. Overview of amino acid absorption.	Disorders associated with amino acid absorption (cystinuria/ Hartnup's disease).		
	General pathways of amino acid catabolism	Overview and biochemical importance of the processes of transamination and oxidative deamination. Enzymes and coenzymes involved in the above processes.			
	Ammonia metabolism	Sources of ammonia in the body. Urea cycle - overview of reactions involved, including regulatory enzyme. Role of glutamine in detoxification of ammonia in the brain. Hepatic coma (hepatic encephalopathy);biochemical basis of clinical features Reference range for blood urea and blood urea nitrogen (BUN).	Overview of disorders of the urea cycle		

	Metabolism of individual amino acids	Functions of individual amino acids. Important specialized products from tyrosine – melanin, catecholamines, thyroid hormones. Formation of tyrosine from phenylalanine. Pathogenesis, clinical features, diagnosis and treatment of phenylketonuria.	Metabolism of methionine and homocysteine Roles of folic acid, vitamin B_{12} and pyridoxine in their metabolism. Role of homocysteine as a risk factor for cardiovascular diseases. Important specialized products from glycine (glutathione, creatine, creatinine, haem and purines) and tryptophan (serotonin, melatonin and niacin). Neurotransmitters derived from amino acids (glutamate – gamma-amino butyric acid [GABA], histidine [histamine], arginine [nitric oxide]).	Uncommon disorders of amino acid metabolism: maple syrup urine disease (MSUD), alkaptonuria, tyrosinemias, methymalonyl aciduria, disorders of glycine metabolism, etc. Importance of neonatal screening for inborn errors of amino acid metabolism. Principle of the technique of chromatography	
	Plasma proteins	Functions of albumin. Examples of specialized transport proteins present in plasma. Reference values of total proteins and albumin. Common clinical conditions in which plasma protein levels are abnormal and the reasons why these changes occur (malnutrition, cirrhosis of the liver, nephrotic syndrome, chronic renal failure, multiple myeloma). Importance of the albumin: globulin ratio (A: G ratio). ‘ Normal value for the A:G ratio	Classification of plasma proteins, based on electrophoretic mobility.	Principle of the technique of electrophoresis	

		and common clinical conditions in which the ratio is abnormal.			
6	**VITAMINS**				**10 hours**
	General properties of vitamins	Definition, classification, comparison of clinically relevant features of fat- and water-soluble vitamins. Concepts of hypo- and hypervitaminosis and recommended dietary allowances (RDA).			
	Fat-soluble vitamins				
	Vitamin A	Dietary sources. Various forms of vitamin A and their functions Precursor form. Biochemical functions. Role in Wald's visual cycle. RDA Deficiency – causes, manifestations and treatment.	Hypervitaminosis A		
	Vitamin D	Dietary sources of vitamin D. Synthesis in the body and conversion to calcitriol. Biochemical functions. Role in calcium absorption in small intestine, calcium homeostasis and bone mineralization. RDA Deficiency (rickets and osteomalacia) – causes, manifestations, biochemical findings in blood			
	Vitamin E	Dietary sources Role as an antioxidant. Relationship to action of glutathione peroxidase. RDA Deficiency leading to fragility of RBCs.			
	Vitamin K	Sources. RDA. Deficiency – causes, manifestations (including hemorrhagic disease of the new born).	Biochemical role in gamma carboxylation reactions. Vitamin K cycle. Basis of action of warfarin and other dicumarol derivatives.		

	Water-soluble vitamins				
	Thiamine	Dietary sources. Functions (coenzyme form, physiologically important reactions for which it is required). RDA Deficiency (beri-beri) – causes and manifestations Wernicke-Korsakoff syndrome - causes, clinical features			
	Riboflavin	Dietary sources. Functions (coenzyme forms, physiologically important reactions for which they are required). RDA Deficiency – causes and manifestations.			
	Niacin	Sources (including from tryptophan). Functions (coenzyme forms, examples of physiologically important reactions for which they are required). RDA Deficiency – causes and manifestations of pellagra.			
	Pyridoxine	Dietary sources. Functions (coenzyme form, physiologically important reactions for which they are required, including transamination and decarboxylation of amino acids). RDA. Deficiency – causes and manifestations. Rationale for supplementation in treatment of tuberculosis.			
	Pantothenic acid	Sources, functions and RDA			
	Biotin	Sources. Role in carboxylation reactions. Examples of important enzymes that require biotin.			
	Folic acid	Dietary sources. Functions (coenzyme forms, physiologically important reactions for which they are required).	Role of folic acid in one-carbon metabolism (one-carbon donor reactions (e.g., serine		

