QUESTIONS FOR EXAMINATION ON BIOCHEMISTRY

MODULE I. STRUCTURE, FUNCTION AND PROPERTIES OF PROTEINS. ENZYMES

1. The functions of proteins in the human body. Physiologically important peptides. Levels of protein structure. Primary, secondary, tertiary, quaternary structures. Chemical bonds, providing their stability. Globular, fibrillar, transmembrane proteins: structural features, examples. Protein folding. Chaperonins. Protein denaturation and renativation. Prion disease.
2. Complex proteins. Classification, examples. Structure and functions of myoglobin.
3. The structure and functions of hemoglobin. T- and R-forms of hemoglobin. Allosteric effects of hemoglobin: cooperative effect, Bohr effect, effect of 2,3-diphosphoglycerate. Features of fetal hemoglobin. The concept of hemoglobinopathies. Sickle-cell anemia. Thalassemia.
4. General characteristics of enzymes. Enzyme specificity: types, examples. The structure of enzymes. Cofactors and coenzymes. Basic reaction types and classes of enzymes. Systematic names of enzymes.
5. Catalytic mechanisms of enzymes. Active catalytic site. Stages of enzymatic reaction. Models of interaction of enzyme with its substrate.
6. Enzyme kinetics. The dependence of enzyme reaction rate on substrate concentration. The Michaelis-Menten equation. The dependence of enzyme reaction rate on amount of enzyme. The dependence of enzyme reaction rate on pH and temperature.
7. Inhibition of enzyme activity. Competitive and noncompetitive inhibition. Irreversible inhibition. Enzyme kinetic changes. Examples.
8. Allosteric enzymes. Structure and functions. Allosteric effectors. Regulation of enzyme activity by protein-protein interactions. Regulatory proteins. Examples. Regulation of enzyme activity by phosphorylation and dephosphorylation and by partial proteolytic cleavage.
9. Isozymes. Examples. Biologic role. Enzymopathy. Examples. Enzymodiagnostics and enzymotherapy. Examples of using enzymes in therapy. Abzymes.

MODULE II. MEMBRANES. BIOLOGIC OXIDATION.

1. Structure of biological membranes. Membrane lipids: structure, function. Membrane proteins. Properties of biological membranes: microviscosity, asymmetry, fluidity. Fluid mosaic model of membrane structure.
2. Transport of substances through biological membranes. Passive transport. Ion channels. Aquaporins. Active transport of substances across membranes. Primary active transport. Structure of Na^+, K^+-ATP-ase. Secondary active transport. Biochemical mechanisms of endocytosis and exocytosis.
3. Transmembrane signal transduction. Membrane receptor proteins. G-proteins: structure, function, regulation.
4. Catabolism and anabolism. The scheme of metabolism and energy transfer in human organism. Specific and common catabolic pathways.
5. Oxidative decarboxylation of pyruvate. Structure of the pyruvate dehydrogenase complex. Stages of the pyruvate oxidative decarboxylation. Regulation of the pyruvate dehydrogenase complex.
6. Tricarboxylic acid cycle. Overview, energetics of the tricarboxylic acid cycle.

7. Reactions of the tricarboxylic acid cycle. Reactions catalyzed by dehydrogenases. Reaction of the substrate-level phosphorylation.
8. Regulation of the tricarboxylic acid cycle. Anabolic functions of TCA cycle. Anaplerotic reactions.
9. Macroergic substrates. Classification of high-energy bond containing substances. ATP as universal "energetic currency".
10. ATP synthesis: substrate-level phosphorylation and oxidative phosphorylation. Examples of the substrate-level phosphorylation reactions.
11. Oxidative phosphorylation of ADP. Mechanism of coupling between oxidation and phosphorylation. Mitchell's chemiosmotic theory.
12. Structure of electron-transport chain: components, complexes, arrangement in the inner mitochondrial membrane. Structure of ATP-synthase. Mechanism of ATP synthesis.
13. Regulation of oxidative phosphorylation. Uncoupling of oxidation and phosphorylation. Physiologic implication. UCP-proteins. Molecular biological aspects of mitochondrial function and dysfunction.
14. Reactive oxygen species and reactive nitrogen species. Nonezymatic and enzymatic mechanisms of generation ROS and RNS. Lipid peroxidation: mechanisms, products. Primary and secondary mechanisms of oxidative damage. Role of peroxidation in cell death.
15. The antioxidant system of the body. Nonenzymatic antioxidants. Enzymatic antioxidant defense system.
16. Physiological importance of free radical oxidation. Free radical oxidation in phagocytosis. Free radical oxidation in the pathology of cardiovascular system.

