QUESTIONNAIRE IN BIOCHEMISTRY FOR STUDENTS OF MEDICINE
II COURSE

▪ GENERAL PART

1. Protein functions. Molecular forms of proteins (hetero-, iso- and aleoproteins). Oligopeptides, polypeptides and proteins. Amino acids – types and classification. Levels of organization of the protein molecule. Primary structure of proteins. Types of bonds in protein molecules - properties of the peptide bond, weak bonds, disulfide bridges.

2. Conformation. Secondary structure - α-helix and β-sheet, random coil characterization. Supersecondary structures – motifs and domains. Tertiary structure. Fibrous and globular proteins.

3. Quaternary structure. Mechanisms maintaining the conformation of proteins. Relation between the structure and the function of proteins - medical importance: defects in receptors (familial hypercholesterolemia, diabetes insipidus); diseases due to impaired conformation (prion disease, Alzheimer's disease); molecular diseases (sickle cell anemia); defects in the post-translational modification of proteins (scurvy and glycated hemoglobin).

4. Proteins as polyelectrolites: isoelectric point, precipitation of protein. Denaturation. Electrophoresis. Methods for protein examination – electrophoresis, chromatography, etc. Electrophoresis of plasma proteins – fractions.

5. Nucleic acids – types and biological role. Chemical composition – structure of nucleotides, chemical bonds. Free nucleotides of biological importance. Features of polynucleotide chains. Watson and Crick model. Purine and pyrimidine analogues as anticancer and antiviral agents.

6. Primary structure of nucleic acids. Conformation of DNA and of the different types of RNA. Nucleosomes. Importance of histone and nonhistone proteins. Denaturation and renaturation of DNA. Ribozymes, RNA maturation, microRNAs – role in the regulation of gene expression.

7. Characteristics of enzymes as biological catalysts. Structure, names and classification of enzymes. Mechanisms of enzyme catalysis. Enzyme–substrate complex. Active site. Specificity of the enzyme action.

8. Water-soluble vitamins – structure, biological role. Vitamin and vitamin derivatives as cofactors. Avitaminoses.

9. Lipid-soluble vitamins – structure, biological role. Hyper- and avitaminoses.

10. Enzyme kinetics. Enzyme units. Factors affecting the enzyme reaction rate: time, temperature, pH, concentration of the enzyme and of the substrate. Michaelis constant. Michaelis – Menten equation and Lineweaver – Burk plot (equation).

11. Reversible and irreversible inhibition. Competitive and noncompetitive inhibitors. Enzyme activators.

12. Enzyme activity regulation. Regulation of the absolute enzyme amount – constitutive and inducible enzymes; control of the half-life of enzymes. Regulation of the catalytic activity – compartmentalization, shuttle mechanisms, multyenzyme complexes, covalent modification (phosphorylation – dephosphorylation) and allosteric control. Retroinhibition.

13. Clinical significance of enzymes: functional and non-functional plasma enzymes. Role in the diagnosis of myocardial infarction and hepatitis. Diagnostic significance of isoenzymes (creatine phosphokinase and lactate dehydrogenase). Hereditary enzyme diseases (Gout, Lesch-Nyhan syndrome). Enzyme therapy. Enzymes and enzyme inhibitors in the treatment of cancer.

- **BIOENERGETICS**

14. Bioenergetics. Features of organisms as open chemical systems. General laws of thermodynamics and their application in living organisms. Coupling of endergonic and exergonic processes. Macroergic compounds. Role of the system ATP/ADP. Characteristics of biological oxidation. Substrates of biological oxidation and final hydrogen acceptors. Oxidoreductases. Redox systems.

15. Oxidative phosphorylation at substrate level: oxidative phosphorylation of glyceraldehyde-3-phosphate, enolase reaction. Oxidative decarboxylation of the α-keto acids pyruvate and α-ketoglutarate; regulation.

16. Respiratory chain – localization, function and molecular structure. Oxidative phosphorylation coefficient (P/O). Respiratory control, phosphate potential. Inhibitors of the electron transport. Chemiosmotic theory for the mechanism of oxidative phosphorylation in the respiratory chain. ATP synthase. Effect of uncoupling agents and inhibitors of the oxidative phosphorylation.

17. Free oxidation. Heat production. Brown adipose tissue. Role of thermogenin. Short electron transport chains. Reactive oxygen and nitrogen species (ROS and RNS) -generation and neutralization. Antioxidant enzymes and non-enzymatic antioxidants.

