

SYLLABUS, ToS & OSPE

M.B.B.S.

FIRST PROFESSIONAL

PART-II

BIOCHEMISTRY

SYLLABUS MBBS 1st PROF. PART-II **BIOCHEMISTRY**

Teaching objectives (Biochemistry Part-II):

The general objectives and overall aim of the teaching course include:

1. To teach sufficient biochemistry to give the student a basic understanding of life processes at the molecular level.
2. To provide an understanding of the normal biochemical processes in the human body in which the function of the various organs and tissues are integrated.
3. To comprehend the principles of metabolic integration that would contribute to the students' understanding of the biochemical basis of various disease processes.
4. To familiarize the students with laboratory instruments / equipment used in biochemistry laboratory.
5. To undertake practical classes that would familiarize the student with the various chemical methods which are used in the diagnosis of disease.
6. To familiarize the students with modern biochemical techniques and their uses in the diagnosis of diseases especially genetic diseases.

Learning objectives (Part-II)

At the end of the Part-II course, the student should be able to demonstrate his knowledge and understanding on the subject with following learning objectives

1. To be familiar with the homeostatic mechanisms through the concepts of inter-regulation of carbohydrates, lipids and protein metabolism and its relation to hormone actions in the human body.
2. Once these basic concepts are understood, it will be straightforward to understand how alterations in the basic processes can lead to a disease state.
3. To have understanding and knowledge about many pathological situations where these can be related to biochemical defects, and to have some experience of biochemical techniques in order to understand the practical/clinical problems in biochemistry.
4. To develop skills as a self-directed learner, recognize continuing educational needs; use appropriate learning resources and critically analyze relevant literature in order to have a comprehensive understanding and knowledge of biochemistry.
5. To learn and understand the basic biochemical processes taking place in the body, since these underline an understanding of normal and abnormal human metabolism. In order to accomplish this, the student should learn how large molecules are synthesized and used (DNA, RNA, and proteins), and how energy is generated, stored, and retrieved (metabolism).

6. To describe digestion assimilation of nutrients & consequences of malnutrition. Integrate the various aspects of metabolism & their regulatory pathways.
7. To explain biochemical basis of inherited disorders with their associated sequelae.
8. To outline the molecular mechanisms of gene expression, the principles of genetic engineering & their applications in medicine.
9. To outline the biochemical basis of cancer & carcinogenesis.
10. To make use of conventional techniques/instruments to perform biochemical analysis relevant to clinical screening & diagnosis. Familiarize with principles of various conventional & specialized lab investigations & instrumentation analysis & interpretation of a given data.
11. Applying basic knowledge of protein synthesis, post translational modification and targeting to its cellular destination.
12. Principles of various conventional and specialized laboratory investigations and instrumentation, analysis and interpretation of a given data; the ability to suggest experiments to support theoretical concepts and clinical diagnosis

1- Bioenergetics and Biologic Oxidation

- a) Endergonic and exergonic reactions, free energy, free energy change, ATP and other compounds as carriers of energy
- b) Electron transport chain: Components and organization of electron transport chain (ETC)
- c) Reactions of electron transport chain, redox potential, methods of electron transfer among the components of electron transport chain, and energy release during electron transport
- d) Oxidative phosphorylation: ATP synthesis in ETC, inhibitors and uncouplers of oxidative phosphorylation, and chemiosmotic hypothesis of oxidative phosphorylation.

2- Metabolism of Carbohydrates

- a) Glycolysis
 - Reactions of aerobic and anaerobic glycolysis occurring in RBCs and other tissues
 - Biomedical significance and energy yield of aerobic and anaerobic glycolysis and its significance, and substrate-level phosphorylation
 - Regulation of glycolytic pathway
 - Metabolic fates of pyruvate
 - Lactic acidosis; genetic deficiency of pyruvate kinase and pyruvate dehydrogenase
- b) Tricarboxylic acid (TCA) cycle
 - Reactions of TCA cycle and their regulation along with energy yield.