MODULE III. METABOLISM OF CARBOHYDRATES

1. The biological role of carbohydrates. The daily requirement for carbohydrates in adults and in children. Dietary carbohydrates of animal and vegetable origin.
2. Structure and function of carbohydrates: monosaccharides, disaccharides, gomopolisaccharides. Derivatives of monosaccharides - acetylhexosamine, glucuronic acid.
3. Digestion of carbohydrates. Enzymes in carbohydrate digestion: salivary α-amylase, pancreatic α-amylase, enzyme complexes in small intestine.
4. Malabsorption of carbohydrates: biochemical mechanisms. Sucrose and lactose intolerance: biochemical causes, consequences and mechanisms of development of symptoms.
5. Transport of monosaccharides through membranes: facilitated diffusion and active transport. Glucose transporters: types, structures, functions. Insulin-dependent glucose transporters.
6. Glucose pathways. Glucose phosphorylation. The role of glucose-6-phosphate.
7. Glucose metabolism in liver: role of glucokinase and glucose-6 phosphatase in the maintenance of a constant concentration of glucose in the blood.
8. Glycogen synthesis from glucose-6-phosphate. Biologic role, reactions, enzymes. Tissue and cellular localization.
9. Degradation of glycogen. Biologic role, reactions, enzymes. Tissue and cellular localization.
10. Features of glycogen metabolism in liver and muscle under certain physiological conditions (food intake, fasting, muscle activity). Hormonal regulation of these processes.
11. Regulation of enzyme activity in metabolism of glycogen - glycogen synthase and glycogen phosphorylase: hormonal regulation - the effect of epinephrine and glucagon (adenylate cyclase mechanism, the role of cyclic AMP and protein kinase A); the role of insulin and phosphodiesterase in decreasing of cAMP concentration in the cell; allosteric regulation of

glycogen phosphorylase activity with the participation of AMP; calcium-dependent activation of glycogen phosphorylase kinase.
12. Genetic disorders of glycogen metabolism: glycogen synthesis and glycogen degradation (liver, muscle and mixed glycogenoses).
13. Metabolic pathways of glucose. The role of glucose-6-phosphate.
14. The process of glycolysis: localization and conditions, the sequence of reactions and enzymes, the final products, involvement of adenine nucleotides and energy effect, irreversible reactions of glycolysis, reactions associated with consumption of ATP, substrate-level phosphorylation reactions, their role, glycolytic oxidoreduction.
15. The process of gluconeogenesis: localization and conditions of the reactions, the substrates, the sequence of reactions and enzymes, reactions associated with the consumption of GTP and ATP, irreversible reactions of gluconeogenesis, the role of gluconeogenesis in fasting and in physical exercises, energy consumption for the synthesis of one molecule of glucose.
16. The reciprocal regulation of glycolysis and gluconeogenesis: hormonal regulation - the role of insulin, epinephrine, cortisol, glucagon; allosteric regulation - role of ATP, ADP, AMP, citrate, fatty acids, glucose-6-phosphate, fructose-6-phosphate, fructose-1,6-diphosphate, acetyl SCoA.
17. Anaerobic oxidation of glucose. Pathways for glycolysis products under anaerobic conditions. Energy effect of the oxidation of glucose and glycogen under anaerobic conditions.
18. Pathways for products of glycolysis under aerobic conditions. Glycerol 3-phosphate shuttle and malate–aspartate shuttle. Energetic effect of aerobic glucose oxidation.
19. Stages of aerobic oxidation of glucose, and the summary reaction of aerobic breakdown of glucose. Advantages of aerobic oxidation of glucose.
20. Pyruvate: metabolic pathways, biologic role, reaction of conversion to acetyl-SCoA and oxaloacetate, the energy balance of oxidation to CO_2 and H_2O.
21. Vitamins as coenzymes in pyruvate metabolism (H, B1, B2, B3, B5): dietary sources, daily requirements, biochemical functions, signs of deficiency.
22. Glucose-lactate cycle (Cori cycle). Biologic role in physical exercises. Sources of lactate in human organism.
23 Glucose-alanine cycle. Biologic role in physical exercises and in fasting.
24. The effect of ethanol on metabolism of carbohydrates in the human body. Causes of hyperlactatemia and hypoglycemia in alcohol intoxication.
25. Features of glucose metabolism in the liver, brain, skeletal muscle, adipose tissue, erythrocytes.
26. Characteristics of the pentose phosphate pathway of glucose oxidation: localization and role of the pentose phosphate pathway, reactions of the oxidative phase, principles of nonoxidative phase, enzymes, coenzymes, interaction with glycolysis, the role of the pentose phosphate pathway in adipose cells, in erythrocytes, in dividing cells.
27. Hereditary deficiency of glucose-6-phosphate dehydrogenase. The factors that trigger manifestations of the disease.
28. The conversion of fructose into glucose. Pathways of fructose metabolism. Disorders of fructose metabolism. Differences in metabolism of fructose in the liver and in muscles. Polyol pathway of fructose synthesis pathway, biologic role.
29. Role of galactose in the body. Galactose metabolism. Key enzymes of galactose metabolism. Galactosemia, molecular causes, clinical manifestations and principles of treatment.