- **METABOLISM**

18. Citric acid cycle – importance for catabolism and anabolism. Chemical reactions, metabolic and energetic balance. Connection of the TCA cycle with the respiratory chain and with the other metabolic pathways. Regulation mechanisms. Pyruvate dehydrogenase deficiency.

19. Digestion and absorption of carbohydrates in the gastrointestinal tract. Glycolysis – importance, chemical reactions, energy production under anaerobic and aerobic conditions, tissue specificity. Metabolic fate of NADH and pyruvate – shuttle systems (malate and glycerophosphate shuttles). Pasteur effect and Warburg effect (in cancer). Clinical aspects - lactic acidosis, enzymopathies, hemolytic anemia.

20. Gluconeogenesis. Cellular compartmentalization and tissue localization, substrates. Importance. Overcoming the irreversible steps of glycolysis. Regulation. Role of gluconeogenesis in the kidney and in the small intestine.

21. Pentose phosphate pathway and NADPH – role in metabolism. Oxidative, isomerase and transferase reactions. Importance of the pentose phosphate pathway for erythrocytes. Glucose-6-phosphate dehydrogenase deficiency.

22. Fructose metabolism – resorption, organ specificity of degradation and relation with other metabolic pathways. Defects in the metabolism of fructose – essential fructosuria and fructose intolerance. Galactose metabolism – resorption; degradation; synthesis of lactose in lactating mammary glands. Defects in the metabolism of galactose – lactase deficiency, galactosemia type I and II.

23. Glycogen metabolism – structure, degradation and synthesis. Regulation of glycogenolysis and glycogenogenesis. Glycogenoses.

24. Regulation of carbohydrate metabolism and blood sugar level. Role of insulin, glucagon and other hormones. Hypoglycemia, hyperglycemia and glucosuria.

25. Features of carbohydrate metabolism in the different tissues and organs: gastrointestinal tract, liver, nervous tissue, muscles, kidneys, adipose tissue, erythrocytes.

26. Lipids – classification. Lipid digestion – enzymes. Composition, origin and functions of the lipoprotein complexes. Receptors, apolipoproteins, enzymes of the lipoprotein metabolism. Familial hypercholesterolemia.

27. Degradation and biosynthesis of triacylglicerols. Metabolism of glycerol. Fate of the fatty acids. Regulation of the degradation of triacylglicerols in the adipose tissue - hormone-sensitive lipase.

28. Oxidation of fatty acids. β-oxidation of fatty acids with an even and an odd number of carbon atoms and of polyunsaturated fatty acids. Carnitine shuttle. Regulation. Energetic balance. Peroxisomal β-oxidation. α-oxidation of branched fatty acids. Peroxide oxidation of unsaturated fatty acids. Enzyme defects in the oxidation of fatty acids.

29. Ketone bodies metabolism. Ketogenesis and ketolysis. Regulation of the ketogenesis. Ketosis and ketoacidosis.

30. Biosynthesis of fatty acids. Citrate shuttle. Acylsintase complex. Regulation of the lipogenesis. Fatty acids chain elongation and synthesis of unsaturated fatty acids.

31. Synthesis and degradation of phospholipids. Biological role of phospholipases A_1, A_2, C and D. Sphingolipids – types, structure and importance. Sphingolipidoses.

32. Essential fatty acids and their derivatives – eicosanoids (prostaglandins, tromboxanes, prostacyclins and leucotrienes). Cyclic and linear pathways of formation. Steroidal and non-steroidal anti-inflamatory drugs – mechanism of action. Essential fatty acids deficiency.

33. Structure and biological role of cholesterol. Cholesterol pathways in the organism. Cholesterol synthesis. Regulation – control by covalent modification and at the transcription level. Removal from the body.

34. Cholesterol derivatives. Synthesis of bile acids, regulation, cholelithiasis (gallstone disease). Steroid hormones – structure, synthesis and functions. Synthesis and biological functions of vitamin D_3.

35. Lipid metabolism disorders. Atherosclerosis. Obesity and fatty liver disease. Adipokines (leptin, adiponectin, etc.) – synthesis, secretion and their role in obesity and in the development of insulin resistance.

36. Digestion and absorption of proteins in the gastro-intestinal tract. Mechanisms for intracellular degradation of proteins. Nitrogen balance and the end products of nitrogen metabolism. General reactions in amino acid metabolism – transamination, oxidative deamination, transdeamination and decarboxylation. Amines of biological significance. Clinical significance of the enzymes called aminotransferases.

