CLINICAL BIOCHEMISTRY (ELECTIVE COURSE)

Guidelines to prepare for practical classes for students of "General Medicine" and "Dentistry" specialities

МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ
Харківський національний медичний університет

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КЛІНІЧНА БІОХІМІЯ (ЕЛЕКТИВНИЙ КУРС)

Навчальний посібник для підготовки до практичних занять здобувачів вищої освіти освітніх програм «Медицина» та «Стоматологія»

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Clinical biochemistry is an applied science, which is based on theoretical questions and methods of biological chemistry studying in the field of clinical medicine, focusing on the studying of the chemical processes' disturbances and methods of its detection and correction. Nowadays clinical biochemistry is essential for qualified diagnosis, the tactics of treatment and the prognosis assessment under different diseases, the development of screening tests for early diagnosis. Clinical biochemistry (elective course) guidelines is a basis for students preparation for practical classes and background for better understanding the molecular mechanisms of patological states formation, sequence for diagnosis of diseases and its effective correction.

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К 60 Клінічна біохімія (елективний курс) : навчальний посібник для підготовки до практичних занять здобувачів вищої освіти освітніх програм «Медицина» та «Стоматологія» / О.А. Наконечна, С.О. Стеценко, Т.О. Брюханова, А.В. Бондарева. Харків : ХНМУ, 2022. 84 с.

Клінічна біохімія – прикладна наука, яка базується на теоретичних питаннях і методах вивчення біологічної хімії в галузі клінічної медицини, зосереджена на вивченні порушень хімічних процесів та методів їх виявлення та корекції. Сьогодні клінічна біохімія має важливе значення для кваліфікованої діагностики, тактики лікування та оцінки прогнозу при різних захворюваннях, розробки скринінгових тестів для ранньої діагностики. Навчальний посібник з клінічної біохімії (елективний курс) є основою для підготовки здобувачів вищої освіти до практичних занять та підґрунтям для кращого розуміння молекулярних механізмів формування патологічних станів, послідовності діагностики захворювань та їх ефективної корекції.

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Basic

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Class 1 (5 hours)

TOPIC 1: Introduction to biochemistry. Significance of clinical biochemistry for disease diagnosis and management. Metabolism disorders, clinical and laboratory investigation for disease diagnosis.

RELEVANCE. Clinical biochemistry is an applied science, which is based on theoretical questions and methods of biological chemistry studying in the field of clinical medicine, focusing on the studying of the chemical processes' disturbances and methods of its detection and correction. Nowadays clinical biochemistry is essential for qualified diagnosis, the tactics of treatment and the prognosis assessment under different diseases, the development of screening tests for early diagnosis. Clinical laboratory tests take an important place among clinical laboratory tests. Very often biochemical laboratories investigate the blood serum (plasma) and urine. But nowadays, biochemistry technologies improve by new methods. Improving of diagnostic sensitivity and specificity facilitate expanding the amount of biochemical analysis test objects. For example, the condensates of the exhaled air, tear fluid, spinal liquor, saliva are used more and more often in diagnosis. On the other hand, a wide use of modern biochemical analyzers, mass spectrometers, flow cytometry allow a conduction of complex analysis in spite of using small amounts of biological samples.

The preparation of a qualified doctor requires a wide range of knowledge about the molecular basis of life and the causal-weird linkages of processes that occur in an organism. Pathogenesis of almost all pathological states includes different kind of disturbances in the molecules structure and function and also in intermolecular interactions. Metabolism disturbances are manifested by increasing or decreasing of metabolites or end products content in biological material, deficiency of enzymes, which catalyze the specific reactions. Changes in the metabolite's concentration, enzymes activity, and the specific clinical symptoms we can evaluate the type of disturbance in a current metabolic pathway.

AIM OF THE CLASS

1. To understand the subject, tasks, role of clinical biochemistry in the general system of doctor's training.
2. To know biochemical research methods.
3. To study the causes and main mechanisms of carbohydrate metabolism disorders, hypo- and hyperglycemic states; to describe the clinical and laboratory investigations used for diagnosis of these states.
4. To study the causes and main mechanisms of disorders of lipid, protein, nucleotide, porphyrin metabolism; describe the clinical and laboratory investigations used for diagnosis of these states.
5. To study the mechanisms of carbohydrate, lipid, protein metabolism disorders under the diabetes.
6. To study plasma protein composition disorders: hypo-, hyper, para- and dysproteinemia.

THEORETICAL QUESTIONS

1. Clinical biochemistry as a science. Subject, tasks, modern directions of the development.
2. Biochemical research methods and their characteristics.
3*. Typical disorders of carbohydrate metabolism.
4*. Hypo- and hyperglycemia: types, mechanisms of development.
5. Mechanisms of carbohydrate metabolism disorders in diabetes mellitus.
6*. Disorders of carbohydrate metabolism regulation.
7*. Typical disorders of lipid metabolism.
8. Mechanisms of lipid metabolism disorders in diabetes mellitus.
9*. Typical disorders of protein metabolism.
10. Metabolic disorders of phenylalanine, tyrosine, methionine, tryptophan metabolism: clinical symptoms, criteria and methods of diagnosis.
11. Disorders of the blood plasma protein composition (hypo-, hyper-, para- and dysproteinemia).
12. Mechanisms of protein metabolism disorders in diabetes mellitus.
13. Typical disorders of nucleotide metabolism: gout, hereditary orotaciduria.
14. Typical disorders of porphyrin metabolism: porphyria, jaundice.

* – *questions for self-study*

Orientative card for self-study theoretical questions processing

Content	***Instruction for learning activities***
1. Typical disorders of carbohydrate metabolism	***1.1. The main carbohydrate metabolism pathways:*** *– hydrolysis and absorption of food carbohydrates in the gastrointestinal tract;* *– intermediate metabolism: carbohydrate entry into cells and their use: anaerobic and aerobic oxidation of glucose, pentose cycle, gluconeogenesis, fatty acid synthesis → synthesis of triacylglycerols, fructose and galactose metabolism, glycosaminoglycan's metabolism;* *– glycogen as a glucose storage form;* *– glucose renal excretion and reabsorption.* ***1.2. Causes of the main carbohydrate metabolism pathways disorders.*** *Deficiency of amylolytic enzymes as a reason of carbohydrates hydrolysis in the gastrointestinal tract disturbances (intestinal diseases, disturbances of pancreatic juice secretion under the pancreatic diseases, defect in genes encoding enzymes).* *Causes of monosaccharides absorption in the intestine disturbances:* *• decrease in the content of sodium ions (for example, adrenal cortex hypofunction leads to disrupted secondary-facilitated transport of carbohydrates);*

	• substances that reduce the phosphorylation of monosaccharides (as monosaccharides are absorbed only in phosphorylated form); *• disturbances of the intestinal wall blood supply.* *Causes of intermediate carbohydrate metabolism disorders:* *• decreased functional activity of hepatocytes (cirrhosis, hepatitis) → impaired glucose synthesis from lactate → decreased glucose (hypoglycemia) and glycogen in the liver; increase the lactate level in blood (hyperlactataemia) → lactic acidosis;* *• hypoxia → increased anaerobic oxidation of glucose → increased lactate formation → lactic acidosis;* *• hypovitaminosis B1, B2, B3, PP, lipoic acid → decreased synthesis of acetyl-CoA from pyruvate → 1) pyruvate is partially converted to lactate → lactic acidosis; 2) decreased synthesis of acetylcholine → impaired transmission of nerve impulses → impaired sensitivity, paresthesia.* *Causes of glucose storage disturbances:* *• decreased glycogenesis (genetic enzymopathy – glycogen synthase deficiency, liver disease – cirrhosis, hepatitis, endocrinopathy – insulin deficiency in diabetes, thiamine hypovitaminosis, ascorbic acid, hypoxia, etc.);* *• increase in glycogenolysis (increased use of glucose by muscles during intense physical activity, increased synthesis and secretion of contra insular hormones, emotional stress, shock, fever, etc.).* *Glycogenosis – a genetic disease associated with a deficiency / absence of glycogen breakdown enzymes and its overaccumulation in the liver and muscles:* *• hepatic glycogenosis → development in the postabsorptive state of hypoglycemia, hepatomegaly, mental retardation (eg, Bitter disease);* *!!! Gierke disease: glucose-6-phosphatase deficiency → glucose-6-phosphate cannot be converted into glucose, so it goes into the pentose cycle → ↑ formation of ribose-5-phosphate → ↑ synthesis of purines → ↑ their decomposition into uric acid → hyperuricemia → possible gout;* *• muscle glycogenosis → impaired energy supply in myocytes, patients have muscle pain and convulsive disorder, muscle weakness, fatigue (eg, McArdle's disease).* *• mixed glycogenosis.* *Aglycogenosis – a genetic disease associated with a deficiency / absence of glycogen synthesis enzymes and their*

	absence in the liver → fasting hypoglycemia (especially in the morning), convulsions, vomiting → delayed psychomotor and mental development. *<u>Disorders of fructose metabolism:</u>* *• essential fructosuria: fructokinase deficiency → fructosemia → fructosuria (without clinical manifestations);* *• hereditary fructose intolerance: fructose-1-phosphataldolase deficiency (manifested by adding juices, fruits to the child's diet) → 1) fructosemia, fructosuria; 2) increase of fructose-1-phosphate level → a) fructose-1-phosphate has a negative effect on the liver and kidneys functioning; b) fructose-1-phosphate causes inhibition of glycogen phosphorylase → blocking the breakdown of glycogen at the stage of formation of glucose-1-phosphate → clinical manifestations: hypoglycemia, cramps after eating, vomiting and other dyspeptic disorders, liver damage; c) increased phosphorylation of fructose to fructose-1-phosphate leads to hypophosphatemia → increased catabolism of adenyl nucleotides to regulate the phosphate content → increased uric acid formation → hyperuricemia → possible development of gout.* *<u>Disorders of galactose metabolism – galactosemia:</u>* *• Type I – galactose-1-phosphate-uridyltransferase deficiency;* *• Type II – galactokinase deficiency;* *• Type III – uridine diphosphate-galactose-4-epimerase deficiency* ↓ *1) increase galactose content in the blood → conversion of galactose to galactitol → accumulation of galactitol in the blood and tissues → excess galactitol in the eye lens provokes the cataract's development; excess in the brain contributes to the swelling of neurons and the formation of pseudotumors in the brain;* *2) excessive accumulation of galactose-1-phosphate (toxic properties) → a) liver damage (hepatomegaly, steatosis), spleen (splenomegaly), kidneys; b) effect on the activity of carbohydrate metabolism enzymes (phosphoglucomutase, glucose-6-phosphate dehydrogenase).* *<u>Mucopolysaccharidosis</u> – diseases associated with impaired metabolism of glycosaminoglycans in connective tissue as a result of their breakdown enzymes deficiency → accumulation of intact or partially destroyed glycosaminoglycans; clinical symptoms: changes in facial features,*

	skeletal changes, joint deformities, damage of liver, spleen, heart, blood vessels, delayed psychomotor and mental development. *Causes of pentose phosphate pathway of glucose oxidation in erythrocytes disturbances are deficiency of the glucose-6-phosphate dehydrogenase enzyme → manifestations of hemolytic anemia: decrease in NADPH2 production → decrease of reduced glutathione level → intensification of lipid membrane peroxidation; clinical symptoms are observed after eating Vicia faba beans (favism), salicylates (acetylsalicylic acid, sulfadimethoxine, etc.), antimalarial drugs (primaquine, acridine), etc.* *Renal blood supply disturbances→ decreased glomerular glucose filtration → decrease of glucose filtration and increase of its reabsorption in the kidney's proximal tubules → lack of glucose in the urine under hyperglycemia conditions (exceeding the renal threshold of 8.8–9.9 mm/l).* *Proximal tubulopathy → decreased reabsorption due to decreased activity or deficiency of enzymes that provide this process → renal glucosuria (glucose may appear in the urine even under normal conditions or hypoglycemia)*
2. Hypo- and hyperglycemia types, mechanisms of development	***2.1. Hypoglycemia*** *– a decrease in blood glucose level less than 3.3 mM/liter.* *2.1.1. Types of hypoglycemia:* *• physiological: compensatory secretion of insulin caused by alimentary hyperglycemia, in women during lactation, during heavy and prolonged physical exercises, prolonged mental stress (because of increased glucose utilization by tissues);* *• exogenous: insufficient intake of carbohydrates from food, overdose of insulin, oral hypoglycemic and other drugs, alcohol consumption;* *• endogenous: impaired carbohydrate absorption, insulinoma, hyperplasia of pancreatic beta cells, extrapancreatic tumors, decreased glycogen synthesis and gluconeogenesis under severe liver damage conditions, deficiency of contra insular hormones, elimination of glucose because of its reabsorption, genetic disturbances of glucose metabolism (deficiency of 1,6-diphosphatases, hepatic glycogenosis, impaired fructose tolerance, etc.)* *2.1.2. The mechanism of hypoglycemia formation: decrease of blood glucose level → 1) deficiency of glucose*

	supply and decrease its level in the brain → decrease in oxygen use → decrease in ATP synthesis → disruption of Na + / K + and Ca2 + / Mg2 + -pumps → disturbance in ion gradients → depolarization of neurons → weakness, irritability, convulsions; 2) compensatory increasing of contra insular hormones secretion; 2) stimulation of the sympathoadrenal system → increased secretion of catecholamines → tachycardia, agitation, hyperhidrosis, tremor, hypertension. ***2.2. Hyperglycemia** - an increase in blood glucose above 6.1 mM/liter.* *2.2.1. Mechanism of hyperglycemia formation: decrease of glucose utilization by cells → activation of glycogenolysis and gluconeogenesis.* *2.2.2. Types of hyperglycemias:* *• physiological: alimentary (overconsumption of easily digestible carbohydrates that provoke a temporary increase of blood glucose level, emotional stress (activation of the sympathoadrenal system → increased secretion of catecholamines, glucocorticoids, glucagon, prolactin → hyperglycemic effects of hormones);* *• pathological: endocrine disorders associated with insulin deficiency, hyperproduction of contra insular hormones (glucagon, corticotropin, glucocorticoids, somatotropin, prolactin, thyroxine, triiodothyronine, etc.); liver diseases accompanied by activation of glycogenolysis and inhibition of glycogenesis; convulsive states (increased muscle glycolgenolysis → increased lactate formation → activation of lactate gluconeogenesis in the liver); anesthesia (excitation of sympathetic centers → increased adrenaline secretion), etc.*
3. Disturbances of carbohydrate metabolism	*3.1. In our organism there is a neuroendocrine regulation of carbohydrate metabolism under physiological conditions by glycogenesis, glycogenolysis, conversion of glucose to triacylglycerols, gluconeogenesis, glycolysis.* *3.2. Disturbances of carbohydrate metabolism neuroendocrine regulation due to:* *• stress reactions, psychic excitement, etc. → activation of sympathoadrenal, hypothalamic-pituitary-adrenal and thyroid systems → increased secretion of hormones – catecholamines, glucocorticoids, T3, T4 → activation of glycolgenolysis, gluconeogenesis, decreased glycogenesis → hyperglycemia;*

	• firing of parasympathetic neurons→ increased insulin secretion → decreased blood glucose (hypoglycemia); *• changes in the ratio between insulin and contra insular hormones;* *• diabetes mellitus: insulin-dependent type (type I), non-insulin-dependent type (type II); clinical manifestations: dry mouth, polyuria, polydipsia, polyphagia, change in body weight (in the case of type I – decrease of body mass, in the case of type II – obesity), etc.; blood parameters: hyperglycemia, ketonemia, metabolic acidosis, increase of glycated hemoglobin level (> 6 %), increase in C-peptide, etc.*
4. Typical disorders of lipid metabolism	*4.1. The main pathways of lipid metabolism.* *– digestion and absorption of food lipids in the gastrointestinal tract;* *– transport of lipids in the blood stream, lipoprotein metabolism;* *– breakdown and mobilization of fats;* *– intermediate metabolism: fatty acid metabolism, ketone body metabolism, cholesterol and its derivatives - bile acids, phospholipid metabolism.* *4.2. Causes of the main pathways of lipid metabolism disorders.* *<u>Disorders of lipid digestion and absorption in the gastrointestinal tract</u> are caused by:* *• pancreatic lipase deficiency (pancreatitis, pancreatic necrosis, etc.) → disturbance of the fat's breakdown in the small intestine;* *• insufficiency of bile acids in the intestine (hepatitis, cirrhosis, cholecystitis, obstructive jaundice, etc.) → disturbance of fats emulsification and breakdown, abnormality of micelles formation;* *• damage of the intestinal epithelium by infectious and toxic agents (enterocolitis of various genesis);* *• hormonal disorders → for example, deficiency of adrenal hormones, including excess adrenaline secretion leads to reduce of fats absorption;* *• deficiency of gastrointestinal tract hormones (cholecystokinin, secretin, etc.) → disturbance of gallbladder walls contraction regulation, abnormality of the emulsification and breakdown of fats processes, disturbances of fats transfer through the intestinal wall;*

	• disorders of lipid metabolism in intestinal cells with the formation of abnormal protein-lipid complexes → decreased fat absorption → the formation of fat accumulations in the intestinal wall, small lymphatic ducts → blockage of lymphatic outflow.
	Impaired digestion and absorption of lipids → excess lipids in feces – steatorrhea → hypovitaminosis of fat-soluble vitamins, deficiency of essential polyunsaturated fatty acids, which leads to impaired synthesis of biologically active substances from arachidonic acid – prostaglandins, thromboxanes, leukotrienes. *Disorders of lipoprotein metabolism – dyslipoproteinemia: conditions characterized by deviations from the normal content, structure and ratio in the blood of different lipoproteins fractions.* *• Hyperlipoproteinemia – a disturbance of the formation, transport and metabolism of lipoproteins, which is manifested by a steady increase in blood cholesterol and/or TAG; main causes: lipoprotein lipase deficiency/defect, decreased density/affinity of lipoprotein receptors, apoprotein deficiency / defect.* *• Hypolipoproteinemia - conditions characterized by a decrease in the content of TAG in the blood → 1) primary: as a result of insufficient of apo-B, deficiency and/or defect of apo-A; 2) secondary: as a result of prolonged starvation, indigestion and/or absorption.* *!!! Disorders of lipoprotein metabolism – the main link in the pathogenesis of atherosclerosis, coronary heart disease, hypertension, pancreatitis etc.* *Obesity – overaccumulation of TAG in adipocytes:* *• absolute or relative insufficiency of leptin (adipose tissue hormone) → increase the synthesis of neuropeptide Y in the hypothalamus → formation disturbances in eating behavior (hunger) → increase in appetite → excessive food intake;* *• insufficiency of thyroid hormones → reduction of lipolysis → reduction of metabolic rates in tissues and energy expenditure;* *• increased synthesis and secretion of glucocorticoids → activation of gluconeogenesis → hyperglycemia → increased glucose transport to adipocytes → increased synthesis of TAG from glucose → accumulation of TAG in adipocytes;*