30. Glucose metabolism in erythrocyte: glycolysis, pentose phosphate pathway, 2,3 bisphosphoglycerate synthesis.
31. Hormonal regulation of carbohydrate metabolism. Influence of insulin, glucagon, epinephrine, cortisol on blood glucose level and on intracellular glucose metabolism. Insulin-dependent tissues. Hormone-sensitive enzymes of carbohydrate metabolism, mechanisms of their regulation.
32. The physiological and pathological hyper- and hypoglycemia.
33. General characteristics of diabetes type 1 and 2. Disorders of carbohydrate metabolism. Biochemical mechanisms of diabetes complications.

MODULE IV. METABOLISM OF LIPIDS

1. Classification of lipids. Polyunsaturated fatty acids: ω-6 (linoleic, γ-linolenic, arachidonic acid), ω-3 (α-linolenic). Chemical structure. Biologic role. Vitamin F. Triacylglycerols, structure, biological role and function. Structure of phospholipids: phosphatidylserin, phosphatidylcholine, phosphatidylinositol, phosphatidylethanolamine. Biologic role.
2. Digestion of lipids. Dietary sources of lipids, daily consumption of lipids. The stages of digestion of lipids in gastro-intestinal tract.
3. The composition of bile and its role. Types of bile acids, their functions, structure. Disorders of bile secretion. Enzymes for digestion of triacylglycerols, phospholipids, cholesterol esters. Localization of synthesis and activation of these enzymes. The role of phospholipase A2 and C.
4. Disorders of digestion and absorption of dietary lipids. Steatorrhea. Vitamin deficiencies associated with steatorrhea. Features of digestion of lipids in children.
5. Resynthesis of lipids in enterocytes. Reactions of resynthesis of triacylglycerols, cholesterol esters and phospholipids in the intestinal wall. Transport of resynthesized triacylglycerols in the body.
6. Fatty acid synthesis from glucose: localization and conditions, scheme of acetylCoA formation from glucose, role of citrate in the transfer of the acetyl group into cytosol, synthesis of malonyl-CoA, role of biotin. Structure of fatty acid synthase, reactions, the final product of the synthesis, regulation of the process.
7. Synthesis of glycerol 3-phosphate from glucose. Localization and biologic role of the process. Synthesis of phosphatidic acid from glycerol 3-phosphate and fatty acids: localization in the cell, the sources of glycerol-3-phosphate, fatty acids and energy, the sequence of reactions, interconnection with carbohydrate metabolism, metabolic pathways for phosphatidic acid.
8. Reactions of synthesis of triacylglycerols (lipogenesis). The fatty acid composition of triacylglycerols. Interconnection with carbohydrate metabolism. Synthesis of triacylglycerol in adipose tissue and in liver.
9. Lipolysis: localization and conditions, a sequence of reactions and enzymes, the final products, hormonal regulation, transport of produced fatty acids and their using, utilization of glycerol. The energy effect of glycerol oxidation.
10. Reactions of fatty acid oxidation to carbon dioxide and water: the role of carnitine, localization and conditions, reactions of β-oxidation, role of vitamins and coenzymes, the final products, connection with the TCA cycle and respiratory chain, the energy yield of the process, the calculation of the energy effect of ß-oxidation of palmitic acid.
11. Triacylglycerol metabolism in different physiologic states (food intake, fasting, muscle activity).