- Importance of TCA cycle and its amphibolic role
- c) Gluconeogenesis
- Reactions of gluconeogenesis using pyruvate and glycerol as precursors, and regulation of gluconeogenesis.
 - Important gluconeogenic precursors: Entrance of amino acids, intermediates of TCA cycle, glycerol, and other compounds as gluconeogenic precursors.
 - Biomedical significance of gluconeogenesis: Role of gluconeogenesis in plasma glucose level regulation, and the Cori cycle, and glucose-alanine cycle.
- d) Glycogen metabolism
- Synthesis and importance of UDP glucose
 - Reactions of glycogenesis and glycogenolysis
 - Regulation of glycogenic synthase and glycogen phosphorylase
 - Importance of allosteric regulation of glycogen phosphorylase 'a' (a plasma glucose sensor) by plasma glucose
 - Disorders of glycogen metabolism (glycogen storage diseases)
- e) The hexose monophosphate pathway and other pathways of hexose metabolism
- Hexose monophosphate (HMP) pathway: Reactions of oxidative and non-oxidative phases of HMP pathway, importance of HMP pathway along with uses of NADPH, and glucose 6-phosphate dehydrogenase deficiency.
 - Reactions of uronic acid pathway along with its biologic importance.
 - Metabolism of fructose: Metabolic fate of fructose in human body, sorbitol metabolism along with effect of hyperglycemia on sorbitol metabolism, essential fructosuria and hereditary fructose intolerance.
 - Metabolism of galactose: Metabolic fate of galactose in body and synthesis of lactose; and disorders of galactose metabolism (galactokinase deficiency and classic galactosemia).
 - Metabolism of ethanol
- f) Regulation of blood glucose level
- Regulation of plasma glucose hormonally (insulin, glucagon, growth hormone, epinephrine, and cortisol) and non-hormonally, and the role of various metabolic pathways in blood glucose level regulation
 - Hypoglycemia and hyperglycemia: An overview of hypoglycemia and hyperglycemia, their important causes, and clinical manifestations.
 - Diabetes mellitus: Types of diabetes mellitus along with its clinical manifestations, metabolic changes in type 1 and type 2 diabetes mellitus, and diagnosis of diabetes mellitus.

3- Metabolism of lipids

- a) de novo synthesis of fatty acids: Production of cytosolic acetyl CoA, fatty acid synthase multienzyme complex, reactions of cytosolic fatty acid synthesis, elongation of fatty acid chain, synthesis of polyunsaturated fatty acid, and regulation of fatty acid synthesis.
- b) Synthesis and storage of triacylglycerols in body.
- c) Mobilization of stored triacylglycerols along with its regulation
- d) Oxidation of fatty acids: Activation of fatty acid, translocation of fatty acyl CoA into mitochondrial matrix, reactions of β -oxidation of saturated and unsaturated fatty acids, energy yield of β -oxidation, fate of acetyl CoA, and other types of fatty acid oxidation (alpha-oxidation, omega-oxidation, and oxidation of odd-carbon fatty acids).
- e) Synthesis and utilization of ketone bodies: Reactions of hepatic ketogenesis, and utilization of ketone bodies by extrahepatic tissues.
- f) Ketoacidosis and regulation of ketogenesis.
- g) Synthesis of eicosanoids, their regulation and functions along with their biomedical importance.
- h) Metabolism of phospholipids and sphingolipids: Synthesis of phospholipids (phosphatidylcholine and phosphatidylethanolamine), synthesis of glycerol ether phospholipids (cardiolipin and platelet activating factor), degradation of phospholipids, deficiency of lung surfactant, metabolism of glycolipids, biosynthesis of ceramide, sphingomyelin, and gangliosides, and degradation of sphingolipids along with sphingolipidoses.
- i) Cholesterol metabolism: Reactions and regulation of cholesterol biosynthesis, and fate and functions of cholesterol in body.
- j) Biosynthesis and fate of bile acids and their significance in health and disease.
- k) Plasma lipoproteins: Synthesis, transport, and fate of chylomicrons, VLDL, IDL, LDL, and HDL; disorders associated with impairment of lipoprotein metabolism, and atherogenic effect of oxidized LDL.
- l) Biochemical defects leading to fatty liver

4- Metabolism of Proteins and Amino Acids

- a) An overview of protein turnover in human body; nitrogen balance (positive and negative).
- b) Inter-organ amino acid exchange in normal post-absorptive state
- c) Degradation of amino acids; removal of nitrogen from amino acids by transamination and deamination; sources of ammonia in body; transport of ammonia, ammonia toxicity; fate of ammonia in body, reactions and regulation of the urea cycle along with metabolic disorders of the urea cycle.
- d) An overview of amphibolic intermediates formed from the carbon skeleton of amino acids.