	• hyperinsulinism → activation of lipogenesis; *• overconsumption of high-calorie food against the background of reducing energy expenditure;* *• mental disorders that are accompanied by a constant desire to eat, for example, provoked by increased activity of serotonin, dopamine, opioidergic systems, which are involved in the formation of feeling of satisfaction;* *• damage of ventromedial and paraventricular nuclei neurons in the hypothalamus (concussion, tumors, encephalitis) → increased synthesis of neuropeptide Y.* *!!! Obesity is a risk factor for hypertension, coronary heart disease, diabetes, diseases of the hepatobiliary system (steatosis), etc.* *The main causes of <u>steatosis</u> formation (fatty liver, liver fatty infiltration) – excessive accumulation of triacylglycerols in hepatocytes, followed by their substitution by connective tissue:* *• disturbances of the synthesized lipoproteins secretion into the blood (for example, damage of membranes with lipid peroxidation intensification and reduction of antioxidant sources);* *• relative deficiency of apoproteins and phospholipids with an excess content of triacylglycerols;* *• deficiency of proteins or essential amino acids in food, toxins and inhibitors affect on protein biosynthesis, which leads to a lack of apoproteins;* *• decreased synthesis of phospholipids associated with the absence of lipotropic factors (methionine, choline, vitamins, polyunsaturated fatty acids), which inhibit the formation of lipoprotein particles membranes;* *• disturbances of lipoproteins formation in the EPR under intoxication conditions.* *<u>Disorders of cholesterol metabolism:</u>* *• hypercholesterolemia: stress (activation of the sympathetic nervous system → increased secretion of catecholamines → activation of lipolysis and cholesterol biosynthesis), inhibition of intestinal and biliary peristalsis, mechanical jaundice (impaired cholesterol excretion from the organism), hypothyroidism and hypercorticism and other endocrine disorders (in this case the reduction of the endogenous cholesterol biosynthesis takes place),*

	excess fat and refined carbohydrates, hereditary defects in cholesterol metabolism enzymes, and others. *!!! Hypercholesterolemia is a risk factor for the development of atherosclerosis, coronary heart disease, obesity, xanthomatosis, cholesteatosis (deposition of cholesterol and its esters in the parenchymal organs with the subsequent development of cirrhosis), etc.* *• hypocholesterolemia: liver disease, hyperthyroidism, hereditary α-, β-lipoproteinemia, insufficient intake of cholesterol rich food, increased excretion of cholesterol under diarrhea conditions, etc.* *!!! Hypocholesterolemia leads to cell membrane damage and disturbance of barrier function, cytolysis, decreased bile acid synthesis and, as a consequence, to impaired digestion, synthesis and secretion of steroid hormones, neurological disorders (ataxia, paresthesia), accompanied by changes in the structure of myelin nerve fibers and nerve conduction pulses, etc.* *<u>Atherosclerosis</u> – a chronic focal lesion of the arteries with deposition in their inner shell (intima) of apoprotein-B-containing lipoproteins and cholesterol, accompanied by structural and cellular changes and growth of connective tissue in the blood vessels middle membrane (media) with the formation of blood vessels fibroids, which leads to local and general circulatory disorders. There are pathological changes in metabolism of cholesterol and lipoproteins in the early stages of atherosclerosis: the content of atherogenic particles in the blood increases, cholesterol is the main component of them, and the protein component is apo-B → local oxidation of LDL → accumulation of modified LDL → atherosclerosis plaque formation. In case of antiatherogenic HDL small amount there is an accelerated atherogenesis takes place even at low level of cholesterol.* *!!! Atherogenic factors - cholesterol, LDL, triacylglycerols, saturated fatty acids.* *!!! Antiatherogenic factors – phospholipids, polyunsaturated fatty acids, HDL.* *<u>Gallstone disease</u> – a disease of the hepatobiliary system caused by impaired metabolism of cholesterol and/or bilirubin, accompanied by the formation of stones in the gallbladder and bile ducts. Reasons:*

	• high content of cholesterol in bile, for example, as a result of reduced biosynthesis of bile acids, which normally maintain cholesterol in bile in a dissolved state; *• deficiency of lecithin, which is broken down with the formation of bile acids;* *• motility disorders of the gallbladder → bile stasis;* *• high content of bilirubin in bile.* *Lysosomal diseases of lipid accumulation: unlike triacylglycerols, other lipids (in particular, sphingolipids and glycolipids) do not perform reserve-energy functions → their accumulation in organs is associated with a hereditary defect of lysosomal enzymes of their decomposition → damage of organs with the most intense glycolipids metabolism - the brain, moreover – organs that rich in macrophages - liver, spleen.* *• Gaucher disease: β-glucocerebrosidase deficiency → accumulation of glucocerebroside in cells of the reticuloendothelial system (liver, spleen, bone marrow) → hepatosplenomegaly, hemorrhagic syndrome, bone pain, defects of joint mobility.* *• Tay-Sachs disease: hexosaminidase deficiency → accumulation of gangliosides in the brain, retina → decline of mental and physical abilities, speech problems, blindness and deafness, muscle atrophy.* *• Neiman-Pick disease: sphingomyelinase deficiency → accumulation of sphingomyelin in cells of the reticuloendothelial system and brain → lesions of the brain and internal organs, physical development, hepatosplenomegaly, muscle hypotension, blindness and deafness.* *Ketonemia – an increase in the level of ketone bodies (acetoacetic, β-oxybutyric acids) in the blood (norm 0.1–0.6 mm/l) as a result of increased but insufficient complete oxidation of fatty acids, which in most cases is associated with a decrease of carbohydrate reserves (starvation, heavy exercise, diabetes, prolonged excitation of the sympathetic nervous system, etc.).*
5. Typical disorders of protein metabolism	*5.1. The main pathways of protein metabolism:* *– digestion of proteins in the gastrointestinal tract;* *– transmembrane transfer of amino acids (absorption of amino acids);* *– use of amino acids for: proteins biosynthesis, biosynthesis*

	of biologically active substances (enzymes, biogenic amines, hormones, nucleotides, vitamins, creatine, etc.), participation in the Krebs cycle in energy deficiency, gluconeogenesis, etc. *– neutralization of ammonia in the liver (ornithine cycle of urea formation) and kidneys (formation of ammonium salts).* *5.2. Causes of the protein metabolism main pathways disorders.* *<u>Imbalance between the amount of dietary proteins and their normal amino acid composition:</u>* *• the causes of protein intake insufficiency are disorders of eating, digestion and absorption → protein starvation; the most severe manifestations are: 1) kwashiorkor – unbalanced dietary protein deficiency → weight loss, severe hypoproteinemia, hypolipoproteinemia, negative nitrogen balance, anemia, edema, immunodeficiency, delayed physical and mental development, etc.; 2) alimentary dystrophy (alimentary insanity) – relatively balanced protein deficiency → increased mobilization of muscle proteins, bones, skin → weight loss, negative nitrogen balance, immunodeficiency, hypoglycemia, ketonemia, ketoacidosis, delayed physical and mental development, etc.;* *• causes of excess intake and/or assimilation of proteins are overeating, unbalanced diet, increased protein synthesis in diabetes and hypersecretion of somatotropin, etc. → increase of nitrogen-containing products – amino acids, ammonia → acidosis, dystrophic changes in brain tissue and parenchymal organs, positive nitrogen balance, hyperproteinemia, dyspeptic disorders, etc.* *• imbalance of the amino acid composition of consumed proteins: 1) deficiency of essential amino acids → negative nitrogen balance, reduced growth and development, reduced plastic processes in organs and tissues, body weight, appetite, specific manifestations (eg tryptophan deficiency – pellagra-like dermatitis, anemia, hypoproteinemia, with methionine deficiency – increased atherogenesis, obesity, hypocatecholaminemia); 2) excess intake and/or biosynthesis of amino acids → decreased appetite, body weight, disorders of other amino acids metabolism, organ and tissue functions, moreover, specific manifestations (eg, excess methionine – hemolytic anemia, liver failure; phenylalanine – psychomotor development delay).*

	Disorders of protein digestion: *• in the stomach due to hypoacid states, decreased pepsin activity, resection of the stomach, etc .;* *• in the intestine due to the action of various factors, including hereditary, causing digestive disorders, including malabsorption syndrome.* *Disorders of transmembrane transfer of amino acids due to various genesis membranopathy → disruption of transport from the intestine into the blood; from blood to hepatocytes and other cells and tissues; from primary urine into the blood → protein dysfunction, protein starvation.* *Disturbances of protein biosynthesis due to their absence in food, energy deficiency in cells, disorders of neuroendocrine regulation, pathology of matrix synthesis → 1) insufficient renewal of structural proteins → development of dystrophic disorders in organs and tissues; 2) slowing down regenerative processes; 3) delay in mental and physical activity; 4) decreased synthesis of hormones, enzymes, accompanied by the development of endocrinopathies, metabolic disorders; 5) decrease in production of antibodies and other protective proteins → decrease in immunological reactivity of an organism; 6) reduction of oncotic blood pressure, etc.* *Hereditary disorders of amino acid metabolism (primary aminoacidopathies) – a defect of various enzymes → the main clinical manifestation - metabolic encephalopathy:* *• phenylketonuria → phenylalanine hydroxylase deficiency (phenylalanine-4-monooxygenase) or tetrahydro-biopterin (phenylalanine hydroxylase cofactor);* *• tyrosinemia (tyrosinosis) → fumarylacetoacetylase deficiency (type I), tyrosine aminotransferase (type II), 4-hydroxyphenylpyruvate hydroxylase (type III);* *• alkaptonuria → deficiency of homogentisic acid dioxygenase;* *• albinism → deficiency of melanocyte tyrosinase;* *• hyperhomocysteinemia → deficiency of cystathionine synthetase, methionine synthetase or methyltetrahydrofolate reductase;* *• histidinemia → deficiency of histidase;* *• hyperlysinemia → deficiency of lysine-α-ketoglutar-reductase;* *• leukemia → deficiency of branched chain α-keto acids dehydrogenase;*

	• *hyperglycinemia → deficiency of glycine cleavage enzyme.* *Disturbances of the protein metabolism final stages:* • *hypernitrogenemia (azotemia) - increasing level of residual nitrogen in the blood! 14.3-28.6 mM / l): 1) productive hypernitrogenemia: disturbance of urea synthesis → decrease the urea level in the blood and urine → increase residual nitrogen level; 2) retention hypernitrogenemia: disturbance of the kidneys excretory function, patency of the urinary tract; 3) mixed form of hypernitrogenemia: a combination of increased protein breakdown in tissues with insufficient excretion in the urine;* • *hyperammonemia – increase in blood ammonia levels due to disorders of its neutralization reactions (genetic defects of enzymes of the ornithine cycle, liver damage due to cirrhosis, hepatitis and other diseases; clinical manifestations: vomiting, nausea, confusion, convulsions, speech disorders, etc.*

TASKS FOR SELF-CONTROL

1. Some person has a hereditary disease associated with a deficiency of the carbohydrate metabolism enzyme. When one of the carbohydrates enters to the blood it leads to increasing of its phosphorylated form level. Symptoms are fructosuria, hepatomegaly, vomiting. The most dangerous complication of the disease is hypoglycemia.

– *Indicate the deficiency of what enzyme takes place in this case and the reaction it catalyzes.*

– *Explain the mechanism of hypoglycemia development in this disease.*

– *What food should be excluded from the diet in this disease?*

2. The patient has sclera and skin yellowing, colorless stool and dark urine. The content of total bilirubin in the serum is increased by the increasing of direct bilirubin fraction.

– *What kind of jaundice does the patient have?*

– *Name the possible causes of jaundice.*

– *Explain the increasing of direct bilirubin in the blood.*

3. A number of enzymes are involved in carbohydrates digestion. One of them is active in early childhood. In some adult people the activity of the enzyme is significantly reduced that leads to diarrhea after drinking whole milk.

– *Name the enzyme and the reaction it catalyzes.*

– *Why not all adults have reduced activity of this enzyme?*

– *Why does diarrhea occur when the enzyme is deficient?*

4. The child lived for a long time in a troubled family. Examination of the child revealed edema, physical and mental retardation, muscle atrophy but with the subcutaneous fat layer. Biochemical analysis of blood showed severe hypoproteinemia (mainly hypoalbuminemia), hypolipoproteinemia, negative nitrogen balance.

– *Name the most probable diagnosis. Justify the answer.*

5. The patient complained of radicular pain in the lumbosacral region, headache, general weakness. For three years proteinuria and hypertension are observed, on the radiograph rounded foci of destruction in the bones of the pelvis and spine. In the biochemical analysis of blood - increased protein levels at normal levels of albumin and globulins, increased erythrocyte clotting rate. In the biochemical analysis of urine - protein level 1.2 g/l, a positive reaction to Bence-Jones proteins.
– *What pathology can be assumed. Justify the answer.*
6. A young man appointed to a doctor. On examination: complaints of heart pain, xanthomas along the tendons of the muscles, xanthomas in the Achilles tendon. At ophthalmoscopy: the presence of gray-white deposits on the periphery of the cornea. The lipid profile of the blood indicates an increase in cholesterol, LDL.
– *What disorder of lipid metabolism can be suspected? Justify the answer.*
7. Diabetes mellitus is accompanied by changes in the metabolism of many compounds, including lipids. In particular, the level of ketone bodies in the blood increases, which can lead to the development of ketoacidosis.
– *Why does the level of ketone bodies increase in diabetes?*
– *Why does ketoacidosis lead to neuropathy?*
8. Absorption of food ingredients from the gastrointestinal tract begins immediately after ingestion and remain about 2–4 hours. At this time, the content of glucose, amino acids, lipids in the blood increases. 4–5 hours after a meal comes the phase of post absorption.
– *Which of the pancreatic hormones predominates in the blood in the absorptive phase, and which - in the post absorbent phase?*
– *Which metabolic pathways are enhanced in the absorptive phase in the liver, muscle, and adipose tissue, and which in the postabsorptive phase?*
9. Hyperglycemia in diabetes is accompanied by serious changes in the metabolism of many organs and systems.
– *Name the main causes of hyperglycemia in type 2 diabetes.*
– *Why and how could hemoglobin function change in diabetes?*
– *How could this affect the heart muscle?*
10. A 7-month-old child was diagnosed with severe megaloblastic anemia, which cannot be treated with folic acid, and deposits of orotic acid crystals in soft tissues. There is an exceed concentration of orotic acid in the urine.
– *What diagnosis can be assumed?*
– *What process is disrupted?*
11. The child has anorexia, vomiting, irritability, enlarged liver, spleen and lymph nodes, decreased visual acuity, cessation of general development, loss of motor skills. Diagnosis: Neiman-Pick's disease.
– *What group of diseases does this pathology belong to?*
– *What are the causes and consequences of these diseases?*
– *Which enzyme deficiency is observed in a child? What reaction does it catalyze?*
– *Which substance accumulates?*

12. The synthesis of fatty acids takes place in the absorbent period in the cytoplasm of cells with acetyl-CoA, synthesized in mitochondria in the process of oxidative decarboxylation of pyruvate.
– What substance is the main source of pyruvate for the synthesis of fatty acids?
– Why in these conditions the use of acetyl-CoA for the synthesis of fatty acids increases and its oxidation in the TCA is inhibited?
– How is acetyl-CoA transported to the cytoplasm?
13. A patient complained of frequent diarrhea with elevated stool lipids.
– What can be the causes of this condition?
14. A child who is breastfeeding often vomits, loses weight. After some time, jaundice, hepatomegaly and clouding of the lens of the eye are observed.
– What pathology can be assumed?
– What metabolic disorder is the pathology associated with?
– Defect of which enzyme causes these symptoms?
– Explain the cause of clouding of the eye lens?
15. Urine of the newborn provides a green color in the test with a solution of ferric chloride. The colored product is formed by the reaction between the reagent and the metabolic product of one of the amino acids. This test indicates the presence of a hereditary disease that results in severe mental retardation. The therapeutic strategy for this disease is a diet low in this amino acid.
– Name this disease.
– Which enzyme defect leads to this pathology?
– What amino acid metabolism is disturbed?
– Why do some patients have fair skin and hair?
16. The child has an enlarged spleen, erythema of the skin, increased sensitivity to sunlight, there is a clinic of hemolytic anemia, leukocytosis. Urine is colored bright red.
– The presence of which pathology can be assumed?
– Deficiency of what factor observed under this pathology?
– What metabolic process disturbance underlies this disease?
17. The child has mental retardation, ectopia of eye lens, osteoporosis, scoliosis, thromboembolism, elevated blood levels of methionine and homocysteine.
– What pathology can be suspected?
– What causes this pathology?
18. The patient complains of skin and sclera yellowing, which occurred during the last week.
– What results of laboratory tests can be expected if jaundice is caused: a) under autoimmune destruction of erythrocytes; b) in a case of bile ducts tumor; c) acute viral hepatitis?
19. Name the pathologies that characterized by excessive amounts of following substances in urine: *1) glucose, acetoacetate, beta-hydroxybutyrate; 2) phenylpyruvic acid, phenylacetic acid, phenyl lactate; 3) albumin.*

20. A two-year-old child has developmental delay, signs of self-aggression. Biochemical study showed severe hyperuricemia.
– *What pathology can be assumed?*
– *What enzyme defect takes place under this pathology?*
– *What process disturbance is the cause of this pathology?*
21. The patient has pellagra-like skin lesions, mental disorders, ataxia. Urine analysis: hyperaminoaciduria, increased amount of indolylacetate, indolylacetylglutamine, indican.
– *What disease can be assumed in this patient? Justify the answer.*
22. The child has periodic attacks of weakness on an empty stomach, periodic loss of consciousness, convulsions. A small child with thin limbs and a big belly. The child has hepatomegaly. Biopsy revealed a significant accumulation of glycogen.
– *What pathology can be suspected in a child?*
– *What factor defect can lead to these clinical manifestations?*
23. Methionine – an essential amino acid for the human body. The active form of this amino acid – S-adenosylmethionine is involved in the methylation reactions of various compounds as a donor of a methyl group.
– *Why methionine used in fatty liver disease and through what mechanisms is its therapeutic effect realized?*
– *How will the long absence or insufficiency of methionine in the diet affect the state of myocytes?*
24. A woman, playing volleyball, lost consciousness. No anamnestic data are known. Examination shows traces of injections on the anterior abdominal wall, on the pads of the fingers. The skin is sticky, the reaction of the pupils to light is weak. Blood pressure – 140/70 mm Hg, heart rate – 90 beats/min. The glycemic level is 1.5 mM/l.
– *What happened to the woman?*
– *What disease can provoke this condition?*
– *What drug should a woman inject?*
– *What types of comatose states can be observed in this disease?*
25. The patient has a hereditary defect of the ornithine cycle. He was prescribed phenylacetate and benzoate.
– Name the main enzymes – regulators of the formation and elimination of ammonia.
– What diet should be recommended to the patient?
– How will the content of urea and ammonia in the blood change under this pathology?
– Explain the mechanism of action of phenylacetate and benzoate.
26. A patient with type I diabetes was advised to increase dietary fats as an energy source.
– *Name the causes of type I diabetes.*
– *Which liver enzyme deficiency is found in patients with diabetes?*
– *How do glucose oxidation processes change in patients with diabetes?*
– *What alternative energy sources can cells use in diabetes?*

27. The obese patient is recommended to go on a medical starvation for several days.
– Name the sources of energy in the human body that can used during starvation?
– How will the hormonal background of the body change during the period from the absorbent state to the postabsorptive state?
– How will the level of the main energy source change during fasting for a few hours?
– How will fasting glucose metabolism change?
28. The child has darkening of the sclera, mucous membranes, nasal cartilage and auricles, urine darkens in the air.
– What disease can be suspected?
– What can provoke the dark color of urine?
– What type of metabolism is disturbed in this disease?
– What is the reason of the pathology?
29. The child has: delayed physical and mental development, deep disorders of the connective tissue structure. Keratan sulfates are found in urine.
– What pathology can be assumed?
– What type of metabolism is disturbed in this pathology?
30. At the patient while examination cone-shaped consolidations in the joints, signs of a nephrolithiasis are revealed. History of two sudden attacks with severe pain and swelling of the big toe, followed by complete remission within 1–2 weeks.
– What diagnosis can be assumed?
– Indicate which metabolite needs to be determined in blood plasma to confirm the diagnosis.
31. To determine the cause of hypoglycemia in newborns, a glucagon test was performed, which did not cause an increase in blood glucose levels.
– What are the effects of glucagon in increasing of blood glucose levels?
– Name the possible reasons for the lack of hyperglycemic effect of glucagon.
– What biochemical tests could diagnose the state of the child?
32. With prolonged stress, diabetes, the content of neutral fat in fat depots decreases and the concentration of free fatty acids in the serum increases.
– Which process is activated? Name the regulatory enzyme of this process
– Explain the mechanism of process activation under prolonged stress?
– Indicate the reasons for the increased activity of the process in diabetes.
33. The girl has hemolytic anemia. Pyruvate kinase deficiency in erythrocytes was established.
– What metabolic process in erythrocytes is disturbed in this case?
– What reaction is catalyzed by pyruvate kinase? What is the value of this reaction?
– Explain the reasons for the development of erythrocytes hemolysis under these conditions.