12. Reactions of the synthesis of ketone bodies. Conditions, localization, biologic role. Reactions of ketone bodies utilization in tissues.
13. Ketoacidosis in starvation and in diabetes mellitus. Role of oxaloacetate deficit in activation of ketogenesis.
14. The fatty acid composition of phospholipids. Reactions of phospholipids biosynthesis in tissues. Two pathways of phospholipid biosynthesis. The role of vitamins B6, B9 and B12, methionine and serine. Disorders of phospholipid synthesis. Hepatic steatosis (fatty liver).
15. Lipidosis: Tay-Sachs disease, Gauchers disease, Niemann-Pick diseases.
16. The chemical structure and biological role of cholesterol. Dietary sources of cholesterol. Pathways of cholesterol metabolism. Removing cholesterol from the body.
17. Cholesterol biosynthesis. Localization, substrates, stages. Reactions for mevalonate synthesis. Scheme of the next stages. Interaction with carbohydrate metabolism. Regulation of cholesterol synthesis. Hormonal and allosteric regulation mechanisms. Drug regulation of cholesterol synthesis.
18. Bile acids, classification, structure and physiological role. Stages of the synthesis of bile acids, Role of vitamins. Primary and secondary bile acids, conjugated bile acids. Enterohepatic circulation of bile acids.
19. Disorder of cholesterol metabolism and gallstone disease. Role of phospholipids. Lipotropic factors.
20. Lipoproteins of blood: classification, structure, stages of formation. Apoprotein: classification, function.
21. Transport of dietary triacylglycerol in organism. Chylomicrons: lipid composition, structure, functions, apoproteins. Localization of chylomicron formation. Role of lipoprotein lipase in chylomicron metabolism.
22. Sources of TAG in the liver. Very low density lipoproteins: lipid composition, structure, functions, apoproteins. Role of lipoprotein lipase in VLDL metabolism.
23. Localization and role of apo B100 receptor. Role of receptor-mediated endocytosis of LDL, pathway of components after endocytosis. Role acyl SCoA: cholesterol acyltransferase (ACAT).
24. Transport of cholesterol and cholesterol esters in blood. Role of high density lipoproteins and low density lipoproteins. Lecithin-cholesterol acyltransferase reaction.
25. Role of essential polyunsaturated fatty acids in cholesterol metabolism. Vitamin F: dietary sources, daily requirements, biochemical functions, signs of deficiency. Polyunsaturated fatty acids ω3: examples, structure, properties, biologic role. Eicosanoids: prostaglandins, thromboxanes, leucotriens. Biologic role. Scheme of synthesis. Role of phospholipase A2, cyclooxygenase, lipooxygenase. Factors affecting the synthesis of eicosanoids.
26. Hyperlipoproteinemia type IIA (familial hypercholesterolemia): mechanisms and clinical simptoms.
27. Atherosclerosis: stages. The role of modified LDL in the initiation of atherosclerosis. Neutrophils and monocytes in pathogenesis of atherosclerosis.
28. Characteristics of disorders of triacylglycerols transport - dyslipoproteinemia types I and V. mechanisms and clinical symptoms.