- e) Concept of glucogenic and ketogenic amino acids; an outline of the metabolism of individual amino acids like glycine, cysteine, arginine, proline, phenylalanine, tyrosine, histidine, tryptophan, methionine amino acids; causes and salient features of important metabolic defects in amino acid metabolism like phenylketonuria, maple syrup urine disease (MSUD), histidinemia, alkaptonuria, cystathioninuria, homocystinuria, hyperprolinemia, cystinuria, cystinosis, tyrosinemias, and albinism.
- f) Metabolism of epinephrine and norepinephrine, creatine, creatinine, histamine, gamma-aminobutyrate, serotonin, melatonin, and melanin

5- Integration and Regulation of Metabolic Pathways

- a) Fed-fast cycle and starvation.
- b) Basic concepts of intermediary metabolism, introduction of anabolic and catabolic pathways.
- c) An overview of regulation and integration of various metabolic pathways (role of liver, heart, brain, skeletal muscle and adipose tissue).

6- Metabolism of Nucleotides

- a) *de novo* Synthesis of purines and pyrimidines; the salvage pathways of nucleotide synthesis; degradation of purine and pyrimidine nucleotides
- b) Disorders associated with purine nucleotide metabolism like adenosine deaminase deficiency, purine nucleoside phosphorylase deficiency, and hyperuricemia
- c) Natural and synthetic derivatives of purines and pyrimidines and their role in health and disease.

7- Biochemical Genetics (Informational Flow in the Cell)

- a) The structural basis of cellular information
- b) Organization of DNA: chromosomes, Karyotyping.
- c) Replication of DNA: Reactions of DNA replication in eukaryotes and prokaryotes; types of damage to DNA and DNA repair; mutations
- d) Transcription (DNA-dependent RNA synthesis): Steps in the transcription of eukaryotic and prokaryotic genes; post-transcriptional modifications (processing) of RNA; reverse transcription in retroviruses and its relation to cancers and AIDS.
- e) Translation (protein synthesis): The genetic code; components required for protein synthesis, composition of eukaryotic and prokaryotic ribosomes; steps of protein synthesis; post-translational modifications of polypeptide chains; protein targeting.
- f) Regulation of gene expression in prokaryotes and eukaryotes

- g) Molecular biology techniques: Basic information and biomedical importance of molecular biology techniques; DNA extraction; recombinant DNA technology; DNA cloning; polymerase chain reaction (PCR); hybridization; blotting techniques.
- h) Oncogenes and their role in carcinogenesis; mechanisms of activation of proto-oncogenes; mechanism of action of oncogenes; tumour suppressor genes and oncogenic viruses.
- i) Genetic basis of disease
- j) Important tumor markers and their clinical significance (Carcinoembryonic Antigen, Alpha fetoprotein, human chorionic gonadotropin, calcitonin and prostatic acid phosphatase).

8- Biochemistry of Endocrine System

- a) An overview of endocrine system; classification of hormones based on their mechanism of action and chemical nature; mechanisms of action of each class of hormone; general characteristics of various types of hormone receptors; types and actions of various kinds of G-proteins in mediating the actions of hormones; signal transduction pathways of various hormones; types and role of various kinds of second messengers
- b) Pituitary and hypothalamic hormones: Structure, biosynthesis, secretion, transport, regulation, catabolism, and biologic actions of all hypothalamic and pituitary hormones; disorders associated with hyper- and hypo-activities of these hormones such as growth hormone deficiency (dwarfism), gigantism, acromegaly, Cushing's syndrome, Addison's disease, Diabetes insipidus, and the inappropriate secretion of ADH (SIADH).
- c) Thyroid Hormones: Structure, biosynthesis, secretion, transport, regulation, catabolism, and biologic actions of all thyroid hormones; disorders associated with hyper- and hypo-activities of these hormones like goiter, hypothyroidism, hyperthyroidism, Graves' disease.
- d) Calcium Regulating Hormones: Structure, biosynthesis, secretion, transport, regulation, catabolism, and biologic actions of parathyroid hormone; disorders associated with hyper- and hypo-activities of these hormones like; role of parathyroid hormone, calcitriol, and calcitonin in calcium homeostasis; hypoparathyroidism, hyperparathyroidism (primary, secondary, and tertiary), pseudohypoparathyroidism, rickets, and osteomalacia).
- e) Adrenal Cortical Hormones: Structure, biosynthesis, secretion, transport, regulation, catabolism, and biologic actions of all adrenal cortical hormones; disorders associated with hyper- and hypo-activities of these hormones like Cushing's disease / syndrome, secondary adrenal deficiency, Addison's disease, primary aldosteronism and secondary aldosteronism.
- f) Adrenal Medullary Hormones: Structure, biosynthesis, secretion, transport, regulation, catabolism, and biologic actions of all adrenal medullary hormones; and associated disorders like pheochromocytoma
- g) Male and Female Gonadal Hormones: Structure, biosynthesis, secretion, transport, regulation, catabolism, and biologic actions of all male and female

gonadal hormones; disorders associated with hyper- and hypo-activities of these hormones like; hypergonadism and hypogonadism in males and females.