		RDA Relationship with vitamin B_{12} and concept of "folate trap". Deficiency – causes and manifestations (megaloblastic anemia). Importance of supplementation in peri-conceptual period. Folate antagonists (action of methotrexate, aminopterin and sulphonamides).	hydroxymethyl transferase), one-carbon acceptor reactions (methionine synthase, thymidylate synthase and de novo purine synthetic pathway).		
	Vitamin B_{12}	Dietary sources. Absorption and role of intrinsic factor of Castle. Functions (coenzyme forms, reactions for which they are required). Role in folic acid metabolism (concept of "folate trap" in B_{12} deficiency) RDA Deficiency – causes and manifestations (megaloblastic and pernicious anemia). Importance of combined B_{12} and folic acid administration in treatment of megaloblastic anemia.			
	Vitamin C	Dietary sources. Functions (in collagen synthesis, iron absorption and as an anti-oxidant). RDA. Deficiency – causes and manifestations of scurvy.		Role of vitamin C in the conversion of tyrosine to catecholamines, cholesterol to bile acids and in catabolism of tyrosine.	
	Vitamin-like substances Lipoic acid			Role in reactions involving pyruvate dehydrogenase and alpha-ketoglutarate dehydrogenase.	

7	**NUCLEOTIDE CHEMISTRY AND METABOLISM**				**6 hours**
	Nucleotide chemistry	Purine and pyrimidine bases found in DNA and RNA. Definition and types of	Examples of synthetic analogues of purine and pyrimidine bases and nucleosides used		

		nucleosides and nucleotides. Functions of physiologically important nucleotides.	as therapeutic agents (anti-cancer drugs, anti-viral drugs and allopurinol).		
	Nucleotide metabolism	Role of folic acid in purine synthesis. Overview of the pathway of degradation of purines to form uric acid, including role of xanthine oxidase. Hyperuricemia and gout (causes, clinical features, principles of treatment, including mechanism of action of allopurinol and probenecid).	Names of compounds required for purine and pyrimidine synthesis. Salvage pathway for purine bases and nucleosides. Lesch- Nyhan syndrome (cause and biochemical basis of clinical features). Mechanism of action of methotrexate and 5-flurouracil, as examples of drugs used in cancer chemotherapy.	Overview of the pathway of de novo synthesis of purine nucleotides (names of only starting material and end products - AMP and GMP - required). Overview of pathway of de novo synthesis of pyrimidine nucleotides, showing only starting material, rate-limiting enzyme and end products. Disorders of pyrimidine metabolism: orotic aciduria	
8.	**INTEGRATED METABOLISM**				**3 hours**
		Overview of metabolism in the fed and fasting states	Overview of metabolism in liver, brain and adipose tissue		
9	**BIOENERGETICS**				**3 hours**
	Role of ATP	Role of ATP as the "energy currency" of the cell.		Role of high energy phosphates in energy capture and transfer e.g., role of creatine phosphate in muscle.	

	The respiratory chain and oxidative phosphorylation	Sources of reducing equivalents in the cell (NADH and $FADH_2$). Role of mitochondria as the "power house" of the cell. Substrate level and oxidative phosphorylation. Schematic representation of the electron transport chain. Role of the respiratory chain as an electron transporter and a proton pump. Chemiosmotic theory of oxidative phosphorylation. Amount of ATP synthesized when NAD and FAD act as hydrogen acceptors.		Transport of cytosolic NADH into the mitochondria (mitochondrial shuttle systems). Examples of inhibitors of electron transport chain (carbon monoxide, cyanide) and uncouplers of oxidative phosphorylation (free fatty acids, thyroxine, thermogenin). Role of brown fat (non-shivering thermogenesis and role of uncoupling protein/ thermogenin). Overview of complex V (ATP synthase).	
10	**HOMEOSTATIC MECHANISMS IN THE BODY**				**4 hours**