MODULE V. NITROGEN METABOLISM

1. Nitrogen balance. Negative, positive nitrogen balance. Equilibrium. Physiologic and pathologic situations with different nitrogen balance. Nitrogen balance in children. Food sources

of proteins. Daily requirement for proteins in adults and in children. The biological value of proteins. Manifestations of protein deficiency. Kwashiorkor.
2. Digesting of proteins in the stomach and in intestine. The mechanism of the synthesis and the biological role of gastric acid. Disorders of gastric acid production. Enzymes of gastric juice, pancreatic juice and intestinal juice involved in the digestion of proteins.
3. Disorders of protein digestion and absorption, connection of these disorders with the development of allergic reactions. Features of protein digestion and absorption of amino acids in children of different ages. Celiac disease.
4. Decomposition of proteins in intestine under influence of microbial enzymes. Substances formed by the decay of proteins. The processes of detoxification in the liver: microsomal oxidation and conjugation system. Reactions of indican formation.
5. The transport of amino acids through cell membranes. Sources and pathways of amino acids in tissues. Glucogenic and ketogenic amino acids.The fate of α-keto acids formed in the process of deamination (for pyruvate, oxaloacetate, alpha-ketoglutarate). The calculation of the energy effect of oxidation of the amino acids.
6. Deamination of amino acids (reductive, hydrolytic, intramolecular, oxidative). Direct and indirect oxidative deamination. Reductive amination.
7. Ttransamination reactions. The role of vitamin B6. The reactions catalyzed by aspartate aminotransferase (AST) and alanine aminotransferase (ALT). Biologic role. Diagnostic value.
8. Synthesis of biogenic amines (γ-aminobutyric acid, histamine, serotonin, dopamine). The role of these biogenic amines. Catabolism of biogenic amines: deamination with monoamine oxidase (MAO) and methylation reactions.
9. Sources of ammonia in tissues. Ammonia toxicity. Transport forms of ammonia in blood (glutamine, asparagine, alanine). The reactions of their formation. Glucose-alanine cycle. The role of the liver, kidney and intestines in the binding and elimination of ammonia.
10. Urea cycle: localization, enzymes, biologic role. Interaction between urea cycle and TCA cycle. Diagnostic value of urea concentration in blood and urine. Reference range.
11. Hyperammoniemia, their causes and consequences. Physiologic concentration of ammonia in the blood. Causes of ammonia toxicity.
12. The purine and pyrimidine nucleotides: structure, functions in the body. Sources of nitrogen and carbon atoms in the purine ring. The scheme of synthesis of purine nucleotides, regulation. Synthesis of deoxyribonucleotides. Enzymes. Role of NADPH and thioredoxin. Reaction dTMP synthesis. The role of folic acid and tetrahydrofolate. The cause of megaloblastic anemia in folate deficiency. The mechanism of the antibacterial activity of sulfanilamides. Inhibitors of timidyl nucleotide synthesis - methotrexate, 5-fluorouracil, azidothymidine.
13. Catabolism of purine nucleotides: decomposition of AMP and GMP; reaction of reutilization of hypoxanthine and guanine, the reaction of formation of uric acid from hypoxanthine and xanthine, the role of xanthine oxidase. Primary and secondary hyperuricemia, their causes and consequences: urolithiasis: causes, biochemical aspects of pathogenesis and treatment; gout: causes, clinical manifestation, biochemical aspects of pathogenesis and treatment. The mechanism of allopurinol effect in the treatment of gout. Lesch Nyhan syndrome, the causes, the principles of treatment, prognosis.
14. The scheme of pathways of glycine and serine. Interconnection of metabolism of glycine, serine, methionine and cysteine, vitamins B6, B9 and B12: reaction of interconversion of serine and glycine, formation of methylene and methyl tetrahydrofolate, S-adenosyl methionine synthesis from homocysteine, the role of vitamin B12; S-adenosyl methionine in transmethylation processes for the synthesis of biologically important substances;

reaction of homocysteine production and the pathway of its transformation into cysteine; role of vitamin B6.
15. Metabolism of phenylalanine and tyrosine. Anabolic and catabolic pathways of tyrosine transformations. The reaction converting phenylalanine to tyrosine. Characteristics of disease phenylketonuria type 1 (classic) and phenylketonuria type 2 (variant): defective enzymes, biochemical aspects of pathogenesis, typical clinical manifestations, principles of treatment.
16. The reactions of conversion of tyrosine to dihydroxyphenylalanine, dopamine, norepinephrine and epinephrine. Disorders of tyrosine metabolism - albinism and parkinsonism. Biochemical aspects of pathogenesis and treatment.
17. Metabolism of arginine. Arginine in the synthesis of urea, creatine, nitric oxide (NO). Reactions of polyamines synthesis (spermine and spermidine). The structure of creatine and creatine phosphate, the reaction of their synthesis, localization of the process. The biological role of creatine phosphate.