- h) Hormones of Pancreas: Structure, biosynthesis, secretion, transport, regulation, catabolism, and biologic actions of all pancreatic hormones (insulin, glucagon, somatostatin and pancreatic polypeptide); disorders associated with hyper- and hypo-activities of these hormones like; pathophysiology of insulin deficiency and diabetes mellitus

9- Biochemistry of Digestive Tract

- a) Introduction, chemical composition, and secretion and regulation of various digestive juices of GIT such as saliva, gastric juice & HCl, pancreatic juice, bile, and succus entericus
- b) Hydrolysis (digestion) of carbohydrates, lipids, proteins, and nucleic acids in gastrointestinal tract
- c) Absorption of carbohydrates, lipids and amino acids.
- d) Disease states associated with GIT disorders like achlorhydria, peptic ulcers, lactose intolerance, cholelithiasis and pernicious anemia, cystic fibrosis and celiac disease.
- e) Site of synthesis and major actions of gastrointestinal hormones like gastrin, cholecystokinin (CCK), secretin, gastric inhibitory peptide (GIP), vasoactive intestinal polypeptide (VIP), motilin, enkephalins, substance P, neurotensin, and enteroglucagon.

10- Metabolism of Xenobiotics

- a) Definition and classes of important xenobiotics of medical relevance, their phases of metabolism and clinical significance (Cytochrome P450: Cytochrome P450 hydroxylase cycle in microsomes; role of cytochrome P450 in phase I metabolism of xenobiotics; induction of cytochrome P450)
- b) Phase II metabolism of xenobiotics; types of phase II reactions;
- c) Responses to xenobiotics including pharmacologic, toxic, immunologic and carcinogenic effects

11- Water & electrolyte balance; acid-base regulation

- a) Biochemical mechanisms to regulate water and electrolyte balance in body: Fluid compartments of the body; gain and loss of body water; regulation of body water balance, effect of pure water deprivation, water excess or water intoxication; and electrolytes of body fluids (sodium, potassium, magnesium and chloride).
- b) Body buffer systems, role of lung and kidney in maintenance of acid-base balance.

- c) Acid-base disturbance in the body like respiratory and metabolic acidosis (lactic acidosis and ketoacidosis); respiratory and metabolic alkalosis; concept of anion gap, base excess and base deficit.
- d) Clinical interpretation of laboratory report of arterial blood gases.

Laboratory Experiments

- The introduction of techniques and instrumentation of clinical biochemistry like centrifugation, spectrophotometry (visible, UV, infra red and atomic absorption), pH metry, chromatography, electrophoresis, enzyme-linked immunosorbent assay (ELISA), micropipetting, flame photometry and ion selective electrode (ISE) technique
- Collection, preservation, and storage of blood sample
- Estimation of various substances in blood and other biological fluids, like glucose, creatinine, urea, protein, albumin, uric acid, and calcium, total cholesterol; HDL cholesterol, and triacylglycerols; demonstration of creatinine clearance; and oral glucose tolerance test (OGTT)
- Determination of plasma enzyme activities of alanine aminotransferase (ALT), aspartate aminotransferase (AST), amylase, creatine phosphokinase (CK), alkaline phosphatase (ALP), and lactate dehydrogenase (LDH)
- Clinical interpretation of common laboratory values of the compounds and enzymes as listed above
- Determination of amino acids in urine by paper chromatography (demonstration)

RECOMMENDED BOOKS

- Harper's Illustrated Biochemistry by Murrar RK, Granner DK and Rodwell VW, latest edition, McGraw Hill
- Lippincott's Illustrated Reviews: Biochemistry by Harvey R and Ferrier D, Latest edition, published by Lippincott Williams & Wilkins
- Marks' Basic Medical Biochemistry – A Clinical Approach, by Smith C, Marks AD, and Lieberman M. Latest edition, published by Lippincott Williams & Wilkins
- Practicals and Viva in Medical Biochemistry by Dandekar SP and Rane SA, latest edition, published by Elsevier.