	Acid base balance	Definitions of acid, base and buffer. Normal pH of body fluids and importance of maintaining normal pH Sources of hydrogen ions in the body. Mechanisms involved in regulation of pH Buffers of body fluids Henderson – Hasselbalch equation. Role of buffers (with emphasis on the bicarbonate buffer system) Role of the lungs and kidneys in maintaining acid- base balance. Simple acid-base disorders: Major causes and clinical features of: • Metabolic acidosis (including importance of anion gap) and alkalosis • Respiratory acidosis and alkalosis. Arterial blood gases (ABG) analysis and interpretation of results. Compensatory mechanisms in metabolic/respiratory acidosis/alkalosis.			

	Fluid and electrolyte balance	Distribution of water in various body compartments. Intra- and extracellular fluid composition (sodium and potassium) Blood volume and osmolality. Major causes and clinical features of dehydration. ***Sodium:*** Normal levels in the blood. Physiological functions. Regulation of sodium homeostasis (including the role of renin-angiotensin-aldosterone system). Major causes, clinical features of hyponatremia and hypernatremia ***Potassium:*** Normal levels in the blood. Physiological functions. Regulation of potassium homeostasis. Major causes and clinical features of hypokalemiaandhyperkalemia.	Regulation of osmolality– role of anti-diuretic hormone (ADH).		
11	**IMMUNOLOGY**				**2 hours**
	Immunology	Introduction to immunoglobulins Types, properties and functions of different classes of immunoglobulins. Multiple myeloma – biochemical abnormalities and laboratory diagnosis.			
12	**MINERALS**				**5 hours**
		Concept of macro and micro minerals and examples. Sources and daily requirement.			
	CALCIUM	Normal blood levels. Functions of calcium. Role of vitamin D in absorption of calcium. Regulation - role of parathyroid hormone (PTH), calcitonin and			

		vitamin D in calcium homeostasis. Important causes, clinical features, laboratory diagnosis of hypocalcemia and hypercalcemia Osteoporosis and osteomalacia - major causes, clinical features.			
	Iron	Sources and daily requirement. Distribution of iron in the body. Functions of iron. Absorption of dietary iron in the duodenum - overview of role of divalent metal transporter-1 (DMT-1), duodenal cytochrome b (dcytb), hephaestin, ferroportin. Storage and transport (role of ferritin and transferrin). Causes, clinical features of iron deficiency anemia.	Iron overload conditions, e.g., hereditary haemochromatosis.		
	Copper	Biochemical functions of copper. Role of ceruloplasmin. Genetic basis, clinical features of Wilson's disease.	Biochemical basis of Menke's disease		
	Zinc	Functions of zinc. Causes and clinical features of zinc deficiency.			
	Magnesium and manganese: **Iodine:** **Flouride:** **Selenium**	 Sources and daily requirement of iodine. Functions of iodine. Causes and clinical features of iodine deficiency. Sources and daily requirement of fluoride. Functions of fluoride. Causes and clinical features of fluorosis. Functions of selenium	Functions of magnesium and manganese.		
13	**HAEM METABOLISM**				**6 hours**
	Heme synthesis	Importance of haem (heme-containing proteins – hemoglobin, myoglobin, cytochromes).	Heme synthesis and its regulation in the liver and bone marrow.		

		Porphyrias: Definition, biochemical basis of clinical features of porphyrias (neurological features and photosensitivity). Acquired porphyria: lead poisoning.			
	Heme degradation	Degradation of haem and fate of bilirubin. Hyperbilirubinemia – causes and role of laboratory investigations in the differential diagnosis of jaundice. Jaundice in the newborn	Congenital disorders of conjugation and excretion of bilirubin – Crigler-Najjar syndrome, Dubin-Johnson syndrome, Gilbert's syndrome and Rotor's syndrome.		
14	**FUNCTION TESTS:**				**4 hours**
	Renal function test:	Functions of the kidney Clinical importance of blood urea and serum creatinine levels in renal disease.			
		Estimation of GFR: Creatinine clearance and its importance. Nephrotic syndrome – major clinical features and laboratory diagnosis.	Proteinuria – types (glomerular, tubular and overflow proteinuria) and characteristic proteins present in urine in each type. Microalbuminuria and its importance. Concepts of tests to assess tubular function – measurement of plasma and urine osmolality	Renal tubular acidosis. Lab investigations in acute kidney injury and chronic kidney disease Laboratory tests to diagnose pre-renal, renal and post- renal causes of acute renal failure.	
	Liver function tests	Functions of the liver. Major causes of liver dysfunction. Tests done to assess liver			