34. Consumption of large carbohydrates amounts enhances lipogenesis in the liver and adipose tissue.
– *Which carbohydrate catabolism products are metabolic precursors for fat synthesis?*
– *What is the difference between fat biosynthesis in the liver and in adipose tissue?*
– *What hormones regulate lipogenesis in adipose tissue?*
35. A child with a point gene mutation has deficiency of glucose-6 phosphatase, also hypoglycemia and hepatomegaly.
– *What is the pathological condition observed in this case?*
– *What reaction does this enzyme catalyze?*
– *How could the activity of the pentose phosphate cycle change under these conditions?*
36. A patient with atherosclerosis after long-term use of statins (drugs that inhibit cholesterol synthesis) developed ketoacidosis.
– *Indicate the general stages in the synthesis of ketone bodies and cholesterol.*
– *Why was the synthesis of ketone bodies activated under these conditions?*
– *Name the normal rate of ketone bodies in the blood.*
37. A chemical worker who has worked with organic solvents for a long time has been diagnosed with fatty liver disease. Lipotropic substances were used for treatment.
– *Describe the mechanism of fatty liver development under these conditions.*
– *What are "lipotropic" substances?*
– *Explain the mechanism of carnitine and choline lipotropic action.*
38. A biochemical study revealed that the activity of oxidative phosphorylation in the cytoplasm of hepatocytes is reduced.
– *How does the ATP / ADP ratio change in hepatocytes?*
– *How does the activity of anaerobic glycolysis change under these conditions?*
– *Explain the mechanism of glycolysis enzyme activity regulation.*
39. In a patient with diabetes, many fatty inclusions were found during the liver biopsy.
– *What pathological process can be suspected.*
– *Indicate the mechanism of development of this pathological process.*
– *Explain the feasibility of enriching a woman's diet with vitamins B6, B9, B12 and B15?*
40. A woman diagnosed with gallstone disease was prescribed chenodeoxycholic acid.
– *Name the main causes of cholesterol crystallization?*
– *Why the patient prescribed chenodeoxycholic acid?*
– *Why does this disease occur more often in women?*
41. During prolonged starvation, proteins are broken down into amino acids.
– *In which process are amino acids involved under these conditions?*
– *What amino acid is actively involved in this process?*
– *What other substances can be involved in this process?*
42. The patient was diagnosed with hypoglycemia on an empty stomach, pyruvate carboxylase deficiency was detected during the liver biopsy.
– *What reaction is catalyzed by pyruvate carboxylase? Name the coenzyme.*
– *Decreased activity of which process is observed in the patient?*
– *Is it advisable to prescribe aspartate to the patient?*

43. A 7-month-old child has vomiting and diarrhea after consuming fruit juices. Fructose consumption leads to hypoglycemia.
– *What pathological condition has the child?*
– *What enzyme deficiency is observed under these conditions?*
– *Explain the cause of hypoglycemia after fructose consumption.*
44. According to observations – the child is lethargic, apathetic. In the morning on an empty stomach, she often has cramps. Liver biopsy revealed a significant deficiency of glycogen.
– *What pathological condition has the child?*
– *Which enzyme deficiency occurs?*
– *What is the reason for the convulsions?*

Class 2 (5 hours)

TOPIC 2: Basic biochemical parameters for diseases diagnosis.

RELEVANCE. Improving laboratory diagnostics is one of the urgent tasks of modern practical medicine. The search for new effective and affordable methods of assessing the state of metabolism is a promising section of laboratory medicine. Blood tests have had an evidenced diagnostic value until recently. But a lot of studies conducted by biochemists and clinicians have provided a diverse database that reveals the informativeness of the diagnostic criteria for various diseases. Moreover, the effective clinical biochemistry study is based on the analysis of laboratory parameters and understanding the mechanisms of diseases pathogenesis. In addition, clarifying the levels of biochemical research, assessing the functional role of the studied parameters, the correct use of laboratory test profiles leads to right assessment of the organism's, organs and tissues current state. The set of laboratory tests is conditionally divided into groups: Group 1 – tests in the system of patient's obligatory examination: hematological (detailed blood test), clinical (urine, feces), biochemical (metabolic parameters, such as blood glucose, etc.); Group 2 – particular disease-specific tests; Group 3 – tests for the diagnosis of comorbidities.

One of the modern clinical biochemistry directions is the creation of research algorithms, identification of abnormalities with the interpretation of physiological or pathological states, the formation of diagnostic assumptions and diagnosis confirmation. Future doctors should know all basic parameters of biochemical analysis and have to know the strategy of biochemical parameters for a particular case selection, analyze their changes for diagnose and choosing of treatment tactics.

AIM OF THE CLASS.

1. Basic parameters of biochemical analysis.
2. Clinical and diagnostic value of protein, carbohydrate, lipid, pigment, mineral metabolism indicators in biological fluids.
3. Clinical and laboratory investigations of diabetes mellitus diagnosis and management.
4. Assimilate indicators of acid-base status and gas composition of blood and their clinical and diagnostic value.
5. To describe the clinical and diagnostic value of the hormonal profile and enzyme activity in biological fluids.

THEORETICAL QUESTIONS

1. Clinical and diagnostic value of protein metabolism indicators determination in biological fluids:
   –* total protein and protein fractions content;
   –* specific serum proteins content;
   – total nitrogen;
   – urea;
   – creatine and creatinine;
   – uric acid.
2. Clinical and diagnostic value of carbohydrate metabolism indicators determination in blood:
   – glucose;
   – pyruvic acid;
   – lactic acid;
   – fructose and galactose;
   –* carbohydrate-containing proteins and their components (seroglycosides, glycated hemoglobin, fructosamine, sialic acids).
   – activity of enzymes involved in carbohydrate metabolism.
3.* Clinical and laboratory diagnosis and monitoring of diabetes mellitus.
4. Clinical and diagnostic value of blood lipid profile determination:
   – cholesterol;
   – triacylglycerols;
   – lipoproteins;
   – coefficient of atherogenicity;
   – ketone bodies;
   –* apolipoproteins.
5. Clinical and diagnostic value of pigment metabolism determination in the blood: total bilirubin and its fractions.
6.* Clinical and diagnostic value of acid-base status and gas composition determination in blood.
7.* Clinical and diagnostic value of some mineral metabolism indicators determination in blood.
8. The value of the hormones content determination for the endocrine system disorders diagnosis.
9. Clinical and diagnostic value of enzymes activity determination in blood and urine (aminotransferases, γ-glutamyltranspeptidase, glutamate dehydrogenase, alkaline and acid phosphatase, creatine kinase, lactate dehydrogenase, amylase, lipase, cholinesichenase, lecinesiterase).

* – questions for self-study

Orientative card for self-study theoretical questions processing

Content	***Instruction for learning activities***
1. Clinical and diagnostic value of total protein and its fractions determination in biological fluids	*In clinical laboratory diagnosis, the main approaches to assess the state of protein metabolism are:* *• determination of total protein content in the blood;* *• determination of the protein fractions content in blood for the assessment of proteins deficiency or excessive content;* *• determination of the specific proteins content in the blood, in particular paraproteins;* *• determination of the initial (amino acids), intermediate and final products of protein metabolism in the blood;* *• study of the genes structure that encode the individual proteins synthesis.* ***1.1. total PROTEIN – blood.*** *– Normal: newborns up to 1 month. – 46–68 g / l, children 1–12 months. – 48–76 g/l; children 1–16 years – 60–80 g/l; adults – 65–85 g/l; after 60 years the level is lower by 2 g/l.* *– Total serum protein is a laboratory indicator that reflects the homeostasis state; proteins are multifunctional compounds: perform transport and protective (immunoglobulins, opsonins, etc.) functions, maintain blood flow and viscosity, form blood volume in the vascular stream, provide blood plasma density, regulate acid-base status, participate in coagulation system, etc.* *– **Hypoproteinemia** – a decrease in total protein content in the blood less than 65 g/l:* *• <u>relative</u>: associated with an increase the water volume in the bloodstream; observed in patients with oliguria, anuria, water load, cardiac decompensation, intravenous administration of a significant amount of glucose solution under renal excretory dysfunction, increased secretion of antidiuretic hormone;* *• <u>absolute</u>: associated with hypoalbuminemia; observed in patients with insufficient protein intake (starvation, esophageal narrowing, enteritis, enterocolitis, etc.), inhibition of proteins synthesis on the background of chronic inflammatory processes in the liver (cirrhosis, hepatitis, intoxication), inborn disorders of certain proteins biosynthesis (eg, Konovalov-Wilson disease), increased protein breakdown (tumors, burns, thyrotoxicosis, postoperative period, etc.), significant protein loss (diabetes, nephrotic syndrome, glomerulonephritis, bleeding, etc.);* *• physiological: observed in some physiological conditions: in women in the last months of pregnancy, during lactation; in patients after prolonged physical exercises.*

	*– **Hyperproteinemia** – an increase of total protein content in the blood:* *• relative: associated with a decrease in the water volume in the bloodstream; observed under diabetes mellitus, diabetic ketoacidosis, chronic nephritis, severe burns, intestinal obstruction, diarrhea, vomiting, generalized peritonitis, increased sweating;* *• absolute: associated with the synthesis of paraproteins, increased synthesis of immunoglobulins and acute phase proteins; observed in acute and chronic infections, autoimmune diseases, chronic polyarthritis, hemoblastosis, sarcoidosis, etc.* ***1.2. total PROTEIN – urine.*** *– Proteinuria – a general concept that means the appearance any protein in the urine in excess of the physiological concentration (the amount of protein in the final urine normally does not exceed 100–150 mg/day).* *– Functional proteinuria:* *• physiological: in newborns during the first 4–10 days as a result of a weak kidney filter;* *• transient: after prolonged physical exercises, overheating or hypothermia; after emotional stress, after eating of protein-rich food, fluid loss in infants, after administration of vasoconstrictors;* *• dehydration: in infants due to feeding disorders, diarrhea, vomiting;* *• pathological: as a result of renal tubules damage, disturbances of protein reabsorption.* *– Forms of proteinuria:* *• prerenal: associated with the synthesis of pathological proteins, increased tissue breakdown, severe hemolysis: under this condition proteins pass through the intact renal filter into the urine (myeloma, lymphoma with paraproteinemia, acute plasmoblastic leukemia, hemolytic anemia, metastasis and anemia abdominal tumors, etc.);* *• renal: 1) glomerular: on the background of cortical lesions (acute and chronic glomerulonephritis, nephropathy in diabetes, nephropathy in pregnancy, nephrosis, etc.); 2) selective glomerular: filtration disorders due to changes in the surface charge of sialoglycoproteins on the glomerular membrane or changes in the surface charge of proteins (in diabetes mellitus); 3) non-selective glomerular: nephrotic syndrome with disturbances of renal filtration; 4) mixed (glomerular-tubular): manifest stage of nephropathy, when a significant amount of plasma proteins is detected in the urine (acute renal failure, renal vein thrombosis, etc.);*

	• postrenal: associated with bleeding and urinary tract infections, polyposis, bladder tumors. ***1.3. PROTEIN total – cerebrospinal fluid.*** *– Normal: children until 1 year – 0.49–0.87 g/l; 1–10 years – 0.24–0.32 g/l; from 11 years to 20 years – 0.23–0.49 g/l; over 21 years – 0.24–0.58 g/l.* *– Hyperproteinrachia – increased total protein content in cerebrospinal fluid; observed under increased blood-brain barrier permeability or in a case of decreasing of protein utilization from the cerebrospinal fluid due to their circulation pathological changes. There are several types of hyperproteinrachia:* *• mild hyperproteinemia (0.46–0.80 g/l) in diabetic neuropathy, myxedema, vascular diseases of the CNS, convulsions, poly-neuritis, degenerative diseases, neurosyphilis, hyperkinetic progressive panencephalitis, multiple sclerosis, serous meningitis;* *• moderate hyperproteinemia (0.81–1.5 g/l) in tuberculous meningitis, poliomyelitis, hematoma, hemorrhage in the subarachnoid space, arachnoiditis, CNS tumors;* *• severe hyperproteinemia (1.5–3.0 g/l) in hemorrhagic stroke, brain injury, etc .;* *• expressed hyperproteinemia (3.1–10.0 g/l) with purulent meningitis, hemorrhage with a breakthrough of blood into the cerebrospinal fluid, spinal cord compression.* *– Hypoproteinrachia – a decrease in total protein content in cerebrospinal fluid; mainly observed in a case of protein utilization increasing rate (increased intracranial pressure, removing of cerebrospinal fluid large amount, hydrocephalus).* ***1.4. Protein fractions.*** *– Separation of serum proteins is carried out by electrophoresis, it is based on different mobility of proteins in an electric field → fractions:* *• albumins (homogeneous);* *• α1-globulins (acute phase proteins – α1-antitrypsin, α1-acid glycoprotein, α1-lipoprotein);* *• α2-globulins (α2-macroglobulin, haptoglobin, ceruloplasmin, apolipoproteins A, B, C);* *• β-globulins (transferrin, C3 component of the complement system, β-lipoproteins, hemopexin);* *• γ-globulins (Ig A, M, G, D, E).* *- The normal content in the serum for adults: albumin – 60.5–74.2 %; α1-globulins – 1.1–4.3 %; α2-globulins – 4.2–11 %; β-globulins – 8.4–12.8 %; γ-globulins – 6.4–17.0 %.*

	– Types of serum proteinogram disorders: *• dysproteinemia – changes in the ratio of protein fractions compared to normal:* *1) changes in α1-globulins (increasing – in acute and chronic inflammatory processes, liver damage, tissue breakdown or cell proliferation; decreasing – in α1-antitrypsin deficiency, hypo-α1-lipoproteinemia);* *2) changes in α2-globulins – increasing – in acute inflammatory processes with a pronounced exudative and purulent nature, diseases associated with involvement in the pathological process connective tissue – collagenosis, rheumatic diseases, autoimmune diseases, malignant tumors, nephrotic syndrome, etc.; reduction – in diabetes mellitus, congenital mechanical jaundice in newborns, toxic hepatitis);* *3) changes in β-globulins (increasing – in hyperlipoproteinemia, liver disease, nephrotic syndrome, hypothyroidism; decreasing – in hypo-β-lipoproteinemia);* *4) changes in γ-globulins (increasing under viral and bacterial infections, inflammation, tissue destruction, burns, decreasing: primary (physiological) hypogammaglobulinemia – in children 3–5 months, secondary hypogammaglobulinemia – in diseases and conditions accompanied by depletion of the immune system;* *• genetic defects in protein biosynthesis:* *1) lack of albumin with normal content of other protein fractions (characterized by edema due to a decrease in oncotic pressure);* *2) hypoglobulinemia – general insufficiency of serum globulins, while the content of total protein is reduced to 40 g/l at normal albumin content;* *3) agammaglobulinemia – a genetic defect in the synthesis of antibodies, while the total amount of protein does not change (characterized by increased susceptibility to bacterial infections while maintaining resistance to viral infections);* *• paraproteinemia – the appearance in the blood of abnormal proteins – immunoglobulins or their fractions (on the electrophoregram there is an additional narrow and sharply limited proteins fraction in the field of γ-globulins) in paraproteinemic hemoblastosis (group of lymphoid tissue tumors), while increasing protein up to 140–170 g/l at constant albumin levels*
2. Clinical and diagnostic value of separate specific blood proteins determination	*Specific blood proteins perform a number of functions: participation in immune reactions, the blood coagulation process, transportation of various compounds, inhibition of proteases etc. In addition, these proteins are characterized by participation in the general reactions of the body in various pathological processes, reflecting the state of organs and tissues,*

	which has found use in clinical practice. The general characteristics of individual specific blood proteins are given below. ***2.1. Haptoglobin:*** *– α2-glycoprotein of blood, acute phase protein, synthesized mainly in the liver;* *– role: 1) protective: forms complexes with released during cell breakdown proteins, in particular, binds free hemoglobin after intravascular hemolysis, which prevents iron loss; 2) transport (transfers vitamin B12); 3) cathepsin inhibitor;* *– the content in the serum is normal depends on age: newborns – 0.5–4.8 g/l, 6 months–16 years – 2.5–14.1g /l, 16–60 years – 1.5–2.0 g/l, over 60 years – 3.5–17.5 g/l;* *– there are three hereditary phenotypes of haptoglobin – Hp 1–1, Hp 2–1, Hp 2–2;* *– hypergaptoglobinaemia is observed: 1) in the acute phase of inflammation compared to other acute phase proteins it is less pronounced due to selective binding to free plasma hemoglobin during hemolysis, which often accompanies acute phase processes; with the results of the other acute phase proteins content); 2) in necrobiotic processes → increase in the haptoglobin content in these case reflects the degree of connective tissue destruction (collagenosis, acute myocardial infarction, sepsis, rheumatism, pneumonia, tumors); 3) under cholestasis; 4) under the treatment by glucocorticoids;* *– Hypogaptoglobinaemia is observed in the suppression of synthesis due to liver damage or increased metabolism under hemolysis of various origins, as well as in pancreatitis, sarcoidosis, DIC syndrome, the use of oral contraceptives.* ***2.2. C-reactive protein:*** *– acute phase protein, has a wide ligand specificity, activates complement, interacts with different cell types;* *– serum content up to 0.5 mg/l is considered normal;* *– role: recognition of various substances present on the cell surfaces in microorganisms or human tissues; activation of the corresponding functional systems and, as a consequence, elimination of pathogens, and also necrotized cells;* *– determined in the blood under the following circumstances: 1) diagnosis of bacterial infection and monitoring of response to antibiotic therapy; 2) diagnosis of the acute stage of systemic lupus erythematosus, ulcerative colitis, etc.; 3) diagnosis of the acute stage of the disease and monitoring of therapy for rheumatoid arthritis; 4) early diagnosis of infectious and inflammatory complications in operated patients; 5) diagnosis*

	of infectious complications in the case of bone marrow and kidney transplantation; 6) risk assessment of cardiovascular pathology, etc. Thus, an increase in the content of C-reactive protein in the blood is a sign of a disease associated with tissue damage, inflammation, infection, tumors. ***2.3. Ceruloplasmin:*** *– α2-blood glycoprotein, acute phase protein;* *– role: transport of copper to tissues, catalyst for iron oxidation (ferroxidase), participation in the oxidation of catecholamines and serotonin, antioxidant effect, anti-inflammatory effect (inhibits the activity of serum histaminase);* *– the content in the serum is normal in adults is 0.2–0.6 g/l;* *– increasing in blood content is observed under chronic inflammatory processes (especially after surgery), in the acute period of infectious diseases, nonspecific pneumonia, pulmonary tuberculosis, rheumatism, malignant neoplasms, liver disease (hepatitis, cirrhosis, gallstone disease), pernicious anemia, dysentery, melanoma, myocardial infarction, etc.;* *– decreasing in blood content is observed under Konovalov-Wilson disease (hepatocerebral degeneration), kidney disease, in particular glomerulonephritis with nephrotic syndrome (loss of protein through the kidney), gastrointestinal tract diseases (disturbances of amino acids absorption), severe liver disease.* ***2.4. α1-Antitrypsin:*** *– α1-glycoprotein of blood, protein of the acute phase;* *– role: inhibitor of proteolytic enzymes of kinin and complement systems, fibrinolytic system, proteases secreted by neutrophils; under the inflammatory process in the lung tissue effectively inhibits the activity of elastase, preventing the degradation of connective tissue protein – elastin in the walls of the alveoli and the development of pulmonary emphysema; modulates the local immune response, has antioxidant and antimicrobial action;* *– the content in the serum is normal conditions depends on age: children till 3 years – 0.8–2.0 g/l, adults till 60 years – 0.78–2.0 g/l, over 60 years – 1,15–2.0 g/l;* *– increasing in blood content is observed under infectious and rheumatic diseases, tissue necrosis, hepatitis;* *– congenital deficiency of α1-antitrypsin: juvenile basal pulmonary emphysema, chronic obstructive pulmonary disease with the development of emphysema, cystic fibrosis (as there is no inhibitory effect on leukocytes elastase activity, which damages the alveoli walls on the epitheliocytes surface);*