REFERENCE BOOKS

- Textbook of Biochemistry with Clinical Correlations by Devlin TM, latest edition, published by Wiley-Liss
- Biochemistry by Berg JM, Tymoczko JL, and Stryer L, latest edition, published by W.H. Freeman and Company
- Lehninger Principles of Biochemistry by David L Nelson and Michael M. Cox
- Tietz Textbook of Clinical Chemistry by Burtis CA and Ashwood ER published by Saunders.
- Fundamentals of Biochemistry Life at Molecular Level by Donald Voet, Judith G Voet and Charlotte W. Pratt
- Biochemistry by Berg JM, Tymoczko JL, and Stryer L, latest edition, published by W.H. Freeman and Company
- Tietz Textbook of Clinical Chemistry by Burtis CA and Ashwood ER published by Saunders.
- Clinical Chemistry and Metabolic Medicine by Martin A. Crook, latest edition, Edward Arnold (Publishers) Ltd
- Practicals and Viva in Medical Biochemistry by Dandekar SP and Rane SA, latest edition, published by Elsevier.

Table of Specifications for Biochemistry Theory Paper MBBS First Professional Examination (Part-II)

CONTENTS	SEQs	MCQs
1. Bioenergetics and biologic oxidation	0.5	2
2. Carbohydrate Metabolism	1.5	6
3. Lipid metabolism	1.5	6
4. Metabolism of proteins and amino acids	1.5	6
5. Metabolism of purines, pyrimidines, and nucleotides	0.5	2
6. Replication of DNA, mutations, and DNA repair	0.5	3
7. Transcription, RNA processing and proteins synthesis Regulation of gene expression, genetic diseases, and basic techniques used in molecular genetics	0.5	3 3
8. Endocrinology	1.0	6
9. Biochemistry of digestive juices of GIT, digestion and absorption in GIT	0.5	3
10. Oncogenesis and metabolism of xenobiotics	0.5	3
11. Water & electrolyte balance; acid-base regulation	0.5	2
Total items	9 SEQs	45 MCQs
Total Marks (5 marks for each SEQ and 1 mark for each MCQ)	45 marks	45 marks

25% of MCQs and SEQs should be clinically oriented or problem-based.

10% marks are allocated for "Internal Assessment"

Total Marks for Theory Paper: SEQ+ MCQ+ Internal Assessment=
45+ 45+ 10=100 Marks

**Table of Specifications for Biochemistry Oral & Practical
Examination
MBBS First Professional Examination (Part-II)**

Oral and Practical Examination carries 100 marks

Examination Component	Marks
A- Internal Assessment	10
B- Practical Notebook/Manual (Internal Examiner)	05
C- Viva voce a. External examiner: 25 Marks b. Internal Examiner: 25 Marks	50
D- OSPE a. Observed stations (6 Marks): There are two observed stations; 3 marks for each station – time allowed is 3 minutes for each observed station) b. Non-observed stations (16 Marks): There are eight non-observed stations; 2 marks for each station – time allowed is 2 minutes for each non-observed station.	22
E- Practical a. Principle, supposed calculation, etc: 4 Marks (External Examiner) b. Performance of the experiment: 4 Marks (Internal Examiner) c. Structured table viva: 5 Marks (External Examiner)	13

Format (Practical Examination / OSPE)
MBBS First Professional Examination (Part-II)
BIOCHEMISTRY (PART-II)

Total Marks: 100

Total marks allocated to Oral and Practical Examination are 100

Internal Assessment: 10 Marks

General Viva (Theory Viva): 50 Marks

25 Marks are allocated to internal examiner and 25 marks to external examiner.

Practical Examination: 40 Marks

Practical examination comprises three components i.e. Yearly Workbook, OSPE and experiment

A- Yearly Workbook: 5 Marks (Internal Examiner)

B- OSPE: 22 marks

OSPE comprises 10 stations (two observed stations carrying 3 marks each and 8 non-observed stations 2 marks each).

List of Tests for Observed Stations (3 minutes at each station)

- i. Spectrophotometer.
- ii. Centrifuge Machine.
- iii. Pipettes.
- iv. Blood samples.

Non-Observed Stations (2 minutes for each station)

- i. Tests to determine the concentration of total cholesterol, HDL cholesterol, and triacylglycerols, in plasma.
- ii. Tests to determine the concentration of total proteins, and glucose in plasma and CSF, and albumin in plasma.
- iii. Determination of plasma uric acid and calcium.
- iv. Determination of creatinine and urea in plasma, and creatinine clearance.
- v. Determination of activities of ALT and alkaline phosphatase in plasma.
Estimation of plasma bilirubin.
- vi. Determination of activities of creatine kinase, LDH, and AST

C- Experiment: 13 marks

- Principle/supposed calculations of the experiment:: 4 Marks (External Examiner)
- Performance of experiment : 4 Marks (Internal Examiner)
- Table viva : 5 Marks (External Examiner)