QUESTIONS FOR EXAMINATION ON BIOCHEMISTRY

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

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.

MODULE II. MEMBRANES. BIOLOGIC OXIDATION.

6. Tricarboxylic acid cycle. Overview, energetics of the tricarboxylic acid cycle.
9. Macroergic substrates. Classification of high-energy bond containing substances. ATP as universal “energetic currency”.
15. The antioxidant system of the body. Nonenzymatic antioxidants. Enzymatic antioxidant defense 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.
7. Glucose metabolism in liver: role of glucokinase and glucose-6 phosphatase in the maintenance of a constant concentration of glucose in the blood.
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).


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.


20. Pyruvate: metabolic pathways, biologic role, reaction of conversion to acetyl-SCoA and oxaloacetate, the energy balance of oxidation to CO₂ and H₂O.


23. Glucose-alanine cycle. Biologic role in physical exercises and in fasting.


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.


32. The physiological and pathological hyper- and hypoglycemia.


MODULE IV. METABOLISM OF LIPIDS


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.


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.


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 β-oxidation of palmitic acid.

11. Triacylglycerol metabolism in different physiologic states (food intake, fasting, muscle activity).
15. Lipidosis: Tay-Sachs disease, Gauchers disease, Niemann-Pick diseases.

**MODULE V. NITROGEN METABOLISM**


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.


7. Transamination 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.


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.
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
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.
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.
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.

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.


13. The biochemical diagnostics of diabetes: glucose tolerance test, the concentration of glycosylated hemoglobin (HbA1c) and C-peptide.


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


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.


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.
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.
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.
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.
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).

**MODULE VIII. BIOCHEMISTRY OF TISSUES**


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.


4. The role of the kidneys in maintaining the acid-base status – reabsorption of bicarbonate, secretion of H^+, ammonium, excretion of organic acids.


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.