	– acquired α1-antitrypsin deficiency: kidney disease with nephrotic syndrome, gastroenteropathy (protein loss), acute phase of thermal burns, viral hepatitis (impaired protein biosynthesis), respiratory distress syndrome (acute pancreatitis). ***2.5. Antistreptolysin O (ASL-O)*** *– antibodies to streptolysin:* *– the content in normal conditions in blood serum in adults is less than 200 IU/ml, children till 14 years – less than 150 IU/ml;* *– a marker of streptococcal infection (the content increases in a week after infection, the peak is registered in 3–5 weeks, decreasing in 6–12 months);* *– increasing in blood content is observed under rheumatism, diseases of streptococcal etiology: scarlet fever, sore throat, chronic tonsillitis, osteomyelitis, etc., as well as related complications (rheumatism, myocarditis, glomerulonephritis, etc.).* ***2.6. Orozomucoid (acidic α1-glycoprotein):*** *– α1-glycoprotein of blood, acute phase protein;* *– role: modulates the selectin's effect (cell surface protein) on the influx of leukocytes to inflammation sites; suppresses immunoreactivity, alters platelet adhesion, binds drugs and hormones with basic properties;* *– the content in the serum is normally 0.5–1.2 g/l;* *– increasing in blood content is observed under bacterial infections, inflammation, Crohn's disease, systemic lupus erythematosus, rheumatoid arthritis, myocardial infarction, malignancies;* *– decreasing blood level is observed under kidney disease with nephrotic syndrome, severe liver damage, gastroenteropathies with protein loss, antimicrobial drugs administration, estrogens and oral contraceptives.* ***2.7. Transferrin:*** *– β-glycoprotein of blood, "negative" acute phase protein (its concentration in the blood is reduced in inflammation and malignant neoplasms), is synthesized mainly in the liver;* *– role: 1) transport of iron in the blood stream between the gastrointestinal tract and organs that store iron (liver, bone marrow, spleen) and hematopoietic tissues; 2) transfer of iron that does not use in heme biosynthesis to the depot; 3) regulation of immune processes;* *– the normally content in the serum: newborns – 1.3–2.75 g/l, adults – 2.0–3.2 g/l;* *– increasing in blood is observed under iron deficiency (increased levels precedes the development of anemia for several days or months), pregnancy, estrogen and oral contraceptives administration;*

	– decreasing in blood content is observed under chronic inflammatory processes, hemochromatosis, liver cirrhosis, protein loss in burns, kidney disease with nephrotic syndrome, gastrointestinal tract pathologies (in particular, malabsorption syndrome), malignant tumors.
3. Clinical and diagnostic value of carbohydrate-containing proteins and their components determination in blood	***3.1. Proteins associated with carbohydrate components are a large group of compounds, in particular:*** ***• glycoproteins****:* *– prosthetic group is represented by a small amount of carbohydrates: hexoses (galactose, mannose), pentoses (xylose, arabinose), deoxy sugars (fucose), amino sugars (acetylgalactosamine, acetylglucosamine), neuraminic acid and its acetate ethers;* *– the most labile fraction of glycoproteins are seroglycosides (seromucoids), accounting for 1 % of all serum proteins, 12 % of all plasma carbohydrates); they include at least 15 different carbohydrate-protein complexes, such as prealbumin, orosomucoid, alpha-1-antitrypsin, alpha-1-glycoprotein, haptoglobin, erythropoietin, etc;* *– role: enzymes (cholinesterase), hormones (thyrotropin, gonadotropins); immunoglobulins, blood plasma proteins (ceruloplasmin, haptoglobin, etc.), membrane proteins, including receptors, etc.* ***• proteoglycans:*** *– prosthetic group is represented by a significant amount of carbohydrates, which are called glycosaminoglycans (GAG); the composition of GAG includes: glucuronic acid (hyaluronic acid, chondroitin-4(6)-sulfate, heparin, heparan sulfate), iduronic acid (dermatansulfate), galactose (keratan sulfate);* *– role: form the main substance of the connective tissue intercellular matrix; provide intercellular interaction; provide the formation and maintenance of cells and organs; provide the formation of the framework during the tissue's formation; specifical interaciont with collagen, elastin, fibronectin, laminin and other proteins of the intercellular matrix; as polyanions attach water, cations (sodium, potassium, calcium), form the turgor of various tissues; perform the role of a molecular sieve in the intercellular matrix; prevent the spread of pathogenic microorganisms; spring function in articular cartilage (hyaluronic acid); renal filtration barrier (heparan-containing proteoglycans); corneal transparency (keratan and dermatan sulfates); anticoagulants (heparin); components of cells plasma membranes, functioning as receptors, involved in adhesion and intercellular interactions (heparan sulfates); components of synaptic vesicles.*

	3.2. Clinical and diagnostic value of seroglycoids determination: *– it is an acute phase indicator in blood;* *– increasing in blood content is observed under inflammatory and necrobiotic processes, malignant neoplasms, exacerbation of chronic cholecystitis, destructive form of pulmonary tuberculosis, rheumatism, myocardial infarction, stroke;* *– a decreasing in the content is observed under disorders of the liver protein-synthesizing function (infectious hepatitis, hepatocellular dystrophy, cirrhosis), multiple sclerosis.* ***3.3. Clinical and diagnostic value of glycated protein determination.*** ***• Glycated hemoglobin (HbA1c):*** *– the product of the non-enzymatic reaction between glucose and hemoglobin → reflects hyperglycemia that occurred during the lifetime of erythrocytes (up to 120 days), but erythrocytes circulating in the blood have different lifetime, so for the average glucose concentration focus on the half-life of erythrocytes 60 days) → the percentage of HbA1c in the blood is judged by the glucose content for the last 4–8 weeks;* *– normal rate up to 4.0–6.5 % of the HB total content;* *– increasing in the content is observed under diabetes mellitus and other conditions with impaired glucose tolerance, iron deficiency, splenoectomy;* *– decreasing in blood content is observed under hypoglycemia, hemolytic anemia, bleeding, blood transfusion.* ***• Fructosamine:*** *– the product of non-enzymatic reaction between glucose and albumin → duration of staying in the vascular bed near 20 days, which corresponds to the time of albumin circulation in the blood → determination of blood content is an integral test that reflects blood glucose levels for the last 3 weeks → determined primarily by control glycemia in patients with diabetes mellitus;* *– normal content in blood: adults – up to 285 mmol/l, children – up to 270.8 mmol/l;* *– increasing in blood content is observed under diabetes mellitus, renal failure, hypothyroidism, uremia, myeloma, acute inflammatory processes, as well as in some physiological conditions, in particular, during pregnancy;* *– decreasing in blood content is observed under hypoalbuminemia, diabetic nephropathy, hyperthyroidism.* ***3.4. Clinical and diagnostic value of sialic acids determination in blood:*** *– sialic acids are neuraminic acid acyl derivatives → they are a part of various carbohydrate compounds: glycoproteins*

	(especially those that are broken down under inflammatory processes, such as glycoproteins of the connective tissue main substance, which are break down by hydrolases action – neuraminidases with removing of sialic acids and their transfer into the blood), glycolipids (gangliosides), oligosaccharides; they are an integral part of the mucus of the respiratory tract, genital tract, stomach, intestine mucous membrane; *– blood rate 2.0–2.36 mmol/l;* *– increasing in blood content is observed under rheumatoid arthritis, polyarthritis, myocardial infarction, tumor processes, acute appendicitis, destructive processes;* *– decreasing in blood content is observed under pernicious anemia, hypochromatosis, degenerative processes in the CNS.* ***3.5. Clinical and diagnostic value of glycosaminoglycans determination in urine:*** *– connective tissue metabolism rate;* *– the level in the daily urine is calculated in mg of glucuronic acid per creatinine content, the norm for adults is less than 13.3 μg of glucuronate/mg of creatinine per day;* *– increasing in urine content – a reliable sign of mucopoly-saccharidosis (to detect enzyme's defects it is essential to conduct additional blood tests).* ***Routine tests:*** *– blood glucose (fasting plasma glucose up to 6.1 mmol/l; > 6.1 mmol/l to 7.0 mmol/l – impaired fasting blood glucose; > 7.0 mmol/l – preliminary diagnosis – sugar diabetes);* *– ketone bodies in the blood and urine;* *– glucose tolerance test: determination of fasting blood glucose and every hour during two hours after glucose challenge (one of the specific methods of examination, which is based on determining the body's tolerance to glucose; the test can detect predisposition to diabetes, diabetes latent form, diabetes of pregnant women, impaired glucose tolerance);* *– glycated hemoglobin;* *– fructosamine;* *– microalbumin in urine (microalbuminuria is a reliable precursor to the development of diabetic nephropathy);* *– creatinine in urine;* *– lipid profile.* ***Additional tests:*** *– determination of insulin content in the blood: the normal content in a healthy person is from 3 to 25 muU/mL, in children – 3–20 muU/mL; increased insulin content is observed in type II diabetes mellitus;*

	– determination of serum antibodies to insulin (IAA) in patients with type I diabetes mellitus (the test has a clear correlation with age: type I diabetes mellitus in children until 5 years – in 100 % cases IAA will be detected, in adults – ≈ in 20 %); *– determination of C-peptide in blood: products of proinsulin breakdown are C-peptide and insulin → these products are secreted into the blood by pancreatic beta cells in equal amounts → C-peptide is a biologically inactive compound, its circulation is characterized by a longer half-life, its level is a more stable indicator of insulin secretion than the rapidly changing level of the insulin → study of the C-peptide level allows to assess insulin secretion in different clinical situations;* *– determination of the antibodies titer to the Langerhans islets cells (ICA): has the most prognostic value for the development of type I diabetes → antibodies appear 1–8 years before the clinical signs of the disease;* *– determination of the titer of tyrosine phosphatase antibodies: tyrosine phosphatase – an open autoantigen of Langerhans islets, localized in the granules of pancreas beta cells → antibodies to antigens of Langerhans islets cells – is an informative marker for the identification of high risk of diabetes mellitus;* *– determination of the titer of antibodies to glutamate decarboxylase (GAD): GAD – antigen, which is the main target for autoantibodies associated with the development of insulin-dependent diabetes;* *– determination of markers-genes of the HLA system and other IDDM genes;* *– determination of the HOMA index (Homeostasis Model Assessment of Insulin Resistance) = fasting glucose content (mmol/l) × fasting insulin content (muU/mL)/22.5 – method of detecting insulin resistance; normally not more than 2.7 c.u.; increase in the value of the HOMA index is observed under insulin resistance, which indicates the possible development of type II diabetes mellitus, as well as atherosclerosis, polycystic ovary syndrome, often on the background of obesity; about gestational diabetes mellitus, endocrine diseases (thyrotoxicosis, pheochromocytoma, etc.), chronic liver diseases, acute infectious diseases;* *– determination of the index caro = fasting glucose content (mmol/l) / fasting insulin content (muU/mL) – a method for detecting insulin resistance; normally not less than 0.33 c.u.; a decrease in the value of the caro index is a sign of insulin resistance.*

5. Clinical and diagnostic value of apolipoproteins determination in the blood	***5.1. Apolipoproteins (apo A, apo B, etc.)*** *– protein components of lipoproteins (LP); role: maintenance of structural integrity of LP, recognition of LP by receptors, regulation of enzymes activity acting on LP.* ***5.2. Apolipoprotein A (apo A):*** *– protein component of HDL;* *– a marker of the cardiovascular risk, which reflects the anti-atherogenic activity of HDL;* *– role: transport of lipids, lecithin-cholesterol-acyltransferase activator → reverse transport of cholesterol from the periphery and vessel walls to the liver → prevention of atherosclerosis;* *– normal content in blood (in a case of determination by an immunoturbidimetric method): men – 0,79–1,70 g/l; women – 0.76–2.14 g/l);* *– increasing in blood content is observed under hereditary hyper-α-lipoproteinemia, alcoholism, pregnancy;* *– decreasing in blood content is observed under hereditary hypo-α-lipoproteinemia, type 1 diabetes mellitus, hemodialysis, cholestasis, hepatocellular pathology, kidney disease with nephrotic syndrome.* ***5.3. Apolipoprotein B (apo B):*** *– LDL protein component;* *– risk marker of atherosclerosis;* *– role: transport of cholesterol from the liver to peripheral cells;* *– normal content in blood (in a case of determination by by an immunoturbidimetric method): men – 0,46–1,74 g/l; women – 0.46–1.42 g/l);* *– increasing in blood content is observed under hyperlipoproteinemias IIa, IIb, IV, V types, hyper-apo-β-lipoproteinemia, coronary heart disease, kidney disease with nephrotic syndrome, diabetes, hypothyroidism, Itsenko-Cushing's syndrome, liver disease, pregnancy dysglobulinemia, porphyria, emotional stress;* *– decreasing in blood content is observed under hypo-β-lipoproteinemia, hyperthyroidism, decompensated diabetes mellitus, hepatocellular disorders, anemia, malabsorption syndrome, inflammatory processes of joints*
6. Clinical and diagnostic value of acid-base status and gas composition of blood indicators determination in blood	***6.1. The main indicators of acid-base status (ABS):*** *– pH – normal 7,35–7,45 (arterial blood); pH displacement in the acidic direction (pH < 7.35) – acidosis, pH 7.25–7.35 – subcompensated acidosis, pH < 7.25 – decompensated acidosis; pH displacement to the alkaline side (pH > 7.45) – alkalosis, pH 7.45–7.55 – subcompensated alkalosis, pH > 7.55 – decompensated alkalosis;*

	– pCO2 – voltage of carbon dioxide in arterial blood; normal 35–45 mm Hg; deviation from the norm indicates respiratory disorders of the ABS; decrease in pCO2 (arterial hypocapnia) – under alveolar hyperventilation, respiratory alkalosis; increase in pCO2 (arterial hypercapnia) – under alveolar hypoventilation, respiratory acidosis; *– [HCO3-] – concentration of bicarbonate ions in arterial blood; norm 21–27 mmol/l; reflects the kidneys participation in the compensation of acidosis or alkalosis;* *– Buffer Base (BB) – the total number of all blood anions; norm 48.0 ± 2.0 mmol/l; since the total amount of BB, in contrast to standard and true bicarbonates, does not depend on pCO2, metabolic disorders of ABS could be assessed by its amount;* *– excess or deficiency of buffer bases (Base Excess, BE) – the most informative indicator of metabolic disorders of ABS, the rate of 0 ± 2.3 mmol/l; when the content of buffer bases increases, the value of BE is positive (excess of bases) → metabolic alkalosis; when the content of buffer bases decreases, the value of BE is negative (base deficiency) → metabolic acidosis.* ***6.2. The main indicators of gas exchange.*** *Respiratory component of oxygen transport: pO_2 – oxygen pressure in arterial blood, it is a pressure that provide saturation of blood by O_2. Normal – 80–107 mm Hg. As higher the pO_2 as more oxygen content in a blood stream and higher rate of oxygen movement to capillary blood to tissues.* *Hemic component of oxygen transport:* *• Total concentration of hemoglobin in the blood (ctHb) – includes the concentration of oxyhemoglobin (cO_2Hb), deoxyhemoglobin (cHHb), dyshemoglobin, unable to bind oxygen: carboxyhemoglobin (cCOHb), methemoglobin (cMetHb) and sulfhemoglobin (SulfHb)* *ctHb = $cO_2Hв$ + cHHв + cCOHв + cMetHb + cSulfHb; norm – newborns 8,7–14,9 g/l, children – 6,8–8,7 g/l, adult men – 8,4–10,9 g/l, adult women – 7,1–9,6 g/l; it uses for anemia diagnosis, assessment the risk of tissue's hypoxia; decreasing in stHb indicates anemia, increasing in stHb is observed under the inhabitants of the highlands;* *• sO2 – the degree of hemoglobin saturation with oxygen; norm: newborns 40–90 %, adults 94–98 %; a decrease in the indicator indicates a disturbance of oxygen absorption*

7. Clinical and diagnostic value of mineral metabolism indicators determination in blood	***7.1. Potassium (K^+):*** *– the main cation of intracellular fluid;* *– role: maintenance of osmotic pressure and acid-base homeostasis; regulation of neuromuscular excitation, heart rate, internal and extracellular volumes, etc;* *– normal content in blood plasma about 3,5–5,3 mmol/l;* *– Hypokalemia is observed under the diuretics use, starvation (lack of food intake), severe diarrhea/vomiting (loss through the gastrointestinal tract), kidney disease, aldosterone hyperproduction, etc. → clinical symptoms: fatigue, muscle weakness, weak irregular heartbeat, weakening of muscle contractions, tendon reflexes, tachycardia, low blood pressure, arrhythmia, etc.;* *– hyperkalemia is observed under burn tissue damage, purulent-septic diseases, tumors (exit from cells into the blood), urinary incontinence, intravenous potassium-containing solutions → clinical symptoms: irritability, abdominal cramps, nausea, vomiting, diarrhea, weakness paresthesia, bradycardia, arrhythmia, up to cardiac arrest (at a content of 7.5–10.0 mmol/l).* ***7.2. Sodium (Na^+):*** *– the main cation of extracellular fluid;* *– role: maintenance of the composition and volume of extracellular fluid, determines the osmolality of blood plasma and extracellular fluid, maintenance of acid-base status, water balance regulation, vascular tone, muscle contraction, nerve impulse conduction, etc.;* *– normal content in blood plasma 131–157 mmol/l;* *– Hyponatremia is observed under heart failure, liver cirrhosis, prolonged vomiting/diarrhea, diuretics, etc. → clinical symptoms: irritability, fatigue, hypotension, dry mucous membranes, tremor, convulsions, apathy, tachycardia, etc.* *– hypernatremia is observed under chronic renal failure, Conn's syndrome, Itsenko-Cushing's disease and syndrome, diabetes insipidus, excessive intravenous sodium salts, etc. → clinical symptoms: hypertension (fluid leakage from cells), edema, strong thirst, fatigue, agitation, tachycardia, etc.* ***7.3. Calcium (Ca^{2+}):*** *– cation of extracellular fluid (1 %);* *– role: structural, participation in the processes of neuromuscular excitability, muscle contraction, myocardial contractility, blood clotting, secretion of mediators, the role as a secondary mediator in the transmission of hormonal signals into the cell, etc.;* *– the rate in the serum of 2.25–3.0 mmol/l;*

	– hypocalcemia is observed under insufficient of vitamin D intake/calcium, hypoparathyroidism, chronic renal failure, chronic liver damage, etc. → clinical symptoms: numbness and tingling in the extremities, increased neuromuscular excitability (possibly before the development of clonic-tonic seizures); *– hypercalcemia is observed under hyperparathyroidism, hypervitaminosis D, sarcoidosis, hypothyroidism, etc. → clinical symptoms: kidney stones, depression, decreased neuromuscular excitability, increased blood clotting, anorexia, nausea, vomiting, arrhythmias.* ***7.4. Magnesium (Mg^{2+}):*** *– the main intracellular cation;* *– role: structural, cofactor, participation in the metabolism of macroergic compounds, the effect on the contractile capacity of the myocardium and smooth muscle, etc.;* *– the rate in the serum is about 0.7–0.99 mmol/l;* *– hypomagnesemia is observed under profuse vomiting, diarrhea, chronic alcoholism, malabsorption syndrome, infusion therapy with low magnesium content, cardiovascular diseases (coronary heart disease, atherosclerosis), kidney disease, thyroid disease, diabetes mellitus, hyperaldosteroidism, deficiency in food, etc. → clinical symptoms: limb cramps, mood swings, hallucinations, confusion, nausea, dysphagia, paresthesia, tachycardia;* *– hypermagnesemia is observed in acute and chronic renal failure, Cushing's disease, taking magnesium-containing drugs, etc. → clinical symptoms: nausea, vomiting, redness of the skin, mental disorders, muscle weakness, hypotension.* ***7.5. Phosphorus:*** *– the main intracellular element;* *– is about 1 % of body weight in the form of inorganic phosphates;* *– role: structural, energy transfer in the form of macroergic bonds (ADP, ATP), participation in phosphorylation reactions, regulation of acid-base status, growth processes, cell division, storage and use of genetic information, etc .;* *– the rate of inorganic phosphates in the serum is about 0.65–1.30 mmol/l;* *– hypophosphatemia is observed under intestinal malabsorption, alcoholism, vomiting, diarrhea, loss of phosphate in the urine, hyperparathyroidism, vitamin D-resistant rickets, osteomalacia, Fanconi syndrome → clinical symptoms: memory impairment, muscle aches, pain weakness, numbness and tingling in the extremities, etc.;*