		function in clinical practice: 1. Tests to assess ability to detoxify and excrete substances: conjugated and unconjugated bilirubin (van den Bergh's test), blood ammonia levels. 2. Tests to assess biosynthetic functions: total protein and serum albumin levels, prothrombin time 3. Markers of liver injury: alanine transaminase (ALT) and aspartate transaminase (AST) 4. Marker of cholestasis: alkaline phosphatase (ALP). Differential diagnosis of jaundice, based on liver function tests.			

	Thyroid function test:	Regulation of secretion of thyroid hormones.		Importance of estimation of TSH in assessment of thyroid function. Measurement of total and free thyroxine levels. Role of TSH and free thyroxine in laboratory diagnosis of hypothyroidism and hyperthyroidism	
	Adrenal function tests			Hormones produced by the adrenal cortex and medulla. Regulation of secretion of adrenocortical	

				hormones. Basic tests done for the laboratory diagnosis of adrenal hypofunction and hyperfunction (serum and urine cortisol)	
15	**MOLECULAR BIOLOGY**				**12 hours**
	The cell cycle, DNA and RNA structure	Watson and Crick model of DNA structure (including simple diagrammatic representation of the salient features of DNA structure). Types and functions of different types of RNA. Overview of organization of DNA in a chromosome.		Overview of the cell cycle Differences between nuclear and mitochondrial DNA.	
	DNA replication and repair	Overview of the process of DNA replication in eukaryotes Roles of DNA polymerase, helicase, primase, topoisomerase and DNA ligase Diagrammatic representation of the events at the replication fork Okazaki fragments and its importance in replication.	Inhibitors of DNA replication as anti-cancer drugs. Overview of role of major DNA repair mechanisms – mismatch repair, base excision repair, nucleotide excision repair and double strand break repair. Diseases associated with abnormalities of DNA repair systems – xeroderma Pigmentosa and hereditary non-polyposis colon cancer (HNPCC).	Importance of telomeres and telomerase	

	Transcription	Structure of a gene - concepts of exons and introns, promoter, enhancers/repressors and response elements. Overview of the process of transcription in eukaryotes – initiation, elongation and termination Post-transcriptional processing – capping, tailing and splicing.			
	Translation and genetic code:	Genetic code - definition. Characteristics of the genetic code – universal, unambiguous, degenerate, without punctuation (continuous/commaless). Basis of degeneracy of the genetic code (wobble hypothesis). Components of eukaryotic ribosomes. Structure of tRNA (diagram of clover leaf model of tRNA structure) and its function in protein synthesis. Function of aminoacyl tRNA synthase.	Overview of the process of translation – initiation, elongation and termination Inhibition of prokaryotic translation by antibiotics. Post-translational modifications – examples.		
	Mutations and regulation of gene expression	**Mutations:** Definition. Mutagens- examples of physical, chemical and biological mutagens. Types of mutations. point mutation (deletion, insertion, substitution – transition and transversion, frame shift mutation, • missense mutation, nonsense mutation and silent mutation • chromosomal mutations (deletion, inversion and	Relationship of mutations with specific diseases – eg, sickle cell anemia and chronic myeloid leukemia.	Prokaryotes: The operon concept in prokaryotes (using Lac operon as an example). Eukaryotes: Overview of regulation of initiation of eukaryotic transcription: role of general and gene-specific transcription	

		translocation).		factors	
	Recombinant DNA technology and techniques in molecular biology:	Importance and applications of recombinant DNA technology Importance and applications of Polymerase chain reaction (PCR) •	Restriction endonucleases. Vectors for cloning – plasmids and phages. Genomic and cDNA libraries. Principles and applications of techniques in molecular biology: (Southern, northern and western blotting, restriction fragment length polymorphism [RFLP]) Applications of recombinant DNA technology in medicine. General principles of production of therapeutic proteins, e.g., insulin Gene therapy Diagnosis of genetic diseases and genetic counseling Forensic investigation	Human genome project DNA fingerprinting DNA sequencing Microarrays Fluorescent in-situ hybridization (FISH) DNA vaccines Transgenic animals	