37. Ammonia toxicity. Detoxification of ammonia. Reductive amination of α-ketoglutarate. Synthesis of glutamine. Amoniogenesis in the kidneys (renal amoniogenesis). Urea cycle – interrelationships with the citric acid cycle, regulation and metabolic disorders. Glucose-alanine cycle.

38. Catabolism of amino acids. General pathways for degradation of the C-skeletons of amino acids. Pathways for degradation of glucogenic and ketogenic amino acids. Single carbon atom units – types, sources, importance. Vitamin B_{12}, folic acid and S-adenosyl methionine. Therapeutic application of folate analogues. Catabolism of phenylalanine and tyrosine. Catabolism of tryptophan. Catabolism of branched amino acids.

39. Essential and nonessential amino acids. Common reactions in the synthesis of nonessential amino acids. Selenocysteine. Conversion of amino acids to specialized products – arginine (synthesis of creatine phosphate, citrulline, nitric oxide and polyamines) and serine (synthesis of ethanolamine, choline and phospholipids).

40. Conversion of amino acids to specialized products – tryptophan (NAD^+, serotonin, melatonin), tyrosine (thyroid hormones, catecholamines, dopamine, melanin). Products of glutamine and glutamate metabolism. The γ-glutamyl cycle. Glutathione as a reducing agent, antioxidant and as a participant in the metabolism of xenobiotics. Tissue specificities in amino acid metabolism.

41. Impairments of amino acids metabolism. Enzymopathies associated with metabolism of tyrosine (phenylketonuria, tyrosinosis, alkaptonuria, albinism), tryptophan (pellagra) and aliphatic amino acids (methylmalonic acidemia). Parkinson's disease and L-DOPA.

42. Synthesis and degradation of purine nucleotides. Regulation of the pathway. Tissue specificities. Hyperuricemia and gout. Inhibition of the enzyme activity of xanthine oxidase. Enzyme defects – Lesch-Nyhan syndrome and immunodeficienscies. Purine analogues used as anticancer and antiviral drugs.

43. Synthesis and degradation of pyrimidine nucleotides. Regulation of the pathway. Synthesis of CTP and TMP from UMP. Ribonucleotide reductase reaction. Thymidylate synthase reaction. Orotaturia.

44. Iron metabolism. Absorption of haem-bound iron and nonhaem iron. Transferrin receptors. Iron-binding and iron storage proteins. Hepcidin. Post-transcriptional control over iron homeostasis. Disorders of iron homeostasis.

45. Synthesis of porphyrins. Organ and intracellular localization of the pathway. Regulation and regulatory enzymes. ALA-synthase and its control – enzyme inducers and repressors. Types of porphyrias. Application of exogenous porphyrins in the treatment of certain cancer diseases.

46. Hemoglobin degradation. Haptoglobin, hemopexin and scavenger receptors. Haem oxygenase. Direct and indirect bilirubin. Bile pigments. Enterohepatic circulation of the bile pigments. Jaundice.

47. Metabolism integrity. Integration at the level of a single protein molecule and multienzyme complexes. Compartmentalization and selective permeability – transport mechanisms and shuttle mechanisms. Role of the key enzymes, metabolites and cofactors. Regulation through limiting metabolites and cofactors. Control at the level of the slowest steps of a metabolic pathway.

48. Metabolism integrity. Tissue and organ specificities – brain, liver, muscles, heart and adipose tissue. Adaptation in starvation.

49. Molecular diseases. Mutations as a reason for the development of molecular diseases. Consequences from the existence of point mutations that affect enzymes of the pathway for synthesis of hemoglobin. Defects that affect enzyme activities. Molecular diseases due to defects in the DNA repair mechanisms.

50. DNA replication – types of DNA polymerases and other proteins involved in the process. Cell cycle and its control – role of the cyclins, cyclin-dependent kinases (CDK), the retinoblastoma protein (Rb), p53 and the inhibitors of the cyclin-dependent kinases (CDI). Replication mechanisms. DNA repair mechanisms.

50. Recombinant DNA technologies. DNA recombination. Role of restrictases, reverse transcriptase and chemical methods. DNA sequences identification – electrophoresis, Southern blotting. Sanger didesoxinucleotid method for DNA sequencing. DNA amplification: cloning, polymerase chain reaction (PCR).

51. Regulation of the gene expression at the level of the process of transcription. Regulation of RNA polymerase II in eukaryotes through phosphorylation and suppressor proteins. Regulatory sites in the promoter regions in eukaryotes. Transcription factors (TF) and transcription complexes. Epigenetic modifications – DNA methylation and covalent modification of histones – role in the processes of replication and transcription.