MODULE VI. HORMONES. HORMONAL REGULATION OF METABOLISM

1. Hormones. Hierarchy of regulatory systems. Classification of hormones according to chemical structure. Cell signaling. Plasma membrane receptors and intracellular binding proteins. Intracellular second messengers.
2. The adenylyl cyclase mechanism of hormonal action: hormones, second messenger, enzymes and processes regulated by this mechanism. Reaction of cAMP synthesis and breakdown. Activation of protein kinase A. The role of activating and inhibitory isoform of α subunit of G protein. The transcription factor CREB. Phosphatidylinositol signalling: hormones, second messengers, enzymes and processes regulated by this mechanism. The reaction of formation of inositol triphosphate (IP3) and diacylglycerol (DAG). Sources of calcium ions.
3. Receptors associated with tyrosine kinase activity: enzymatic cascade that is associated with the activation of Ras-protein, its scheme, the sequence of events, the main participants, the role for cell metabolism. Cytosolic mechanism of hormonal signals: stages, hormones, features of intracellular receptors.
4. Hypothalamic-pituitary-adrenocortical system: biological role, components, regulation. Glucocorticoids: regulation of synthesis and secretion, the main stages of the synthesis, mechanism of action and target organs, the effect on metabolism - regulated processes. Hypo- and hyperproduction of glucocorticoids - metabolic disorders, biochemical aspects, principles of treatment.
5. Hypothalamic-pituitary-thyroid system, the biological role, components, regulation. Thyroid-stimulating hormone: regulation of synthesis and secretion, structure, mechanism of action and target organs, biological effects.
6. Thyroid hormones: chemical structure, regulation of synthesis and secretion, the main stages of the synthesis, mechanism of action and target organs effect on metabolism: processes, regulated by thyroid hormones. Hypo-and hyperthyroidism - metabolic disorders, biochemical aspects. Principles of treatment.
7. Hormonal regulation of absorptive and post absorptive period. Glucagon: biological importance, regulation of synthesis and secretion, mechanism of action, target organs, the effect on metabolism - regulated enzymes and processes.
8. Epinephrine: biological role, chemical structure, reactions of synthesis, regulation of secretion, adrenergic receptors, their distribution, the mechanism of action, depending on the receptor, target organs, effects on metabolism depending on receptor: regulated enzymes and processes.

Hypo- and hyperproduction of epinephrine - metabolic disorders, biochemical aspects. Principles of treatment.
9. Insulin: the biological role, the main stages of the synthesis, regulation of secretion, mechanism of action of insulin, the molecular effects of insulin - the metabolic and mitogenic pathway.
10. Insulin. Very fast, fast, slow, very slow effects. The enzymatic cascade that is associated with the activation of Ras-protein, its scheme, the sequence of events, the main participants, role for cell metabolism, enzymatic cascade that is associated with the activation of phosphoinositol-3-kinase and protein kinase B (AKT), its scheme, the sequence of events, the main participants, role for the cell metabolism. Glucose transporters, their types and tissue localization.
11. Insulin. Effect on metabolism of carbohydrates, lipids and proteins.
12. Diabetes mellitus type 1 and 2. Causes of absolute and relative insulin deficiency. Similarities and differences in metabolic disorders in types 1 and type 2 diabetes. Biochemical mechanisms of clinical manifestations. Causes of insulin resistance. Biochemical mechanisms of diabetes complications.
13. The biochemical diagnostics of diabetes: glucose tolerance test, the concentration of glycosylated hemoglobin (HbA1c) and C-peptide.
14. Changes in metabolism of carbohydrates and lipids in fasting and in stress. Stages of fasting.
15. The growth hormone: regulation of the synthesis and secretion, structure, the target organs, mechanism of action, the role of somatomedins, effect on metabolism - regulated processes, hypo- and hyper production - metabolic disorders, biochemical aspects. Principles of treatment.
16. Vitamin A: sources, structure, active forms, biochemical functions, clinical signs of hypo- and hypervitaminosis. Retinoic acid, its receptors, the role in cell differentiation.