16.	**METABOLISM OF XENOBIOTICS**				**2 hours**
		Xenobiotics- definition and examples Biochemical importance of the two phases of xenobiotic metabolism Conjugation reactions: • Biochemical role of conjugation reactions (with suitable, clinically relevant examples) - glucuronidation,	The cytochrome P450 enzyme system • Functions • Properties (especially induction by drugs) Overview of metabolism of alcohol. Health hazards associated with alcohol consumption.		

		sulfation, conjugation with glutathione, acetylation.	Metabolic alterations induced by alcohol metabolism.		
17.	**OXIDATIVE STRESS**				**1 hour**
				Concepts of reactive oxygen species (ROS), free radicals and oxidative stress and antioxidants. Mechanisms of generation of reactive oxygen species (ROS) in cells. Role of antioxidants – vitamin E and glutathione. Role of antioxidant enzymes – glutathione peroxidase, superoxide dismutase	
18.	**NUTRITION**				**3 hours**
		Importance of various macro and micro-nutrients in diet. Components and importance of each type in diet. Concept of balanced diet and glycemic index of food. Importance of dietary fibre. Basal metabolic rate. Specific dynamic action (thermogenic effect of food) and respiratory quotient Common sources of saturated, polyunsaturated and monounsaturated fats in diet and	Calorific value of various macronutrients. Principles of calculation of energy requirements of a person.	Dietary protein quality – biological value and net protein utilization. Concept of nitrogen balance.	

		their impact on health. Importance of trans fats Concept of limiting amino acids and supplementary action of dietary proteins. Protein-energy malnutrition (PEM): marasmus and kwashiorkor - causes and main differences. Obesity (including calculation and interpretation of body mass index [BMI]; health risks associated with obesity)			
19.	**IMPORTANCE OF LABORATORY MEDICINE ETHICAL ISSUES IN LABORATORY MEDICINE**				**2 hours**
		The concept that laboratory testing should respect principles of medical ethics (non-maleficence, beneficence, patient autonomy, informed consent, respect for patient, etc)		Ensuring quality and integrity of laboratory services, role and responsibilities when participating in clinical research, optimal use of resources, confidentiality of laboratory results, use of results from screening and testing programs, etc.	

PRACTICAL SYLLABUS

Estimation of important biochemical analytes in blood (glucose, creatinine, urea, uric acid and total protein)

Identification of abnormal constituents in urine; interpretation of the findings and correlation of the findings with pathological states
Tests (including dipstick tests) to detect abnormal constituents in urine include heat coagulation test, sulphosalicylic acid test and Heller's test for proteins, Benedict's test for reducing sugar, benzidine test for blood, Rothera's test for ketone bodies, Hay's test for bile salts and Fouchet's test for bile pigments
Interpretation of laboratory results in the context of a patient's presenting complaints.

Principles of spectrophotometry (including the Beer-Lambert Law)

Principles of electrophoresis (with specific reference to separation of serum proteins) and paper chromatography

Practical classes: Total: 125 hours

Serial no.	***Topic***	***Number of hours***
1.	Estimations of biochemical analytes	40
2.	Qualitative tests	20
3	Demonstrations	15
4	Charts and integrated teaching	25
5	Small group discussions/tutorials	25
	Total	125 hours

INTERNAL ASSESSMENT : (40 marks)

(Theory 20 marks + Practical 15 marks + Record 5 marks)

Theory - To access knowledge.

Practical - To access skill.

Vivo voce - To access communication.

Internal Assessment test will be conducted on 3rd Saturday.