	– hyperphosphatemia is observed under excess intake, cell destruction, glomerular damage, hypoparathyroidism, acromegaly, diabetes mellitus → clinical symptoms: anorexia, nausea, vomiting, muscle weakness, hyperreflexia, tetany, tachycardia. ***7.6. Iron:*** *– 1) heme (cellular) – as part of hemoglobin, myoglobin, cytochromes, catalase, peroxidases; 2)non-heme; 3) extracellular – free plasma iron and iron-binding serum proteins (transferrin, lactoferrin), which are involved in iron transport; 4) iron depot – in the form of protein compounds – ferritin and hemosiderin;* *– the role of iron: structural (as part of iron-containing proteins of hemoglobin, myoglobin, cytochromes, etc.), participation in redox processes, transport, etc .;* *– the role of iron-containing proteins: transport and deposition of oxygen (hemoglobin, myoglobin); participation in redox processes (oxidases, cytochromes, peroxidases), hematopoiesis, detoxification, cell division, regulation of immune responses (ensuring the activity of interferon and killer cells), etc .;* *– the rate in the serum of 12.5–30.4 mmol/l;* *– almost all serum iron is in the transferrin;* *– decreasing in blood content is observed under insufficient food intake, impaired absorption in the gastrointestinal tract (anacid and hypoacid gastritis, resection of the stomach and intestines); increased utilization in organs and tissues (pregnancy, growth of the body in childhood, increased physical activity), increased lost (hemorrhages), redistribution (systemic connective tissue diseases - collagenosis, rheumatism, rheumatoid arthritis, tumors - lymphogranulomatosis, acute and chronic hepatic; cirrhosis, myocardial infarction), etc. → accompanied by hypochromic microcytic anemia (cell-color ratio – 0.8 and less), trophic disorders in organs and tissues, mental disorders, decreased immune resistance;* *– increase in iron content in the blood is observed under excessive intake, insufficient use in the hematopoietic organs → accompanied with hepatosis, cirrhosis, splenomegaly, the development of copper deficiency and zinc ions; excess iron is deposited in the parenchymal organs in the form of hemosiderin*

EXAMPLES OF BIOCHEMICAL ANALYSIS INTERPRETATION RESULTS IN BLOOD

Patient 1, female, 69 years old (height – 157 cm, body weight – 87 kg)

Blood	
Cholesterol – 4,15 mmol/l	Direct bilirubin – 3,2 mcmol/l
Triacylglycerols – 1,12 mmol/l	Glucose – 4,0 mmol/l
Total protein – 79,0 g/l	Creatine phosphokinase – 107 IU/l
Urea – 6,32 mmol/l	Lactate dehydrogenase – 265 IU/l
Uric acid – 0,23 mmol/l	Aspartate aminotransferase – 33 IU/l
Total bilirubin – 13,8 mcmol/l	Alanine aminotransferase – 32 IU/l
Potassium – 3,8 mmol/l	Amylase – 22,1 g/l·h
Sodium – 138 mmol/l	Albumin – 49 g/l
Hemoglobin – 130 g/l	
Protein fractions	
Albumins – 58,0 %	α1-globulins – 4,5 %
α2-globulins – 8,5 %	β-globulins – 9,4 %
γ-globulins – 19,6 %	

According to these results in patient 1 there is a finding of the studied indicators within the norm. Therefore, we can assume that these are the results of a healthy person.

Patient 2, female, 57 years old (height – 165 cm, body weight – 67 kg)

Blood	
Cholesterol – 5,8 mmol/l	Direct bilirubin – 72,0 mcmol/l
Triacylglycerols –1,3 mmol/l	Glucose – 4,9 mmol/l
Total protein – 69,8 g/l	Creatine phosphokinase – 115 IU/l
Urea – 6,0 mmol/	Lactate dehydrogenase – 188 IU/l
Uric acid – 0,22 mmol/l	Aspartate aminotransferase – 23,0 IU/l
Total bilirubin – 92,4 mcmol/l	Alanine aminotransferase – 26,2 IU/l
Potassium – 5,6 mmol/l	Amylase – 27,0 g/l·h
Sodium – 148 mmol/l	Albumin – 45,4 g/l
Hemoglobin – 132 g/l	
Protein fractions	
Albumins – 40,4 %	α1-globulins – 2,2 %
α2-globulins – 14,6 %	β-globulins – 18,0 %
γ-globulins – 25,2 %	

According to these results, patient 2 has:

– mild hypercholesterolemia, hyperbilirubinemia due to direct bilirubin;

– increase in α2-, γ- and β-globulins against the background of decreased albumin.

The increase in the level of bilirubin due to the direct suggests cholestatic jaundice, which is characterized by pronounced dysproteinemia.

Patient 3, male, 37 years old (height – 180 cm, body weight – 86 kg)

Blood	
Cholesterol – 4,7 mmol/l	Direct bilirubin – 3,2 mcmol/l
Triacylglycerols –1,64 mmol/l	Glucose – 5,2 mmol/l
Total protein – 70,0 g/l	Creatine phosphokinase – 125 IU/l
Urea – 7,3 mmol/l	Lactate dehydrogenase – 253 IU/l
Uric acid – 0,85 mmol/l	Aspartate aminotransferase – 25,2 IU/l
Total bilirubin – 18,8 mcmol/l	Alanine aminotransferase – 24,5 IU/l
Potassium – 4,2 mmol/l	Amylase – 25,4 g/l per h
Sodium – 144 mmol/l	Albumin – 46,0 g/l
Hemoglobin – 160 g/l	
Protein fractions	
Albumins – 56,0 %	α1-globulins – 3,8 %
α2-globulins – 8,2 %	β-globulins - 13,5 %
γ-globulins – 18,5 %	

According to these results, patient 3 has severe hyperuricemia on the background of normal values of other indicators. The patient can be assumed – gout.

Patient 4, female, 60 years old (height – 167 cm, body weight – 68 kg)

Blood	
Cholesterol – 5,8 mmol/l	Direct bilirubin – 12,2 mcmol/l
Triacylglycerols –1,3 mmol/l	Glucose – 4,95 mmol /l
Total protein – 69,8 g/l	Creatine phosphokinase – 115 IU/l
Urea – 6,0 mmol/l	Lactate dehydrogenase – 588 IU/l
Uric acid – 0,22 mmol/l	Aspartate aminotransferase – 53,0 IU/l
Total bilirubin – 102,4 mcmol/l	Alanine aminotransferase – 26,2 IU/l
Potassium – 6,5 mmol/l	Amylase – 27,0 g/l per h
Sodium – 147 mmol/l	Albumin – 45,4 g/l
Hemoglobin – 92 g/l	
Protein fractions	
Albumins – 40,3 %	α1-globulins – 2,2 %
α2-globulins – 14,6 %	β-globulins – 18,0 %
γ-globulins – 25,2 %	

According to these results, patient 4 has:

– mild hypercholesterolemia, hyperbilirubinemia due to indirect bilirubin, hyperkalemia;

– a slight increase in the activity of AST and LDH;

– increase in α2-, γ- and β-globulins against the background of decreased albumin.

Increased bilirubin levels due to indirect suggests hemolytic jaundice. In this regard, hyperkalemia, a slight increase in the activity of AST and LDH are due to their excretion from erythrocytes into the blood. Jaundice is characterized by dysproteinemia.

Patient 5, male, 50 years old (height – 180 cm, body weight – 98 kg)

Blood	
Cholesterol – 5,2 mmol/l	Direct bilirubin – 3,2 mcmol/l
Triacylglycerols –12,4 mmol/l	Glucose – 6,5 mmol /l
Total protein – 78,2 g/l	Creatine phosphokinase – 125 IU/l
Urea – 6,5 mmol/l	Lactate dehydrogenase – 329 IU/l
Uric acid – 0,22 mmol/l	Aspartate aminotransferase – 27,0 IU/l
Total bilirubin – 14,7 mcmol/l	Alanine aminotransferase – 29,2 IU/l
Potassium – 4,2 mmol/l	Amylase – 126,0 g/l per h
Sodium – 145 mmol/l	Albumin – 48,4 g/l
Hemoglobin – 156 g/l	
Protein fractions	
Albumins – 57,3 %	α1-globulins – 3,5 %
α2-globulins – 9,9 %	β-globulins – 10,1 %
γ-globulins – 19,3 %	

According to these results, patient 5 has:

– severe hypertriacylglycerolemia;

– slight hyperglycemia;

– increase in amylase activity.

Increased amylase activity is organ-specific for pancreatic lesions. As a result, hyperglycemia is probably due to decreased production of insulin by pancreatic cells. Increased levels of triacylglycerols often occur on the background of pancreatitis. The patient can be assumed – acute pancreatitis.

Patient 6, female, 55 years old (height – 160 cm, body weight – 77 kg)

Blood	
Cholesterol – 5,9 mmol/l	Direct bilirubin – 4,2 mcmol/l,
Triacylglycerols – 0,86 mmol/l	Glucose – 5,1 mmol/l
Total protein – 78,2 g/l	Creatine phosphokinase – 175 IU/l
Urea – 1,32 mmol/l	Lactate dehydrogenase – 525 IU/l
Uric acid – 0,22 mmol/l	Aspartate aminotransferase – 39,0 IU/l
Total bilirubin – 25,8 mcmol/l	Alanine aminotransferase – 250 IU/l
Potassium – 4,2 mmol/l	Amylase – 21,2 g/l per h
Sodium – 141 mmol/l	Albumin – 25,2 g/l
Hemoglobin – 134 g/l	
Protein fractions	
Albumins – 41,5 %	α1-globulins – 3,5 %
α2-globulins – 4,5 %	β-globulins - 18,3 %
γ-globulins – 32,2 %	

According to these results, patient 6 has:

– mild hypercholesterolemia, mild hyperbilirubinemia due to indirect bilirubin;

– decrease in urea and albumin levels;

– increase in the activity of LDH and ALT;

– increase in γ- and β-globulins against the background of decrease in α2-globulins and albumin.

Increased activity of LDH and ALT is organ-specific for the liver – hepatocyte damage. An increase in bilirubin due to indirect bilirubin indicates an inability of hepatocytes to conjugate bilirubin, and a decrease in urea and albumin indicates a decrease in the synthesizing function of the liver. The observed dysproteinemia is characteristic of toxic, viral hepatitis, cirrhosis. The patient can be assumed – liver disease.

Patient 7, male, 50 years old (height – 176 cm, body weight – 75 kg)

Blood	
Cholesterol – 7,3 mmol/l	Direct bilirubin – 3,3 mcmol/l
Triacylglycerols – 3,3 mmol/l	Glucose – 16,5 mmol/l
Total protein -75,5 g/l	Creatine phosphokinase – 102 IU/l
Urea – 10,3 mmol/l	Lactate dehydrogenase – 198 IU/l
Uric acid – 0,20 mmol/l	Aspartate aminotransferase – 27,3 IU/l
Total bilirubin – 14,8 mcmol/l	Alanine aminotransferase – 28,0 IU/l
Potassium – 4,3 mmol/l	Amylase – 22,6 g/l per h
Sodium – 143 mmol/l	Albumin – 25,2 g/l
Hemoglobin – 150 g/l	
Protein fractions	
Albumins – 60,0 %	α1-globulins – 4,5 %
α2-globulins – 8,3 %	β-globulins - 11,7 %
γ-globulins – 15,6 %	

According to these results, patient 7 has severe hyperglycemia, hypercholesterolemia, hypertriacylglycerolemia, increased urea (uremia).

Hyperglycemia suggests the presence of diabetes. In addition, an increase in urea levels is also characteristic of this pathology due to increased protein breakdown. Hyperlipidemia can be explained by increased formation of atherogenic lipoproteins and impaired degradation due to decreased activity of the enzyme lipoprotein lipase. The patient can be assumed - diabetes mellitus.

Patient 8, female, 65 years old (height – 160 cm, body weight – 85 kg)

Blood	
Cholesterol – 4,2 mmol /l	Direct bilirubin – 3,2 mcmol /l
Triacylglycerols – 1,15 mmol /l	Glucose – 4,2 mmol /l
Total protein – 80,0 g/l	Creatine phosphokinase – 107 IU /l
Urea – 6,3 mmol /l	Lactate dehydrogenase – 265 IU /l
Uric acid – 0,23 mmol /l	Aspartate aminotransferase – 33,3 IU /l
Total bilirubin – 13,8 mcmol /l	Alanine aminotransferase – 32,0 IU /l
Potassium – 3,8 mmol /l	Amylase – 22,1 g/l per h
Sodium – 138 mmol /l	Albumin – 49,2 g/l
Hemoglobin – 84 g/l	
Protein fractions	
Albumins – 58,0 %	α1-globulins – 4,5 %
α2-globulins – 8,5 %	β-globulins – 9,4 %
γ-globulins – 19,6 %	

According to these results, patient 8 has a decrease in hemoglobin, the rest of the indicators are within normal limits. The patient can be assumed – anemia.

Patient 9, female, 60 years old (height – 165 cm, body weight – 90 kg)

Blood	
Cholesterol – 3,0 mmol/l	Direct bilirubin – 4,2 mcmol/l
Triacylglycerols – 3,0 mmol/l	Glucose – 5,1 mmol/l
Total protein – 68,0 g/l	Creatine phosphokinase – 900 IU/l
Urea – 7,32 mmol/l	Lactate dehydrogenase – 615 IU/l
Uric acid – 0,23 mmol/l	Aspartate aminotransferase – 139 IU/l
Total bilirubin – 16,8 mcmol/l	Alanine aminotransferase – 20 IU/l
Potassium – 3,95 mmol/l	Amylase – 21,1 g/l per h
Sodium – 137 mmol/l	Albumin – 36,2 g/l
Hemoglobin – 135 g/l	
Protein fractions	
Albumins – 44,0 %	α1-globulins – 7,5 %
α2-globulins – 14,2 %	β-globulins – 13,8 %
γ-globulins – 20,5 %	

According to these results, patient 9 has:

– severe hypercholesterolemia, hypertriacylglycerolemia;

– increasing the activity of CPK, LDH, AST;

– increase in α1- and α2-globulins.

Hyperlipidemia can be considered a risk factor for atherosclerosis and coronary heart disease. The revealed dysproteinemia testifies to acute inflammatory process. Increased activity of CPK, LDH, AST is organ-specific for the heart muscle – damage to its cells.

The patient can be assumed – heart disease, in particular, myocardial infarction.

TASKS FOR SELF-CONTROL

1. The patient has a sharply increased content of acetoacetate and β-hydroxybutyrate in the blood and urine.

– *What could be the cause of this changes?*

– *What do you remember about acetoacetate and β-hydroxybutyrate; what hormones regulate their synthesis; what additional biochemical tests should be performed to confirm the diagnosis?*

– *What diseases and pathological conditions are accompanied by an increase of these substances content?*

2. A patient with liver disease was conducted a study of blood urea content.

– *What was the aim of this analysis?*

– *What enzymes should be tested in the blood to prove the liver disease development?*

– *What purpose is for determination of the total bilirubin and its fractions content?*

– *What urine tests should be performed to confirm the diagnosis?*

3. The patient complains of progressive muscle weakness, loss of muscle mass.

– *What tests should be prescribed during the biochemical examination of the patient? Justify the answer.*

4. There are three isoforms of the enzyme creatine phosphokinase in the body – BB, CF, MM.
– What reaction is catalyzed by creatine phosphokinase?
– Which organs contain enzyme isoforms?
– What pathological conditions can be diagnosed by increased activity of these isoforms in the blood?
– Explain why in clinical practice the activity in the blood of the BB isoform is practically does not investigated?
5. The patient has recently complained of yellowing of the skin and dark urine.
– Suggest tactics of biochemical investigation to substantiate of correct diagnosis.
– What type of jaundice can cause this condition?
– What indicators of biochemical analysis should be paid special attention for differentiation of pathological condition?
– What does the presence or absence of mesobilinogen in the urine indicate?
6. The patient showed a decrease of blood pressure, biochemical investigation revealed an increase in serum amylase activity on the first day and a significant increase in lipase activity on the second day of hospital stay.
– What disease is possible in the patient?
– Offer recommendations for the patient treatment.
7. The patient's blood uric acid content is 1.1 mmol/l, creatinine – 130 mmol/l.
– What disease can be assumed in a patient?
– What class of compounds uric acid and creatinine are belonged to? From what compounds they are formed; compare the indicators with the norm.
8. Biochemical examination of the patient's blood revealed a significant increase in the activity of aspartate and alanine aminotransferases. The de Ritis coefficient is 4.25.
– What disease can be assumed?
– What other enzymes could be increased in the patient's serum?
9. The patient complains of periodic chest pain. The examination revealed the presence of atherosclerotic plaques in the coronary and cerebral arteries. Plasma cholesterol levels are 8.4 mmol/l, LDL is 4.3 mmol/l, and LDL is 3.9 mmol/l. To clarify the diagnosis, the patient had a liver biopsy, which revealed a significant reduction in the number of receptors for LDL and LDL.
– Describe the patient's condition by the ratio of lipoproteins.
– Specify the pathogenesis of hypercholesterolemia in the patient.
– What is the prevention strategy of this pathology?
10. The content of urea in the patient's serum (analysis was performed on an empty stomach) is 9.3 mmol/l.
– Is it the normal content?
– In what pathological conditions does the level of urea in the blood change?
– What additional biochemical tests should be prescribed to the patient?

11. A child with hypertension and edema was admitted to the clinic. The content of sodium in the blood is 170 mmol/l, potassium – 2 mmol/l. 0.5 g of sodium and 4 g of potassium are excreted per day.

– Name the causes of such symptoms.

– What are the functions of potassium and sodium ions in the body?

– How will the deficiency of these ions be detected?

– What is the regulatory mechanism for the normal content of potassium and sodium in the blood?

12. The man in the last two years noted an increase in weight by 14 kg with a predominant deposition of adipose tissue on the torso and face, the appearance in the abdomen of burgundy stripes and depigmented with peeling spots on the back. The face turned a deep red color. Blood tests revealed: cortisol content exceeds the reference interval by 1.5 times; urinary excretion of free cortisol is 5.5 times higher than normal. The man was diagnosed with an adenoma.

– What is the possible diagnosis and what additional investigations are needed to confirm it?

– What is the cause of adipose tissue redistribution?

– What are the indications for cortisol testing?

– What the mechanism of glucocorticoids, in particular cortisol, affection on metabolic processes in the body?

13. The patient has uremia, convulsions, loss of consciousness.

– How will the level of residual nitrogen, urea, creatinine in the blood and urine change in this case?

– To justify the answer, remember: what is uremia, residual nitrogen?

– What pathology can be identifying by measurement of creatinine content in the blood and urine?

14. In the biochemical laboratory, two namesakes were investigated protein in blood plasma, but the initials were not indicated on the form. The protein content in one analysis was 30 g/l, in another – 100 g/l. One patient had significant edema and the other had pneumonia.

– Indicate which result corresponded to each patient. Justify the conclusion.

– What the causes of hyper- and hypoproteinemia? What protein fractions changes caused the results of analysis?

15. The patient complains of low body temperature, weight gain, lethargy, drowsiness. The content of T4 and T3 in the blood plasma is reduced.

– Name the pathology, which is characterized by these symptoms.

– How do the biochemical parameters of blood and urine change under this pathology?

– What are the biological effects of T4 and T3?

– Explain the mechanism of action of T4 and T3.

– Explain the difference between T4 and T3 deficiency in children and adults.