MODULE VII. ROLE OF LIVER IN HOMEOSTASIS. BIOCHEMISTRY OF BLOOD

1. The role of the liver in the metabolism of proteins and other nitrogen-containing compounds. Diagnostic tests (urea, creatinine, plasma proteins), physiologic range, clinical and diagnostic value. Plasma proteins: albumin, α1- and α2-globulins, β-globulins, γ-globulins. Acute phase proteins.
2. Role of the liver in carbohydrate metabolism: homeostasis of blood glucose, its hormonal and metabolic regulation. Diagnostic tests (blood glucose, glucose tolerance test), physiologic range, clinical and diagnostic value.
3. Role of the liver in lipid metabolism: the main stages of the synthesis of triacylglycerols, cholesterol, phospholipids, their hormonal and metabolic regulation; lipoproteins formed in the liver, their structure and role; fatty liver disease, its causes; diagnostic tests (cholesterol, TAG, HDL-Cholesterol, LDL-Cholesterol, atherogenic index), physiologic range, clinical and diagnostic value.
4. The role of the liver in digestion. The composition of bile and its role. The structure and types of bile acids and the reactions of their synthesis. Causes of disorders of synthesis and secretion of bile, consequences.
5. The biotransformation of xenobiotics in the body. The role of the liver in the general scheme of conversion of xenobiotics, its interaction with other organs. The scheme of the process of microsomal oxidation. NADPH-dependent and NADH-dependent pathways. Sources of NADH and NADPH, the components of the electron-transport chains of microsomal system. The role of cytochrome P450. The substrates of microsomal oxidation. Inducers and inhibitors of microsomal oxidation.

6. The process of conjugation. The structure of UDP-glucuronic acid and phosphoadenosine - phosphosulfate. Reactions of formation of conjugated bilirubin and indican. Glycine conjugation, it's role. Metabolism of ethanol. Alcohol dehydrogenase and MEOS pathways. Toxicity of acetaldehyde. Causes of lactic acidosis, ketoacidosis and hypoglycemia in alcohol intoxication.
7. The structure and synthesis of heme. Formation of porphobilinogen, scheme of synthesis of proto-porphyrin IX and its transformation into a heme. Role of ferrochelatase. Regulation of the process. Disorders of the synthesis of heme and hemoglobin: porphyria and thalassemia.
8. The degradation of hemoglobin and formation of bilirubin in the reticuloendothelial system. Transport of bilirubin to the liver. Stages of bilirubin metabolism in the liver. The role of the enzyme UDP-glucuronyl transferase. Steps of bilirubin metabolism in the intestine.
9. Jaundice, types, causes, laboratory criteria. Neonatal jaundice. Pathological jaundice.
10. Metabolism of iron: daily requirement, nutritional sources, mechanism of absorption, transport in blood, mechanism of transport across the cell membrane, storage form. Iron-containing proteins. Regulation of iron metabolism. The role of hepcidin and cytokines.
11. Deficit of iron and excess of iron in organism: causes, biochemical effects and clinical manifestations. Hemochromatosis. Iron deficiency state.
12. Role of blood in transport of oxygen. Scheme of reactions occurring in the erythrocyte in capillaries of lungs and in peripheral tissues. Transport of carbon dioxide. The role of carbonic anhydrase. An influence of processes in erythrocytes on concentration of bicarbonate in plasma. The mechanism of binding of the heme of hemoglobin with oxygen, a role in the regulation of acid-base balance.
13. Acid-base status of the blood. The role of constant concentration of H+ ions. Sources of H+ ions in cells. Key indicators of acid-base balance (pH, pCO2, pO2, HbO2, SO2, anion gap), normal range. Effect of liver, secretion of stomach, pancreas and intestine on acid-base status of the body.
14. The chemical mechanisms of regulation of acid-base status. The buffer system of blood (phosphate buffer, proteins, bicarbonate buffer, hemoglobin). Physiological compensation of acid-base imbalance - the role of the lungs, kidneys and bones, the mechanisms.
15. The main types of disorders of acid-base balance - respiratory acidosis and alkalosis, metabolic acidosis and alkalosis, their causes. Changes of the basic indicators of acid-base status in acidosis and alkalosis.
16. System of hemostasis: role, components. Role of endothelium in hemostasis. Anticoagulant properties of intact endothelium. Pro-coagulant properties of activated endothelium and subendothelial layer.
17. Role of platelets in the blood clotting process. Platelet receptors (GPIIbIIIa, GPIb), their ligands and functions. Vascular-platelet hemostasis. Stages. The mechanism of platelet activation.
18. The secondary hemostasis. Plasma coagulation proteins. General characteristics. Thrombin formation. The functions of thrombin. The conversion of fibrinogen to insoluble fibrin. The role of thrombin and factor XIII.
19. The cell model of blood coagulation, the basic processes occurring at each stage. Stages: initiation, amplification, propagation (formation of fibrin).
20. Vitamin K-dependent coagulation factors. The physiological role of γ-carboxylation. Warfarin, mechanism of action, the main side effects. Vitamin K, food sources, daily requirement, biochemical functions, causes and symptoms of deficiency.