Given below is a division of topics for periodic assessments.

Unit I - September

Cell and chemistry carbohydrates, lipids and proteins

Unit II - October

Enzymes and vitamins

Unit III - December

Metabolism of carbohydrates and biological oxidation and electron transport chain

Unit IV - January

Metabolism of lipids

Unit V - February

Metabolism ofproteins and metabolism of heme

Unit VI - April

Organ function tests, acid–base homeostasis and associated disorders, water and electrolyte balance and associated disorders

Unit VII - May

Nutrition, minerals and metabolism of xenobiotics

Unit VIII - June

Chemistry and metabolism of nucleotides and molecular biology

Model exam -1st week of July

RECOMMENDED TEXTBOOKS

The most recent editions of the following books are suggested.

1. Text book of Biochemistry for Medical Students by DM Vasudevan, SreeKumari S and Kannan Vaidyanathan
2. Medical Biochemistry by AR Aroor
3. Principles and Applications of Biochemistry in Medicine by Rafi
4. Biochemistry – Lippincott's Illustrated Reviews

5. Harpers Illustrated Biochemistry

Theory Examination - Pattern of Question Paper I and II

Essays	1 X 10 Marks	=	10 Marks
Brief Answers	5 X 4 Marks	=	20 Marks
Short Answers	10 X 2 Marks	=	20 Marks
	TOTAL		**50 Marks**

PRACTICAL EXAMINATION (Total: 40 marks)

1. A short paper-based clinical scenario will be given to each student. The student will be asked to estimate one of the relevant analytes (glucose, creatinine, urea, uric acid and total protein) in a serum sample provided and asked to interpret this in the context of the given clinical scenario. The clinical relevance and metabolism of the analytes estimated will be discussed. (12 marks)

2. Clinical case histories and laboratory results with 3 clinical charts
Students will be expected to interpret laboratory results supplied, with reference to the history of the patient and to make a provisional diagnosis. (12 marks)

3. Identification of abnormal constituents in urine
Students will be expected to carry out of relevant tests and interpret and discuss their results (12 marks)

4. Objective structured practical exercise (OSPE) (2 stations x 2 marks each = 4 marks)
Only performance stations may be kept. Suggested questions for OSPE are given below.

a. Perform a test to identify the presence of bile salts in the given sample.
b. Perform a test to demonstrate the presence of areducing sugar /protein/ ketone bodies in the given sample.
c. Demonstrate the presence of heat-coagulable proteins in the given sample.

VIVA VOCE: 20 marks
The viva voce is meant to assess understanding, comprehension and applications of the subject and not rote memory.

The topics in Biochemistry will be divided into 4, as detailed below, for the viva voce. Each examiner will assess the students in one of these areas and will award marks out of 5.

Serial no.	***Topics***	***Marks***
1.	Carbohydrates, cell, biological oxidation and vitamins	5 marks
2.	Proteins, enzymes, plasma proteins, function tests, metabolism of xenobiotics, basics of immunology	5 marks
3	Lipids, minerals, nutrition, metabolism of haem, oxidative stress	5 marks
4	Nucleic acids, molecular biology, water and electrolyte balance, acid- base balance	5 marks

5		
	Total marks	20 marks

RECORD BOOKS

It is suggested that students be issued a printed Biochemistry Record Notebook in which they are expected to write only the observations, inferences and calculations of experiments they do in the practical classes conducted.

INTEGRATED TEACHING:

Suggested topics that may be used for integrated teaching:

Clinically important enzymes, plasma markers of myocardial, infarction and liver and renal damage, rationale of oral rehydration solutions, lactose intolerance, galactosemia, diabetes mellitus, ketoacidosis, dyslipidemias, atherosclerosis and coronary artery disease, liver disease, haemoglobinopathies, phenylketonuria, hyperuricemia and gout, deficiencies of vitamins A, D, K, B_{12}, thiamine, pyridoxine and folic acid, acid-base and electrolyte disorders, disorders of calcium homeostasis, iron deficiency anemia, iodine deficiency, disorders of bilirubin metabolism, renal and thyroid function tests, protein-energy malnutrition.

RECORD

Record should be followed as recommended by the University.