52. Regulation of the gene expression. Post-transcriptional control of the gene expression – splicing. Regulation through the transport and stability of mRNA molecules. Post-transcriptional editing of mRNA molecules. Control at the level of translation. Regulation of the synthesis of ferritin at the level of translation.

53. Regulation at the post-translational level. Proteolytic cleavage of proteins. Post-translational modifications – methylation, acetylation, myristoylation and prenylation. Phosphorylation and sulfation. Vitamin C and vitamin K-dependent modifications. Selenoproteins. Ubiquitin, ubiquitination and targeted degradation of proteins.

▪ FUNCTIONAL BIOCHEMISTRY

54. Principles of the intercellular communication and signal transduction. Types of intercellular interactions: endocrine, paracrine, autocrine mechanisms and intercellular junctions. Principles in cell signaling: signaling molecules and receptors. Intracellular participants in cell signaling: a signal cascade. Adaptor proteins and effector molecules: G-proteins, protein kinases and phosphatases. General features of the signal cascades: convergence, divergence and cross-talk.

55. Types of plasma membrane receptors. Receptors associated with ion channels. G-protein coupled receptors. Receptors with intrinsic enzyme activity. Receptors, associated with enzyme activity molecules (tyrosine kinase activity).

56. Secondary messengers in signal transduction. Types of secondary messenger. The adenylyl cyclase system, cyclic AMP (cAMP), cyclic GMP (cGMP), G-proteins and nitric oxide (NO).

57. Secondary messenger in signal transduction. Calcium and calmoduline. Lipid mediators: inositol-3-phosphate, diacylgrlycerols (DAG), eicosanoids, ceramides and sphingosine-1-phosphate.

58. Pituitary and hypothalamic hormones. Hypothalamo-pituitary axis: releasing hormones. Hormones of the anterior pituitary. The hypothalamo-pituitary-thyroid (HPT) axis. Synthesis, secretion and biological effects of the thyrotropin-releasing hormone (TRH) and thyroid-stimulating hormone (TSH). Synthesis, secretion and effects on metabolism of the thyroid hormones. Deiodinases. Thyroid gland diseases.

59. The hypothalamo-pituitary-adrenal (HPA) axis. General characteristics of the steroid hormones. Synthesis of mineralocorticoids and glucocorticoids. Hormonal control over synthesis of steroid hormones: corticotropin-releasing hormone (CRH), proopiomelanocortin (POMC) and adrenocorticotropic hormone (ACTH). Regulatory mechanisms that control synthesis of glucocorticoids and mineralocorticoids in the adrenal cortex. Biological and metabolic effects of cortisol. Clinical cases with increased or decreased secretion of cortisol.

60. The hypothalamo-pituitary-gonadal (HPG) axis. Gonadotropin-releasing hormone (GnRH). Folicle stimulating hormone (FSH) and luteinizing hormone (LH). Synthesis of sex hormones. The hypothalamic–pituitary–somatotropic (HPS) axis. Defects in synthesis and the signaling pathways of growth hormone. Insulin-like growth factors (IGF-1, 2). Hormones of the posterior pituitary.

61. Hormones that regulate water and salt balance. Renin-angiotensin-aldosterone system. Natriuretic peptides. Antidiuretic hormone (ADH or vasopressin). Calcitonin and parathyroid hormone (PTH). Synthesis, secretion and signaling.

62. Hormones of the pancreas – insulin, glucagon and somatostatin. Synthesis, secretion, signaling pathways and biological effects.

63. Catecholamines. Hormones of the gastrointestinal tract. Synthesis, secretion, signaling pathways and biological effects.

64. Hormones that bind intracellular receptors. General characteristics of nuclear receptors. Different types of intracellular receptors. Retinoic acid receptors (RAR). Receptors that bind thyroid hormones. Receptors that bind steroid hormones. Anti-inflammatory effects of the glucocorticoids through inhibition the NF-kB-signaling pathway. Antiestrogens. The intracellular signaling pathways of vitamin D_3. Other families of intracellular receptors: retinoid X receptors (RXR's), liver X receptors (LXR's), peroxisome proliferator-activated receptors (PPAR's), farnesoid X receptor (FXR) and pregnane X receptor (PXR).