21. Anticoagulants: characterization, function and role: tissue factor pathway inhibitor (TFPI), antithrombin III, heparin, protein C and S. The system of fibrinolysis. The main components of fibrinolytic system (plasminogen, tissue plasminogen activator, urokinase). The main physiological mechanism of activation. Degradation of fibrin by plasmin, degradation products.

MODULE VIII. BIOCHEMISTRY OF TISSUES

1. Metabolism of the kidneys. Features and differences of metabolism in renal cortex and in renal medulla. Aerobic and anaerobic oxidation processes, their localization in the kidney. Gluconeogenesis. Role of kidneys in the synthesis of biologically active substances (creatine, erythropoietin, 1,25-dihydroxycholecalciferol). The processes of formation of urine: filtration, reabsorption and secretion.
2. Water balance. The role of the skin, lungs, gastrointestinal tract and kidneys in removing water. Factors of water balance in the body - blood osmolality, volume of blood, blood pressure, concentration of sodium and potassium. The regulation of water reabsorption. The role of antidiuretic hormone. Hypoproduction of antidiuretic hormone, manifestations.
3. The regulation of sodium reabsorption. Renin-angiotensin-aldosterone system (RAAS). The scheme, role of the RAAS in sodium reabsorption. The mechanism of hypertension in hypoperfusion of kidneys.
4. The role of the kidneys in maintaining the acid-base status – reabsorption of bicarbonate, secretion of H^+, ammonium, excretion of organic acids.
5. General properties of urine: quantity, color, clarity, relative density, pH. Changes in pathological situations. Organic and inorganic components of urine. Pathological components - protein, glucose, bile pigments, ketones, erythrocytes, enzymes.
6. Muscle proteins. The structure of the myofibrils and myofibrillar proteins. Structure and properties of myosin. The enzymatic activity of myosin. Thin (actin) filaments, structure, composition. Structure of the thick filament.
7. Features, stage and the chemistry of muscle contraction. Function of troponin subunits. Energy supply for muscle contraction. The regulation of contraction and relaxation of muscles.
8. Changes in metabolism during muscular work. Features of metabolism in muscle tissue. Types of muscles.
9. Features of the biochemistry of the myocardium and the smooth muscle. The regulation of contractility and relaxation of smooth muscle.
10. The role of oxygen to the myocardium and metabolic disorder of the heart muscle in patients with coronary disease. Effects of reactive oxygen species and lipid peroxidation on the myocardium. Myocardial biochemical changes in patients with coronary heart disease. Modern markers of heart failure. Markers of acute myocardial infarction.
11. White adipose tissue. Functions. Features of carbohydrate and lipid metabolism in white adipocytes. Endocrine function of white adipose tissue.
12. Brown and beige adipose tissue. Functions. Features of the metabolism of brown and beige adipocytes.
13. The proteins of connective tissue: classification, functions. Features of the structure and function of collagen, ellastin, fibronectin. Stages of formation of collagen fibers. The role of vitamins and minerals. Scurvy.
14. Glycosaminoglycans of connective tissue. Features of the structure and function. Matrix metalloproteinases: classification, functions.