16. In patient was found: facial edema, significant proteinuria, hypoproteinemia, dysproteinemia, hyperlipidemia.
– *What diagnosis can be assumed? Justify the answer.*
– *What additional clinical and biochemical investigations of the biomaterial should be performed in this case? Justify the answer.*
17. A patient consulted a doctor with complaints that can be regarded as symptoms of an active form of rheumatism – damage of connective tissue, which is accompanied by the destruction of heteropolysaccharides in the glycoproteins.
– *What specific biochemical parameters of blood and urine should be examined to clarify the diagnosis? Justify the answer.*
18. Examination of the patient detected C-reactive protein at a concentration well above 0.5 mg/liter.in the blood.
– *Could this person be considered healthy?*
– *What information does the detection of C-reactive protein in the blood provide?*
19. In the experiment, the experimental animals had hypophysectomy.
– *How will the blood glucose change?*
– *To justify the answer: name the sources of blood glucose; name the causes of hypo- and hyperglycemia; What hormones regulate blood glucose levels?*
20. Hereditary diseases – mucopolysaccharidosis are manifested by metabolic disorders in connective tissue, pathology of bones and joints.
– *What indicators of blood and urine tests indicate the presence of this pathology?*
21. The patient has symptoms of connective tissue pathology.
× *Which blood serum and urine biochemical parameters determination will confirm the assumption of connective tissue pathology?*
22. A person suffers from diabetes mellitus accompanied by fasting hyperglycemia (more than 7.2 mmol/l).
– *Which plasma protein level allows you to assess (for the previous 4–8 weeks before the investigation) the level of glycemia? Justify the answer.*
23. In a child operated on for goiter, the level of calcium in the blood is 1.25 mmol/liter. The child has seizures.
– *What is the probable cause of low blood calcium and seizures?*
– *What functions do calcium ions provide?*
– *What is the normal concentration of these ions in the blood of a child and an adult?*
– *How is the normal level of calcium in the blood plasma maintained?*
24. A patient with jaundice was found an increase in the content of total bilirubin in the blood plasma due to the indirect fraction, in the feces and urine – a high content of stercobilin. The level of direct bilirubin in blood plasma is within normal limits.
– *What pathology can be assumed?*
– *Name its possible causes.*
– *To substantiate the answer, remember: the scheme of hemoglobin breakdown, bilirubin fractions, their norms in the blood.*

25. The patient went to the clinic with complaints of general weakness, aching abdominal pain, poor appetite, yellowing of the skin. 77.3 mmol/l of total bilirubin and 70.76 mmol/l of conjugated bilirubin were detected in the serum.
– *What pathology can be assumed?*
– *Name its possible causes.*
26. The patient has low blood pH and hydrocarbonate ions, increased levels of lactic and pyruvic acids in the blood and urine.
– *What type of acid-base disorder is observed?*
– *Name its possible causes.*
27. During the probe of blood plasma for the study of the isoenzyme spectrum of lactate dehydrogenase sampling hemolysis of erythrocytes was occurred.
– *Which of the enzyme isoenzyme forms will necessarily be increased in the investigation of this sample?*
28. The patient's level of total cholesterol is 6.1 mmol/l.
– *What recommendations should be given to the patient?*
– *Remember the scheme of cholesterol synthesis, its role in the body, possible metabolic disorders.*
– *What are the key enzymes involved in cholesterol synthesis?*
– *What is the principle of hypocholesterolemic therapy?*
29. The patient's serum α-amylase activity is increased.
× *What additional biochemical tests and why should be performed to confirm the diagnosis - pancreatitis?*
30. The following biochemical results were obtained in several patients: 1) total cholesterol (cholesterol) – 4.6 mmol/l; HDL cholesterol – 1.2 mmol/l; 2) total cholesterol – 6.7 mmol/l; HDL cholesterol – 1.2 mmol/l; 3) total cholesterol – 6.7 mmol/l; HDL cholesterol – 0.8 mmol/l.
– *Which of the patients has tendency for atherosclerosis formation? Justify the answer.*
31. Which hormones insufficiency could be indicated by the detection of a persistent increase of urinary excretion of sodium and chlorine ions?
– *What are the functions of these ions?*
– *How are they distributed between cells and plasma?*
– *What the clinical manifestation of these ions' deficiency or excess?*
32. The pensioner went to the doctor with complaints of pain in the epigastric region with irradiation in the back, not related to eating. Urine is dark, feces is light. Biochemical results: in serum total protein – 72 g/l; albumin – 40 g/l; total bilirubin – 380 mmol/l; alkaline phosphatase – 510 IU/l.
– *Describe the content of total protein compared to normal?*
– *What does the increase in alkaline phosphatase activity indicate?*
– *What is the normal albumin content?*
– *What are the reference limits of total serum bilirubin?*
– *What can be associated with changes in bilirubin in the blood?*
– *What diagnosis can be assumed?*

33. The patient was treated with prednisolone for infectious polyarthritis. The patient felt better and spontaneously stopped taking prednisolone. Over time, the patient felt worse. The examination revealed a decrease in blood glucose, lower blood pressure, decreased urinary excretion of 17-ketosteroids.
– *Why did the patient's condition worsen after the discontinuation of prednisolone?*
– *Which hormone secretion was suppressed before the prednisolone withdrawal.*
– *Explain whether the patient's condition will improve with corticotropin.*
– *Schematically show the effect of corticotropin on effector cells.*
34. The patient, 50 years old, first consulted a doctor with complaints of chest pain when climbing stairs, increased fatigue at work, memory loss. The examination revealed an increase in blood pressure to 156/94 mm Hg. In the biochemical study of fasting blood: glucose – 6.3 mmol/l, total cholesterol – 7.4 mmol/l, HDL cholesterol – 0.6 mmol/l, LDL cholesterol – 4.3 mmol/l.
– *Does the patient have a disorder of lipid metabolism? What pathology is described in the question?*
35. The patient has high blood pressure, basal metabolism, glucose and free fatty acids in the blood. Plasma adrenaline levels are significantly elevated.
– *What organ pathology do these data indicate? Justify the answer.*
36. The patient complains of weight gain, shortness of breath, palpitations, fatigue, intermittent headache, menstrual disorders. Appetite is increased. The woman's height is 157 cm, body weight is 110 kg, pulse is 96/min, blood pressure is 152/98 mm Hg. Elevated levels of cholesterol, triglycerides, LDL and VLDL were detected in the blood. The basic metabolism is at the lower limit of the norm.
– *Explain the mechanisms of these symptoms' development.*
– *What is the possible pathogenesis of obesity in patients?*
37. Blood fasting glucose content – 6.4 mmol/l, and 2 hours after a carbohydrate breakfast – 12.6 mmol/l in patient.
– *Specify the normal glucose content on an empty stomach and 2 hours after a carbohydrate breakfast.*
– *Analyze the results of the patient's glucose tolerance test and make conclusions.*
– *Is it possible to develop glucosuria in this patient?*
38. Blood the fasting glucose content is 5.8 mmol/l, and 2 hours after a carbohydrate breakfast – 8.4 mmol/l.
– *Analyze the results of the patient's glucose tolerance test and make conclusions.*
– *Which disease risk does increases in the patient?*
– *Name the biochemical indicator of long-term glycemia, indicate its normal indicators and diagnostic value.*
39. At the examination of the patient, a thickening of the carotid artery wall was found, the content of total cholesterol in the blood serum is 7.4 mmol/l, and HDL cholesterol – 0.9 mmol/l.
– *Evaluate the results of biochemical studies.*
– *Which pathology is characterized by such changes?*
– *Name the lipoproteins that transport cholesterol and describe their biological role.*

40. The patient's total plasma cholesterol is 4.5 mmol/l, LDL – 4.0 mmol/l, HDL – 1.2 mmol/l.

– Assess the analysis results.

– What pathology high risk takes place in this case?

– How will the risk of this pathology development change if the serum HDL content will be 0.7 mmol/l?

CLASS 3 (5 hours)

TOPIC 3: Clinical and biochemical investigation of cardiovascular diseases. Clinical and biochemical investigation of the kidney and urinary tract diseases

RELEVANCE. The heart and blood vessels are the main transport system of the human body, which provides metabolic processes. It is a component of various functional systems that determine homeostasis. The cardiovascular system diseases remain the leading cause of death in the world. There are a number of the most common cardiovascular diseases: coronary heart disease, hypertension, pericarditis, myocarditis, congenital and acquired heart defects, cardiac arrhythmias and conduction, infectious endocarditis. Myocardial infarction and stroke are acute diseases caused by impaired blood flow due to blockage of blood vessels. Heredity, unhealthy lifestyle (smoking, hypodynamia), malnutrition (fatty food, excessive amount of salt), obesity, lipid metabolism disorders, hyperhomocysteinemia, endocrine disorders, diseases of other internal organs are among the risk factors for cardiovascular disease. Early diagnosis and adequate therapy can not only increase life expectancy, but also achieve stable normalization and abolition the pathology. A set of special blood tests to assess risk factors, detect early and hidden lesions of the cardiovascular system, the risk of atherosclerosis, coronary heart disease and heart failure, to assess the likelihood of myocardial infarction is prescribed for cardiovascular disease (cardiac profile).

The kidneys are one of the most important organs, the main function of this organ is to maintain the dynamic stability of homeostasis. The kidneys are involved in the regulation of water-electrolyte balance, blood pressure, maintenance of acid-base status, osmotic pressure of body fluids, stimulation of erythropoiesis, etc. The kidneys produce urine from the components of blood plasma. Up to 150 different substances are excreted in the urine. Daily urine contains an average of about 40 g of organic and 20 g of inorganic substances.

They are divided into several groups depending on the mechanism of various substances entry into the urine: 1) as a result of glomerular filtration (creatinine, urea, etc.); 2) as a result of secretion and reabsorption in the renal tubules (electrolytes); 3) as a result of excretion in proximal nephron (organic acids, bases); 4) from the cells of the renal tubules (ammonia, some enzymes); 5) as a result of complete reabsorption from the ultrafiltrate in the proximal nephron (sugars, amino acids). Substances of the first four groups are called non-threshold, because their presence in the urine is not associated with blood

concentrations. Substances of the last group are called threshold, because in unaffected kidneys, they appear in the urine when their concentration in the blood is more than a certain value – the threshold. The appearance of threshold substances in the urine can occur against the background of normal blood levels under disturbances of the reabsorption mechanisms. Kidney diseases are numerous and diverse in both clinical and morphological manifestations. Biochemical analysis of urine and detection of biochemical changes in the blood have a great importance in determination of the pathological process activity, the renal function state. These methods play a crucial role in the diagnosis and appointment of adequate therapy in many cases in the absence of anamnestic data.

AIM OF THE CLASS.

1. Types, risk factors, classification of cardiovascular diseases and their biochemical markers.

2. To identify metabolic changes that develop in acute myocardial infarction and characterize biochemical markers of myocardial damage.

3. Assimilate biochemical parameters changes in atherosclerosis, hypertension and coronary heart disease.

4. Types, risk factors, classification of kidney diseases and their laboratory diagnosis.

5. To formulate the value of the urine general analysis at patients examination with diseases of kidneys and urinary tracts.

6. To study the biochemical parameters of acute and chronic renal failure and assess their clinical and diagnostic value.

7. To learn biochemical diagnostic algorithms for nephotic syndrome, pyelonephritis, glomerulonephritis, nephrolithiasis, amyloidosis.

THEORETICAL QUESTIONS

1. Cardiovascular diseases: types, risk factors, classification.
2.* Classification of biochemical markers of cardiovascular pathology.
3.* Disorders of oxidative metabolism under acute myocardial infarction.
4. Biochemical markers of myocardial damage.
5. Changes in metabolic biochemical parameters under atherosclerosis, their assessment, ways of correction.
6. Changes in biochemical parameters at different stages of arterial hypertension, evaluation of laboratory results.
7. Kidney disease: types, risk factors, classification.
8. General analysis of urine in the patient's examination under diseases of the kidneys and urinary tract.
9. Clinical and biochemical analysis of blood in the diagnosis of renal pathology.
10.* Functional tests in renal pathology. Endogenous creatinine clearance.
11.* Biochemical tests for assessment of renal pathology.

12.* Biochemical markers of acute renal failure.
13. Biochemical markers of chronic renal failure.
14.* Changes in biochemical parameters of blood and urine under glomerulonephritis and pyelonephritis, their assessment and diagnostic value.
15. Changes in biochemical parameters of blood and urine under nephrolithiasis, their assessment and diagnostic value.
16.* Biochemical parameters change in renal amyloidosis, their assessment and diagnostic value.
17. Biochemical parameters change in nephrotic syndrome, their assessment and diagnos tic value.

* – questions for self-study

Orientative card for self-study theoretical questions processing

Content	***Instruction for learning activities***
1. Classification of cardiovascular pathology biochemical markers.	***1.1. Markers of dyslipidemia and lipoproteins modification.*** ***Total cholesterol*** *(indirectly reflects the risk of atherosclerosis; the rate of 3.2–5.2 mmol/l);* ***LDL*** *(one of the most atherogenic, "harmful" fractions of lipids; rich of cholesterol and, transporting it to the cells of endothelial vessels, forming atherosclerotic plaques; the norm: 1.7–3.5 mmol/l).* ***HDL*** *(prevent the formation of atherosclerotic plaques in blood vessels; antiatherogenic effect due to the ability to transport cholesterol to the liver, where it is utilized and excreted from the body; normal > 0.9 mmol/l).* ***Triacylglycerols*** *(neutral fats in blood plasma, normal content 0,4–1,8 mmol/l).* ***Coefficient of atherogenicity*** *(indicator of the atherogenic and antiatherogenic lipid fractions ratio; normal content < 3).* ***Apo A, Apo B*** *(see class 2).* ***1.2. Markers of instability and rupture of atherosclerotic plaque*** *(periods of exacerbation of cardiovascular disease are characterized by the appearance of unstable atherosclerotic plaques, which cells begin to express proteins involved in damage to the fibrous capsule and the atherothrombosis development).* ***Matrix metalloproteinases (MMPs) –*** *family of zinc- and calcium-dependent endopeptidases, which hydrolyze the main components of the extracellular matrix – collagen of the intima and basement membrane.*

	Tissue inhibitors of MMP (TIMP). *!!! Determination of MMP and TIMP levels allows to diagnose atherosclerotic plaque instability in the early stages and identify patients with high risk of cardiovascular complications; inflammatory activity are elevated levels of MMP-9 and decreased levels of TIMP-1 are typical indicators for unstable plaques → they are used as markers of the acute phase (plaque rupture).* ***Placental growth factor (PlGF)*** *– glycoprotein of the vasculoendothelial growth factors family; participates in key mechanisms of atherosclerotic plaques destabilization; it determination in the blood helps to identify people with high cardiovascular disease risk.* ***Pregnancy-associated plasma protein A (PAPP-A)*** *– circulating protein in the blood, which belongs to zinc-containing metalloproteinases; its content in damaged atherosclerotic plaques is several times higher than in stable → the level of protein in the blood reflects the activity of endogenous plaque destruction and is a predictor of cardiovascular disease unfavorable prognosis.* ***Soluble form of CD40 ligand (sCD40L)*** *– transmembrane glycoprotein of the tumor necrosis factors family, as well as its receptor, is expressed by atherosclerotic plaque cells; increases the synthesis of cell adhesion molecules and various chemokines, enhances the expression of tissue factor and matrix metalloproteinases, which leads to instability of atherosclerotic plaque; considered as a potential indicator of the cardiovascular disease risk.* ***1.3. Markers of inflammation*** *(systemic inflammation is a predictor of adverse course and high cardiovascular risk).* ***Cytokine profile →*** *balance between pro-inflammatory (tumor necrosis factor alpha, interleukins 1, 6, 8, 12) and anti-inflammatory (interleukins 4, 10, 11, 13) cytokines.* ***C-reactive protein*** *– an important independent marker of the inflammatory process, high level of C-reactive protein reflects the increased activity of inflammatory cytokines associated with vascular endothelial damage and coagulation.* ***Lipoprotein-associated phospholipase A2*** *– enzyme formed in the early stages of atherosclerotic plaque formation, stimulates inflammation and contributes to its instability; considered as a marker of specific vascular inflammation.*

	Fibrinogen *– plasma protein synthesized in the liver, then converted into fibrin - the basis of a blood clot that forms a blood clot, thus completing the process of blood clotting → fibrinogen as a marker of inflammation and thrombosis is directly related to cardiovascular disease, in particular, its elevated levels are associated with thickening of the blood vessels intima and sub-clinical manifestations of atherosclerotic lesions.* ***Homocysteine*** *– sulfur-containing amino acid, a product of methionine metabolism; high concentrations are cytotoxic to endothelial cells, which is considered as a factor of atherosclerosis (along with levels of cholesterol, LDL, HDL, C-reactive protein, fibrinogen), increased levels activate thrombosis, which determines the high risk of cardiovascular disease and other complications.* ***1.4. Markers of ischemia and necrosis.*** ***Cardiospecific troponins I and T*** *(Troponin I rate < 0.04 ng/ml, chemiluminescent method; Troponin T normal rate – < 0.05 ng/ml, immunochromatographic method) – 4–6 hours after myocardial damage are released into the blood, reaching a maximum level in 12–24 hours, normalization of the level – in 7–14 days.)* *!!! The troponin content is determined at the first treatment of patients with complaints of chest pain, then repeat the analysis after 6 hours and if the complaints and suspicion of myocardial damage – after 12 hours. Cardiac muscle ischemia can only be excluded in a case of negative troponin after 12 hours the onset of symptoms. To distinguish between ischemic and non-ischemic causes of myocardial damage, the troponin content is monitored in the dynamics of observations. Troponin levels can also be increased in non-ischemic myocardial damage (myocarditis, pericarditis, heart failure, hypertension, etc.).* ***Myoglobin*** *(normal content 0–70 mcg/l, immunoturbide metric method) – increase in level is noted in 2–3 hours after myocardial damage, reaches a maximum for 6–12 hours and is normalized for 24–48 hours; the advantage of myoglobin among other markers is its early appearance in the blood, but a negative result of the analysis for myoglobin excludes a heart attack, a positive one – needs to be confirmed by troponin; if there is no increase in myoglobin within 12 hours of chest pain, the likelihood of myocardial infarction is unlikely.*

	Creatine phosphokinase MB form *(normal content 0–24 IU/l) – creatine phosphokinase isoenzyme specific for the myocardium; 4–6 hours after chest pain, the activity of the enzyme in the blood begins to increase, after 12–24 hours - reaches a maximum, after 2– days – returns to baseline values).* ***Lactate dehydrogenase-1*** *(normal content for adults 72–182 IU/ml): increased activity in the blood during the first three days after the onset of pain allows with a high probability to diagnose myocardial infarction; 16–20 hours after the pain attack, the total LDH activity does not exceed the normal range, but there is an increase in LDH-1 activity, in addition, LDH-1 activity remains increased after the total LDH activity returns to normal.* ***Aspartate aminotransferase*** *(normal content: women – no more than 31 IU/l, men – no more than 37 IU/l) – activity in the blood increases in 6–8 hours after chest pain, reaches a maximum level in 24–36 hours and normalizes up to 5–6-day after myocardial infarction; it is noted that the activity of the enzyme may increase even before the appearance of electrocardiographic signs of myocardial infarction, and the lack of its reduction after 3–4 days of illness is an unfavorable sign; alanine aminotransferase activity in this pathology increases slightly, so the de Ritis coefficient (AST/ALT) increases sharply.* ***Cardioprotein, which binds fatty acids (Heart-FABP, FABP3)*** *– the main energy substrate of cardiomyocytes, has a low molecular weight, freely located in the cytoplasm of cardiomyocytes, under necrosis quickly enters the bloodstream; kinetics are similar to myoglobin, the content in the blood increases in 2–3 hours after chest pain, reaches a maximum level in 8–10 hours and normalizes in 18–30 hours.* ***Free fatty acids not bound to albumin*** *– increasing the level leads to a decrease in antiatherogenic HDL, the formation of atherogenic LDL and increased plasma levels of TAG; elevated levels of free fatty acids cause the synthesis of reactive oxygen species in the mitochondria of macrovascular endothelial cells, which leads to oxidation of LDL and modification of HDL, which induces inflammation in the walls of blood vessels, the formation and as a result, accumulation of cholesterol plaques.*