65. Molecular mechanisms of oncogenesis. Tumor cells features. Tumor markers. Factors that cause cancer. Direct carcinogens and pro-carcinogens. Pro-carcinogen metabolic activation. Stages of chemical carcinogenesis. Oncogenes and proto-oncogenes. Mechanisms of transformation of oncogenes into proto-oncogenes. Oncogenes and growth factors. Oncogenic viruses. Oncogenes and signal transduction. Tumor-suppressor genes. Mechanisms of tumor cell progression and metastasis. Telomerase and cancer. Anticancer therapy drugs – mechanism of action. P-glycoproteins.

66. Apoptosis – molecular mechanisms and biological role. Internal and external pathways of apoptosis. The role of mitochondria in apoptosis. Signals from death-receptors. The role of caspases in apoptosis. TNFR and Fas signal pathways. Anti-apoptotic signals for cell survival – the role of PI3K and PKB/Akt. p53 signal pathway. Regulation and clinical significance of programmed cell death.

67. Pathobiochemical mechanisms of *Diabetes mellitus (DM)*. Classification. Genetic and environmental factors as a predisposition for the development of DM. Type I diabetes (T1DM) and Type II diabetes (T2DM). Metabolic disorders and complications of T1DM and T2DM. Glucose as a regulator of gene transcription – the role of carbohydrate-responsive element-binding protein (ChREBP) protein. T2DM and hyperglycemia: oxidative stress, the sorbitol pathway, advanced glycation end-products and their receptors (AGE's and RAGE's), activation of the DAG/PKC cascade. Diabetes and obesity. Biochemical indicators in the diagnosis of diabetes.

68. Blood. Biochemical features and biomedical importance. Blood cells. Erythrocytes: erythropoiesis, erythropoietin, hematocrit. Bioenergetics and specificities in metabolism of erythrocytes – enzymopathies and anemias. Metabolism of leucocytes – bioenergetics and phagocytosis. Regulation of metabolism in T-lymphocytes. T-cell receptor complex (TCR).

69. Biochemistry of the blood. Blood serum and plasma. Biological role of the plasma proteins. Albumin. Acute-phase proteins: C-reactive protein (CRP), serum amyloid-A (SAA) haptoglobin and hemopexin. Complement system. Matrix metalloproteinases. Immunoglobulins. Plasma proteins and inflammation.

70. Hemostasis and thrombosis. Blood coagulation cascade: intrinsic and extrinsic pathways. Conversion of fibrinogen to active fibrin. Proteins, involved in hemostasis. Vitamin K-dependent post-translational modifications. Fibrinolysis. Regulation of hemostasis.

71. Mechanisms of cellular adhesion. Types of adhesion molecules – structure and biological role – integrins, cadherins, immunoglobulin-like cell adhesion molecules (IgSF CAM's). Cytoskeleton and cell adhesion. Types of cell contacts. Actin and actin filaments – assembly and regulation of actin filaments. Clinical significance.

72. Extracellular matrix (connective tissue). Types and functions of the structural proteins. Types and functions of the proteoglycans and glycosaminoglycans. Diseases due to mutations in genes that encode for structural proteins. Mucopolysaccharidosises.

73. Bones as a mineralized connective tissue. Chemical composition of the bones. Osteoblasts, osteocytes and osteoclasts – role in the formation and remodeling of bones. Biochemistry of the ossification and bone resorption. Regulation of the bone metabolism. Metabolic and genetic disorders that affect the bones. Biochemistry of cartilage. Calcium homeostasis and factors that affect calcium homeostasis.

74. Nutrition and digestion. Food and its biological meaning and value. Some clinical aspects of feeding. Digestion and absorption of carbohydrates, lipids, proteins, vitamins and minerals. Processes in the colon. Secretion of molecules, involved in digestion, in the lumen of the gastrointestinal tract. Disorders of digestion and absorption.

75. Biochemistry of the liver. Metabolic functions. Synthesis of specific products. Metabolism of xenobiotics.

LITERATURE FOR SELF-STUDY

1. ***Lecture course in Biochemistry, Prof. Tatyana Vlaykova, PhD***
2. Bivolarska A***. Biochemistry guide book for students in Medicine, Dental medicine and Pharmacy.*** Lax book, 2021.
3. Rodwell V, D Bender, K Botham, P Kennelly, P Weil. ***Harper's Illustrated Biochemistry***. Thirtieth Edition., 2015.
4. Ferrier D. ***Lippincott Biochemistry*** *6th Edition.* Editor R. Harvey. 2014.
5. Lieberman M. and Marks A. ***Marks' Basic Medical Biochemistry a Clinical Approach***, (2009), Lippincott Williams & Wilkins.