	1.5. Markers of myocardial stress. ***Natriuretic peptides*** *– a family of vasoactive compounds that are synthesized by cardiomyocytes in response to stretching and increased pressure in the chambers of the heart: atrial natriuretic peptide (ANP), cerebral natriuretic peptide (BNP); ANP – mainly reflects the secretory activity of the atria, BNP - the ventricles of the heart (so this peptide is often called ANP-B type, rather than "brain peptide"); an increase in the content of these peptides indicates an increased risk of cardiovascular complications and death.* ***Galectin-3*** *– belongs to the family of β-galactoside-binding proteins, due to the presence of a collagen-like domain in the structure, it can bind to a wide range of extracellular matrix proteins; practically not found in cardiomyocytes, while myocardial fibroblasts express its high levels → increase in blood levels – under cardiac pathology, accompanied by the development of fibrosis, as well as under myocardial dysfunction.* ***Copeptin*** *(CT-proAVP, carboxy-terminated-proarginin-vasopressin) – glycoprotein synthesized in the hypothalamus from the C-terminal part of the hormone vasopressin; blood level rises during stroke, myocardial infarction, which allows it to be considered as a marker of acute stressful situations.* ***1.6. Markers of kidney damage*** *(kidney disease is closely related to cardiovascular disease).* ***Microalbuminuria*** *(urinary albumin excretion up to 20 mg/l) – is considered not only as an early sign of kidney damage, but also as a sign of initial stages of vascular pathology (atherosclerosis, endothelial dysfunction, etc.); is an unfavorable predictor of cardiovascular disease; insignificant levels of albumin excretion indicate a significant risk of cardiovascular complications, and the transition from microalbuminuria to proteinuria clearly indicates deterioration of vascular status* ***Cystatin C*** *– protein from the family of cysteine proteinase inhibitors, expressed in constant concentration in all nuclear cells, participates in the processes of extra- and intracellular proteolysis, preventing its excessive activation by proteases; its level is independent of gender, age and muscle mass and is considered to be the earliest than creatinine level, a marker of kidney*

	damage, as well as a highly sensitive marker of cardiovascular disease, independent of cardiomarkers such as cardiotroponins, natriuretic peptides, C- reactive protein, etc. ***Lipocaline associated with neutrophil gelatinase (NGAL)*** *(other names lipocalin-2, siderocalin, 24p33 or LCN2) – a protein, main functions are: 1) bacteriostatic (forms complexes with microbial siderophores, binds iron needed by microbes, and inhibits their growth); 2) normalization of damaged tissues due to participation in apoptosis; 3) restoration of damaged epithelium by stimulating differentiation and structural reorganization of epithelial cells, etc.; in pathological conditions may be involved in the remodeling of atherosclerotic plaques and myocytes in ischemic myocardial damage; the level increases significantly in urine and blood in the first hours after the development of acute renal damage.* ***1.7. Endocrine indicators*** *as markers of cardiovascular risk:* *– aldosterone, renin, potassium, sodium (to exclude hyperaldosteronism);* *– thyrotropin, T3, T4 (to assess thyroid function);* *– sex hormones.* ***1.8. Indicators of the metabolic syndrome:*** *Metabolic syndrome is a condition that combines a group of risk factors (obesity, hypertension, hyperglycemia as an indicator of development, insulin-resistant diabetes, hypercholesterolemia), the development of cardiovascular disease, etc.* *Biochemical criteria of metabolic syndrome:* *• increase in blood cholesterol levels (≥ 5.2 mmol/l);* *• increase in blood TAG levels (≥ 1.7 mmol/l);* *• decrease in the level of HDL cholesterol (< 1.0–1.2 mmol/l);* *• increase in the level of LDL cholesterol(≥ 3,0 mmol/l);* *• impaired glucose tolerance – increase in plasma glucose 2 hours after exercise in the oral glucose tolerance test (OGTT) (≥ 7.8 mmol/l and < 11.1 mmol/l) at a fasting level of < 7.0 mmol/l;* *• disturbances in fasting glycaemia – increase in the plasma glucose level ((≥ 6,1 mmol/l and < 7,0 mmol/l) in case if the glucose level after 2 hours at OGTT < 7.8 mmol/l;* *• combined impairment of fasting glucose and fasting glucose – increase in fasting plasma glucose (≥ 6.1 mmol/l and < 7.0 mmol/l) in combination with glucose after 2 hours at OGTT (≥ 7.8 mmol/l and < 11.1mmol l);*

	Laboratory studies of metabolic syndrome also include C-reactive protein, C-peptide, insulin, HOMA, glycated hemoglobin, homocysteine (increase), microalbuminuria
2. Disorders of oxidative metabolism in acute myocardial infarction	***2.1.*** *Myocardial infarction is a disease characterized by necrosis of heart muscle certain areas under the background of ischemia, which occurs due to acute vascular insufficiency.* ***2.2.*** *Energy supply of the heart muscle: occurs due to aerobic resynthesis of ATP (as energy sources the myocardium uses various substances that are supplied by the blood – glucose, fatty acids, ketone bodies, glycerol; own glycogen reserves are practically not used, they are needed for energy supply during intensive physical exercises); anaerobic pathways of ATP resynthesis are included, as a rule, at intensive physical exercises.* ***2.3.*** *Disorders of myocardial metabolism under ischemia:* *– oxygen deficiency → disturbances of cardiomyocytes energy supply;* *– deficiency of metabolic substrates → decreased tissue respiration, increased glycogenolysis and glycolysis due to increased intracellular concentrations of catecholamines and cAMP, which activate phosphorylase and phosphofructokinase – a key enzyme of glycolysis (but maximally enhanced anaerobic metabolism is not able to long-term, which inhibits phosphofructokinase);* *– damage and destruction of cell cytoplasmic membranes, mitochondrial membranes → decrease in activity of enzymes in a myocardium, their reflux from cells and increasing activity in blood;* *– metabolic disorders of carbohydrates, proteins, lipids → in particular, reducing the oxidation of fatty acids, increasing their inclusion in triacylglycerols → fatty infiltration of the myocardium*
3. Functional tests under renal pathology. Endogenous creatinine clearance	***3.1.*** *Functional tests are based on a comparison of the certain substances content in blood and urine → assessment of the kidneys ability to excrete a substance from the body (called clearance from "clear" – to clean).* ***3.2.*** *Clearance – a term used to assess the process of any substance excretion from the blood when passing through the kidneys; reflects the equivalent volume of blood plasma, which contains the amount of substance excreted in the urine per minute (for example, 1 ml of*

	blood plasma contains 1 mg of substance → when blood passes through the kidneys every minute 1 mg of this substance is excreted in urine → clearance (purification) is 1 ml/min). In clinical practice, the creatine chosen for this substance → creatinine clearance is the volume of blood plasma that is cleared of creatinine in 1 minute when passing through the kidneys → a decrease in creatinine clearance indicates kidney damage. ***3.3.*** *Creatinine is a non-threshold substance, it is only filtered by the kidneys and cannot be reabsorbed → creatinine clearance is equal to glomerular filtration.* ***3.4.*** *Creatinine clearance is calculated by the formula: C = (Cc – V) / Ccr, where C is the creatinine clearance; V – volume of urine excreted per minute; Cc – concentration of creatinine in urine, Ccr – concentration of creatinine in blood as object of renal filtration depending on growth and weight of the person, creatinine clearance is retrained on size of body's average level (≈ 1,73 m^2) for "normalization" of clearance indicators; in this regard, determine the height and weight of persons).* ***3.5.*** *Creatinine clearance norm in man organism 97–137 ml/min·1,73 m^2, in woman – 88–128 ml/min·1,73 m^2 (after 40 years – creatinine clearance decreasing);* ***3.6.*** *Decreased creatinine clearance is observed under: decreased glomerular filtration due to hemodynamic renal disorders – blood loss, shock, severe dehydration, prolonged heart failure; acute glomerulonephritis, nephrotic syndrome, pyelonephritis, amyloidosis, urinary tract obstruction, acute tubular dysfunction, etc.* ***3.7.*** *Increased creatinine clearance is observed under nephropathy, hypertension, pregnancy and others*
4. Biochemical tests for renal pathology assessment	***4.1. Plasma urea concentration:*** *– evaluated as plasma urea nitrogen; normal content – 3.33–8.35 mmol/l;* *– increase in plasma urea nitrogen – azotemia (uremia):* *• <u>renal:</u> associated with renal pathology, when the ↓ excretory function (glomerulonephritis, pyelonephritis, renal tuberculosis, renal amyloidosis, etc.).* *!!! In acute renal failure, an increase in blood urea up to 16 mmol/l = renal dysfunction of moderate severity, up to 33 mmol/l – severe, more than 50 mmol/ – very severe (unfavorable prognosis);*

	• *extrarenal: associated with ↓ renal blood flow (circulatory failure, ↓ AP) or with the prevention of the urine outflow (with urolithiasis, tumors in the urinary system, after surgery complications).* ***4.2. Concentration of urea in urine:*** *– significant indicator of kidneys excretory function;* *– normal content – 333–835 mmol/day;* *– ↓ in urine → ↓ kidneys excretory function → in pyelonephritis, glomerulonephritis, amyloidosis, acute and chronic renal failure.* ***4.3. The ratio of urea in urine and plasma:** 1) > 10 : 1 – prerenal renal failure; < 3 : 1 – renal failure.* ***4.4. Cystatin C – "gold standard" for determining the glomerular filtration rate:*** *– by chemical nature – protein;* *– role: inhibitor of cysteine proteinases;* *– properties: 1) synthesized at a constant rate by all nucleated cells; 2) freely filtered through the glomerular membrane; 3) completely metabolized in the kidneys; 4) is not secreted by the proximal renal tubules; 5) the synthesis is not affected by age, sex, muscle mass, diet, the presence of inflammatory reactions;* *– under renal pathology, the filtration of cystatin C deteriorates →↑ blood level (considered the most informative endogenous marker of glomerular filtration rate).* ***4.5. Sodium ion content in blood plasma and urine:** necrosis of the renal tubules leads to ↑ content in the urine (> 40 mmol/l) while ↓ in the blood plasma.* ***4.6. Glycinamidinotransferase activity in blood serum:** organ-specific enzyme, the activity of which ↑ in the blood under necrosis of the proximal nephron.* ***4.7. N-acetyl-β-D-glucosaminidase activity in serum and urine:** renal tubular endothelial enzyme, used to assess the degree of renal tubules necrosis; after kidney transplantation ↑ enzyme activity in the blood – a signal of graft rejection*
5. Biochemical markers of acute renal failure	***5.1.** Acute renal failure is a rapid disorder of the kidneys homeostatic function, often with ischemic or toxic origin, which is manifested by rapidly increasing azotemia, severe water-electrolyte disorders. Depending on the mechanism of development, there are three types: 1) prerenal (hemodynamic), due to acute renal failure; 2) renal (parenchymal), caused by damage to the renal*

	parenchyma; 3) postrenal (obstructive), which develops as a result of acute urinary incontinence. ***5.2.*** *The most characteristic manifestations for acute renal failure are: anuria (diuresis less than 50 ml); oliguria (diuresis less than 500 ml); azotemia – increased urea and creatinine in the blood; hyperkalemia – an increase in serum potassium to a level of more than 5.5 meq/l; metabolic acidosis associated with a decrease in serum bicarbonate levels up to 13 mmol/l.* ***5.3. Biochemical markers of kidneys excretory function:*** *creatinine; cystatin C.* ***5.4. Biochemical markers of kidney structural damage.*** ***KIM-1 (kidney injury molecule-1)*** *– surface cell protein of the immunoglobulin family, which has the properties of renal damage ideal marker f, which is associated with the lack of normal expression → a significant sharp increase in blood and urine in acute damage to the proximal renal tubules.* ***NGAL (neutrophil gelatinase–associated lipocalin)*** *– lipocalin, associated with neutrophil gelatinase: protein – a component of the inflammation acute phase; participates in stimulating the proliferation of damaged cells, especially epithelial; counteraction to bacterial infections, etc.; depending on various pathological conditions, it is expressed and secreted by a significant number of different cells, in particular, renal tubules, prostate, hepatocytes, immune cells, epithelial cells of the respiratory and digestive tract; ↑ NGAL synthesis in proximal tubular cells is caused by disorders associated with renal parenchymal ischemia and its nephrotoxic lesions → in response to renal tubular damage there is a sharp ↑ in blood plasma and urine NGAL levels.* ***Uromodulin*** *– glycoprotein, synthesized exclusively by the kidneys, is the main protein of urine; participates in the kidney stones formation, modulation of systemic immune responses, etc.; specific localization of the protein allows to use as a marker of the epithelium of the distal nephron functional state → in the initial acute kidney damage ↑ synthesis and secretion of uromodulin.* ***β2-Macroglobulin*** *– protein, is part of the light chain of membrane-bound HLA antigens → plays an important role in cellular immunity; due to its small size – passes through the membranes of the glomeruli and is absorbed*

	in the proximal tubules; in glomerular pathology – ↓ filtration rate → ↑ level of beta2-microglobulin in the blood and ↓ in the urine; in tubular damage – ↓ amount of reabsorbed beta2-microglobulin → ↑ level of beta2-microglobulin in urine and ↓ in blood. ***Interleukin-18*** *– proinflammatory cytokine, involved in the reaction of tubular epithelium damage → ↑ excretion in the urine (detected in the urine in acute renal failure of ischemic origin at the earliest time – 4–6 hours, reaching a maximum at 12 hour).* ***N-acetylglucosamidinase*** *– lysosomal enzyme, the highest activity – in the kidneys, where the enzyme is secreted by the epithelium of the proximal tubules and is involved in the degradation of mucopolysaccharides and glycoproteins, which form structural components in tissues; normally the enzyme does not cross the glomerular barrier; under damage of epithelial cells the enzyme release→ ↑ level in the urine is released (this allows us to consider it as a marker of early, subclinical damage to the proximal tubules in acute kidney disease)*
6. Changes in biochemical parameters under pyelonephritis and glomerulonephritis, their assessment and diagnostic value	***6.1. Glomerulonephritis*** *– kidney disease of immunoinflammatory nature, in which the glomeruli are affected with the involvement of tubules and interstitial tissue. Laboratory diagnostics:* *• <u>general urine test:</u>* *– proteinuria up to 3 g/l (massive could be during 1–3 weeks, moderate – several months); may be selective (detection of albumin in urine) or non-selective (detection of other proteins in urine);* *– microhematuria – a permanent symptom with a longer duration than proteinuria;* *• <u>blood test:</u>* *– dysproteinemia with a decrease in the protein ratio of albumin/globulin due to α2- and γ-globulins;* *– compensated metabolic acidosis;* *– hyperkalemia (only in severe disease);* *– hypernatremia;* *– hypeuricemia;* *!!! In the case of chronic glomerulonephritis: hypoproteinemia, hypercholesterolemia, signs of chronic renal failure.* ***6.2.*** *Pyelonephritis is a nonspecific bacterial disease with damage to the renal parenchyma, mainly interstitial tissue, pelvis and calyces. Laboratory diagnostics:*

	• general analysis of urine: leukocyturia, pyuria, bacteriuria, leukocyte cylinders, hematuria due to destruction of the renal papillae; *• blood test: dysproteinemia with decreased protein ratio, hypergammaglobulinemia, increased levels of C-reactive protein, azotemia and acidosis (especially in the case of bilateral kidney damage).*
7. Changes in biochemical parameters under renal amyloidosis, their assessment and diagnostic value	*Renal amyloidosis – a disease in which there is a deposition in the kidney tissue of a special insoluble protein – amyloid, followed by its defeat. Laboratory diagnostics:* *• general urine test: proteinuria (starting from the proteinuric stage), possible detection of Bence-Jones proteins in the case of amyloidosis under myeloma;* *• blood test: steady and significant increase in erythrocyte sedimentation rate in the early stages; decrease in hemoglobin and the number of erythrocytes (with the development of renal failure); increase in platelets (in case of involvement in the pathological process of the spleen); hypoproteinemia, hypoalbuminemia (in the case of nephrotic stage), hypercholesterolemia, hyperlipoproteinemia (due to LDL)*

TASKS FOR SELF-CONTROL

1. Patients suffering from cardiovascular system diseases are prescribed a drug similar to endogenous creatine phosphate for the treatment and prevention of myocardial damage.

– What is the biological role of creatine phosphate?

– Where is creatine phosphate synthesized?

– What enzyme is used in creatine phosphate metabolism? Name its role in enzyme diagnostics.

– Name the final product of creatine phosphate metabolism

2. It has been experimentally proven that fatty acids are a natural energy "fuel" for the heart.

– Calculate and compare the energy effect of aerobic oxidation of glucose and palmitic acid.

– To do this, write the total β-oxidation of palmitic acid and calculate the energy balance of palmitic acid oxidation to carbon dioxide and water; write a diagram of aerobic oxidation of glucose and calculate the energy yield in the oxidation of glucose to carbon dioxide and water.

3. A child with hypertension and edema was admitted to the clinic. The content of sodium in the blood – 170 mmol/l, potassium – 2 mmol/l. 0.5 g of sodium and 4 g of potassium are excreted in the urine per day.

– Name the causes of these symptoms and possible treatments.
– What are the functions of potassium ions in the body?
– How will the deficiency of these ions manifest itself?
– How is the maintenance of normal levels of sodium and potassium in the blood plasma?

4. An overweight man complained of intermittent heart pain and shortness of breath. Analysis of fasting blood lipids showed: total cholesterol – 6.5 mmol/l, HDL cholesterol – 1.4 mmol/l, TAG – 8 mmol/l.
– Which pathology is characterized by the above changes in blood plasma parameters?
– What is the atherogenic factor? What is its normal value?
– What is the atherogenic factor in this case?
– What is the effect of drugs that lower blood cholesterol?
– Why are obese people recommended a diet low in carbohydrates?

5. A young man with symptoms of coronary heart disease due to atherosclerosis was admitted to the hospital. During the examination it was found that the patient's lipoproteins contain the inactive enzyme lecithincholesterolacyltransferase (LHAT).
– Why LHAT insufficiency can lead to the development of atherosclerosis?
– Write a reaction that is catalyzed by LHAT.
– Indicate which fractions of lipoproteins are rich in LHAT?

6. Examination of the patient revealed a sharp increase in the de Ritis coefficient - the ratio of AST/ALT.
– What disease can be assumed in a patient?
– Which enzyme activity should be determined to clarify the diagnosis?

7. One of the reasons for the development of myocardial infarction in old age is associated with a disturbance in LDL liver receptor's structure.
– What disease, leading to myocardial infarction, lead to these disorders?
– Remember what LDL is, their composition and structure.
– What is the biological role of LDL?
– What disorders of lipid metabolism could develop in this case?

8. Patient with atherosclerosis after hospital returnee has a recommendation about a diet that stimulates bile flow and increases intestinal motility? Why?

9. The patient has a sharp weakness, temperature 36.8 ºC, pallor, heart pain. High activity of AST, creatine kinase, LGD1, 2 is defined in blood.
– In what disease is it observed? Why?

10. Biochemical examination in the patient's blood revealed a sharp increase in the activity of AST and ALT. De Ritis coefficient = 4.25.
– What disease could be assumed in a patient?
– What other enzymes could be increased in the patient's serum?

11. Which enzymes activity increases in the blood in the first two days after myocardial infarction?

12. A patient with heart failure was recommended as a biological supplement betaine (trimethylglycine - a donor of methyl groups).
– Explain this recommendation.

13. After heart failure, the patient was prescribed as a bioadditive carnitine and arginine. Explain the purpose of this recommendation.
14. The cause of angina is ischemia and myocardial hypoxia. In this disease, for more economic consumption of oxygen in the heart muscle prescribe mildronate – an inhibitor of carnitine synthesis.
– *The speed of which biochemical process is reduced?*
– *Describe this biochemical process.*
15. Examination of a teenager suffering from xanthomatosis revealed familial hypercholesterolemia.
– *The concentration of which lipid's transport forms increases in this disease?*
– *Describe the classification, chemical composition, functions, metabolism of lipid transport forms.*
16. Biochemical analysis of blood revealed a high content of cholesterol in the β-lipoprotein fraction.
– *What are the possible consequences of this phenomenon? Justify the answer.*
17. A patient suffering from hypertension and atherosclerotic vascular disease is prescribed a diet.
– *Indicate which of the lipids should be reduced in his daily diet?*
– *Describe the scheme of synthesis of this lipid and the peculiarities of process regulation.*
18. Cardiospecific marker of myocardial necrosis is: *a) lactate dehydrogenase; b) myoglobin; c) troponin I; d) total creatine phosphokinase.*
19. The level of triacylglycerols as a risk factor for cardiovascular disease are: *a) 1.9 mmol/l; b) 1.2 mmol/l; c) 1.0 mmol/l; d) 0.7 mmol/l.*
20. Hypertension under pheochromocytoma is caused by: *a) increased renin secretion; b) excessive secretion of mineralocorticoids; c) increasing angiotensin synthesis; d) increased secretion of catecholamines.*
21. The cause of hypertension under the defeat of the renal parenchyma are: *a) increase the secretion of catecholamines; b) activation of the renin-angiotensin system; c) excessive secretion of mineralocorticoids; d) increase the synthesis of angiotensin.*
22. At high risk of cardiovascular complications, LDL cholesterol levels should not be higher: *a) 3.5 mmol/l; b) 3.0 mmol/l; c) 2.0 mmol/l; d) 1.8 mmol/l.*
23. The most specific method of diagnosing hypertension under Itsenko-Cushing's syndrome is determination of: *a) thyrotropin; b) renin; c) 17-oxycorticosteroid; d) creatinine.*
24. Normalization of blood levels of MB-creatine phosphokinase under the development of myocardial infarction is observed through: *a) 14 days; b) 5–6 days; c) one day; d) 2–3 days.*
25. LDL is a part: *a) apolipoprotein A; b) apolipoprotein B-100; c) apolipoprotein B-48; d) apolipoprotein C.*

26. High density lipoproteins: *a) are part of chylomicrons; b) promote the entry of cholesterol into the blood; c) ensure the removal of cholesterol from peripheral tissues; d) are atherogenic lipoproteins.*
27. Hyperlipoproteinemia type IIa is characterized by an increase in blood plasma: *a) VLDL; b) LDL and VLDL; c) general LP; d) LDL.*
28. What is the activation to the depressive neurohumoral mechanism under the development of heart failure: *a) cerebral and atrial natriuretic factors; b) sympathoadrenal system; c) renin-angiotensin-aldosterone system; d) vasopressin.*
29. The most informative method of detecting necrotic changes in the myocardium is: *a) the level of transaminases in the blood; b) total creatine phosphokinase in the blood; c) the level of the MB fraction of creatine phosphokinase in the blood; d) lactate dehydrogenase in the blood.*
30. Atherogenic lipoproteins do not include: *a) VLDL; b) HDL; c) TAG; d) chylomicrons.*
31. Hyperlipoproteinemia type IIb is characterized by an increase in blood plasma: *a) VLDL; b) LDL and VLDL; c) general LP; d) LDL.*
32. Cholesterol in the human body: *a) synthesized in the liver and kidneys; b) comes exclusively with food; c) synthesized in the liver and adrenal glands; d) is synthesized in the liver and comes with food.*
33. The change in blood characteristic of the myocardial infarction acute stage is: *a) increase in amylase activity; b) reduction of the de Ritis coefficient; c) increase in troponin levels; d) increasing the activity of γ-glutamyltranspeptidase.*
34. The earliest biochemical marker of necrosis in the development of myocardial infarction is an increase in blood: *a) MV KFC; b) troponin I; c) myoglobin; d) LDH4.*
35. The patient had atherosclerosis complicated by thrombosis of the lower extremity's vessels, gangrene of the left foot toes. Excessive thrombosis is most likely associated with increased: *a) platelet adhesion; b) prothrombinase activation; c) conversion of prothrombin to thrombin; d) conversion of fibrinogen to fibrin; e) synthesis of heparin.*
36. A protease is formed in the kidneys, which triggers a cascade of reactions in the blood, culminating in the formation of a compound that regulates blood pressure. The secretion of this protease into the blood occurs in response to a decrease in the blood supply of the afferent glomerular arterioles and an increase in the concentration of sodium ions in the distal nephron.
– *Name the protease synthesized in the kidneys.*
– *Name the place of synthesis.*
– *Write a cascade of reactions triggered by renal protease.*
– *What hormone is formed in response to the interaction of adrenal cells with the final product of the reaction's cascade.*
37. It is important for the formation of kidney stones: *a) alkaline reaction of urine, oversaturation with salts, features of nutrition; b) the content of acetone in the urine; c) acid reaction of urine; d) features of nutrition; e) frequency of urination.*
38. Most accurately reflects the degree of chronic renal failure increasing in serum: *a) urea; b) ammonium salts; c) creatinine; d) indicators do not change; e) glucose.*

39. Obstructive anuria is caused: *a) kidney cyst; b) renal infarction; c) ureteral stones; d) liver damage; e) wrinkling of the kidney.*

40. How does the concentration of urea in the urine change with the progression of chronic renal failure? *a) decreases; b) increases; c) at the beginning of the disease increases, at the end – decreases; d) at the beginning of the disease decreases, at the end – increases; e) remains constant.*

41. How does the concentration of urea in the blood change with the progression of chronic renal failure? *a) decreases; b) increases; c) at the beginning of the disease increases, at the end - decreases; d) at the beginning of the disease decreases, at the end - increases; e) remains constant.*

42. Choose the metabolic consequences of chronic renal failure: *a) acid-base disorders; b) anemia; c) hypocalcemia; d) imbalance of sodium and water, hyperkalemia.*

43. The diagnosis of chronic renal failure includes the following: *a) increase in blood creatinine, azotemia in the late stages; b) decrease in relative density of urine (Zemnitsky's test); c) reduction of kidney size (ultrasound, radiography, CT); d) signs of glomerulitis and interstitium (biopsy).*

44. The combination of which features reflects the functionality of the kidneys? *a) protein content in urine, isostenuria; b) isostenuria, increased plasma creatinine; c) reduction of glomerular filtration; d) increase in plasma creatinine.*

45. Match the items presented in the marked columns. For each component of the left column, select the numbered element of the right column (each numbered element of the right column can be selected once).

➢ **Change in creatinine clearance**	The reasons for the corresponding change in creatinine clearance
A) enhancement; *B) reduction*	*1) renal failure;* *2) nephropathy;* *3) burns;* *4) eclampsia;* *5) hypercatabolic states.*
➢ **Kidney pathology syndrome**	A characteristic feature of the syndrome
A) nephritis syndrome; *B) nephrotic syndrome*	*1) the main symptom is proteinuria > 3 g/day;* *2) blood in the urine as a result of glomerular bleeding;* *3) hypercholesterolemia;* *4) often develops after infection with hemolytic streptococcus;* *5) edema.*
➢ **Albumin in urine**	Diagnostic value
A) microalbuminuria (in daily or single urine); *B) macroalbuminuria.*	*1) severe glomerular dysfunction;* *2) early sign of glomerular function of the kidneys;* *3) answer to medical treatment;* *4) the level of protein in the urine 0.02–0.2 g/l;* *5) changes in the glomeruli of the kidneys are irreversible.*

➢ **Proteinuria**	It is developing
A) prerenal; *B) selective renal;* *C) nonselective renal;* *D) postrenal;* *E) functional in nephrotic syndrome*	*1) with long walks (marching);* *2) with massive protein loss (more than 3 g/day);* *3) with tumors of the urinary tract, bladder, urethra;* *4) with paraproteinuria under myeloma;* *5) with microalbuminemia under diabetes.*

46. The patient is in the nephrology department. Complaints of swelling on the face, legs, headache, fever over 38 °C. Laboratory tests. In the blood: urea – 9.4 mmol/l, creatinine – 112 mmol/l, uric acid – 0.73 mmol/l, total protein – 62 g/l. In urine: color – dull brown, relative density – 1032, protein – 2.4 g/l, under microscopy – erythrocytes – 28–30 in the field of view in clusters, leukocytes – 10–14 in the field of view. Mucus, epithelium, erythrocyte cylinders.
– *What diagnosis can be assumed?*
– *Does the patient have renal failure? Justify.*
– *What additional tests should be prescribed in this case?*
47. The patient's urine volume is 70 ml; color – light yellow; turbid; pH – 7.0; smell – ordinary; relative density – 1,030; protein – 30 g/l. Microscopy: mucus – a little; leukocytes – 30–40 in the field of view; erythrocytes – unchanged, 2 in the field of view; renal epithelial cells, partially in a state of fatty dystrophy, 15–20 in the field of view; transitional epithelial cells – 0–1 in the field of view; cylinders – hyaline and granular, 8–10 in the field of view; epithelial – 3 in the field of view; granular-fatty and hyaline droplets – 2–3 in the field of view, waxy – single in the drug. In the blood hypoalbuminemia, hypercholesterolemia. The most likely diagnosis: *a) cystitis; b) nephrotic syndrome; c) pyelonephritis; d) acute renal failure; e) chronic renal failure.*
48. The patient's urine volume is 160 ml; color yellow; transparency – cloudy; pH – 5.0; smell – ordinary; relative density – 1,010; protein – 0.99 g/l; sediment – bulky, viscous. Microscopy: mucus – in moderation; leukocytes – mainly neutrophilic granulocytes, individually and in groups of up to 100 in the field of view; erythrocytes are changed, 2–3 in the field of view; renal epithelial cells – 1–2 in the field of view; transitional epithelium – 1–3 in the field of view; cylinders – hyaline, granular and epithelial, 3–4 in the drug; salts – urate. The most likely diagnosis: *a) cystitis; b) urethritis; c) glomerulonephritis; d) pyelonephritis; e) acute renal failure.*
49. The patient's urine volume is 40 ml, brown, cloudy, pH – 6.0; smell – ordinary; relative density – 1,040; protein – 3 g/l; sediment abundant, loose, brown. Microscopy: leukocytes – 8–10 in the field of view; erythrocytes – dehemoglobinized, partially fragmented, up to 150–200 in the field of view; renal epithelium – 8–10 in the field of view, transitional epithelium – 0–1 in the field of view; cylinders – hyaline, granular, epithelial, partially burpigmented, 2–3 in the field of view; salts – crystals of uric acid – single. The most likely diagnosis: *a) cystitis; b) nephrotic*

syndrome; c) pyelonephritis; d) acute glomerulonephritis, hematuria variant; e) chronic renal failure.

50. To diagnose renal complications under diabetes use a test to determine: *a) microalbuminuria; b) ketonuria, c) glucosuria; d) orataciduria.*

51. Which enzyme is organ-specific for the kidneys: *lactate dehydrogenase, succinate dehydrogenase, aspartate aminotransferase, transamidinase, creatine phosphokinase.*

– For the synthesis of which substance is this enzyme needed?

– Write the reactions of this substance synthesis that occur in the kidneys and liver.

– Specify the names of the enzymes.

– What compound is obtained?

– What is formed during the phosphorylation of this compound?

52. Renal proteinuria is caused by: a*) impaired filtration and reabsorption of proteins; b) dysproteinemia; c) ingestion of exudate under inflammation of the urinary tract; d) kidney stones; e) hypofunction of the renin-angiotensin system.*

53. Postrenal proteinuria is caused: *a) passing through an intact renal filter of low molecular weight proteins; b) filtration of normal plasma proteins through a damaged renal filter; c) impaired protein reabsorption in the proximal tubules; d) ingestion of inflammatory exudate in the urine under diseases of the urinary tract; d) the formation of Bence-Jones protein.*

54. The absence of urobilin in the urine indicates: *a) on hemolytic jaundice; b) obstructive jaundice; c) parenchymal jaundice; d) Gilbert's disease; e) intestinal dysbacteriosis.*

55. The cause of renal glucosuria is a disturbance: *a) glucose reabsorption in the proximal tubules; b) glucose filtration through an intact renal filter; c) glucose reabsorption in the distal tubules; d) glucose secretion by the renal epithelium; e) synthesis in the kidneys of erythropoietin.*

56. Excretion of more than three liters of urine per day is observed at: *a) cystitis; b) diabetes mellitus; c) pyelonephritis; d) acute glomerulonephritis; e) acute renal failure.*

57. Acute renal failure is characterized by: *a) increase in daily diuresis; b) reduction or complete cessation of urine output; c) the predominance of nocturnal diuresis; d) frequent urination; e) painful urination.*

58. In the urine of patients with acute glomerulonephritis is observed: *a) leukocyturia; b) transitional epithelium; c) many salts of uric acid; d) glucosuria; e) hematuria.*

59. Pyuria is characteristic of: *a) chronic nephritis; b) pyelonephritis; c) nephrotic syndrome; d) acute renal failure; e) chronic renal failure.*

60. Determination of endogenous creatinine clearance can be used for: *a) assessment of the secretory function of the renal tubules; b) determination of the concentrating function of the kidneys; c) estimates of the functioning nephrons number; d) determination of the renal filtration amount; e) diagnosis of cystitis.*

61. Clinical syndrome accompanied by renal proteinuria: *a) heart failure; b) cystitis; c) glomerulonephritis; d) tumor of the bladder; e) a stone in the bladder.*

62. Physiological proteinuria occurs when: *a) lipoid nephrosis; b) pyelonephritis; c) diabetic nephropathy; d) after overheating or supercooling; e) paraproteinemia.*
63. Microalbuminuria is defined as: *a) as urinary excretion of more than 30 mg of albumin per day in the absence of severe proteinuria; b) urinary excretion of more than 300 mg of albumin per day; c) the appearance of albumin in the urine when loaded with carbohydrates; d) the dominance of albumin in the protein fractions of daily urine; e) excretion in the urine of more than 600 mg of albumin per day.*
64. An early sign of diabetic nephropathy is: *a) glucosuria; b) disturbance in the glucose tolerance test; c) hyperglycemia; d) microalbuminuria; e) proteinuria.*
65. The cause of uremic osteodystrophy in chronic renal failure is: *a) increase in parathyroid level; b) increase in creatinine levels; c) increase in urea levels; d) decrease in erythropoietin levels.*
66. The most typical in acute glomerulonephritis is the appearance in urine: *a) hypostenuria; b) proteinuria; c) leukocyturia; d) bacteriuria.*
67. It is characteristic of the nephrotic syndrome: *a) hyperfibrinogenemia and hyperenzymemia; b) hyperproteinemia and dysproteinemia; c) hypoproteinemia and hyperlipidemia; d) hyperlipidemia and hyperbilirubinemia.*
68. The most likely sign of chronic kidney disease is: *a) arterial hypertension; b) nephrotic syndrome; c) significant proteinuria; d) azotemia.*
69. In the biochemical analysis of blood, the functional state of the kidneys reflects the level: *a) urea; b) residual nitrogen; c) creatinine; e) uric acid.*

Class 4 (5 hours)

TOPIC 1 (5 hours): Clinical and biochemical studies under digestive system diseases

RELEVANCE. The main condition of the vital function is a supplying of nutrients. The digestive system ensures their breakdown into simple organic substances, which are absorbed and used by cells and tissues as a plastic and energetic material. Digestive organs include the digestive tract through which food passes (mouth, esophagus, stomach, intestines), and digestive glands (salivary, pancreatic, liver, etc.). Digestive diseases today are quite common among all diseases of the internal organs. In modern conditions of life full of constant stress, poor nutrition, adverse environmental conditions, the body's reaction to this, in particular, affects the state of the digestive system. The incidence of this area is only growing every year, with the most common transition to a chronic form. In this regard, there is a need for continuous improvement of diagnostic methods, as well as the creation and development of new methods that can detect the disease at an early stage, assess the degree of damage to the digestive system, monitor the results of therapy. Biochemical and clinical blood tests, analysis of gastric and duodenal juice remain one of the important laboratory methods for diagnosing diseases of the digestive system, which allow to assess the general condition of the body, characterize the functional state of individual organs, the degree of structural tissue damage.

AIM OF THE CLASS.

1. Types, risk factors, classification of digestive system diseases and their laboratory diagnosis.

2. To study the biochemical parameters of stomach and pancreas diseases and be able to assess their clinical and diagnostic value.

3. To know the dynamics of changes in biochemical parameters that characterize hepatobiliary system (hepatitis, cirrhosis, steatosis, gallstone disease, malignant neoplasms) diseases.

THEORETICAL QUESTIONS

1. Digestive diseases: types, risk factors, classification.
2. Biochemical markers of gastric diseases:
   –* gastrin of blood;
   –* pepsinogen I, pepsinogen II in the blood;
   – analysis of gastric juice.
3. Biochemical markers of pancreatic diseases:
   – assessment of endocrine deficiency: determination of C-peptide, insulin, glucose, HOMA-IR insulin resistance index in the blood;
   –* assessment of exocrine deficiency by determination of blood and fecal activity of pancreatic enzymes;
   –* some pancreas tumor markers.

4.* General characteristics of biochemical parameters that characterize diseases of the hepatobiliary system.

5. Enzymodiagnostics of liver diseases.
6. Changes in biochemical parameters under chronic hepatitis, their assessment and diagnostic value.
7. Changes in biochemical parameters under cirrhosis, their assessment and diagnostic value.
8. Changes in biochemical parameters under gallstone disease, their assessment and diagnostic value.
9. Changes in biochemical parameters under fatty infiltration of the liver (steatosis), their assessment and diagnostic value.
10. Clinical and diagnostic value of indican determination in urine.

* – questions for self-study

Orientative card for self-study theoretical questions processing

Content	***Instruction for learning activities***
1. Biochemical markers of gastric diseases	***1.1. Gastrin – a marker of upper digestive system pathology:*** *– gastrointestinal hormone, the most well-known forms (depending on the number of amino acids) – G-17, G-34, G-14; G-34 (progastrin) – a form that circulates in the blood and is converted into active gastrin in target cells, produced in the pancreas and intestines, G-17 and G-14 – produced in G-cells of the gastric mucosa;*

	– role: enhances the production of hydrochloric acid by parietal cells of the stomach, pepsinogen, Castle's intrinsic factor, stimulates the synthesis of other digestive hormones secreted by the small intestine; *!!! G-17 – the main hormone that regulates the production of HCl;* *– increase in blood levels – a sign of gastric juice decreased acidity → indicates the gastritis development;* *– increase in blood levels is observed under: chronic gastritis with atrophy of the mucous membrane; pernicious anemia (B12 deficiency); peptic ulcer of the stomach and duodenum; gastrinoma (Zollinger-Ellison syndrome) – a malignant tumor of the pancreas; gastric tumors;* *– a decrease in blood levels is observed during antrectomy with vagotomy, hyperthyroidism.* ***1.2. Pepsinogen I – an indicator of the structure and functioning of the gastric mucosa, a marker of atrophic gastritis**:* *– proenzyme of pepsin, produced by the main cells of the stomach, which are only in the stomach's body (there is also synthesized hydrochloric acid, Castle's intrinsic factor) → under stomach diseases, the synthesis of pepsinogen I, HCl, Castle factor – is significantly reduced;* *– decrease in blood content is observed under: atrophic gastritis of the stomach, pernicious anemia, gastric resection, tumor processes, etc .;* *– increase in blood content is observed under: peptic ulcer of the duodenum, H. pylori infection and others.* ***1.3. Pepsinogen II – an indicator of the structure and function of the entire gastric mucosa, a marker of H. pylori-associated gastritis, gastric ulcer and duodenal ulcer:*** *– proenzyme of pepsin, produced in the cells of the body, cardiac and pyloric parts of the stomach, as well as in the duodenum;* *– increase in blood is observed under: acute or chronic H. pylori-associated gastritis; gastric and duodenal ulcers; Zollinger-Ellison syndrome, the use of proton pump inhibitors;* *– decrease in blood content is observed under: stomach resection, gastrectomy, hypothyroidism, etc.* *!!! Determination of pepsinogen I, II levels together with determination of gastrin content (in particular gastrin-17) and H. pylori test – assessment of the mucous membrane state of all parts of the stomach*

2. Assessment of exocrine pancreas deficiency by determination activity of pancreatic enzymes in the blood and feces	***2.1. Elastase-1 in the stool – a marker of exocrine insufficiency of the pancreas:*** *– pancreatic elastase-1 – proteolytic enzyme produced by acinar cells, excreted as proelastase in the duodenum, under the action of trypsin is converted into elastase.* *– the enzyme when passing through the intestinal tract is not exposed to any influences → the level in the stool is a standard marker of exocrine insufficiency of the pancreas;* *– decrease level in feces is observed under: chronic pancreas inflammatory defeat; destructive processes of the pancreas; destruction of the exocrine gland parenchyma; congenital dysfunction of pancreatic secretion with secondary fibrous degeneration; outflow disturbance of secretion into the duodenum for various reasons.* ***2.2. Alpha-amylase in blood and urine:*** *– pancreatic enzyme that catalyzes the breakdown of starch, glycogen and other polysaccharides to maltose;* *– there are two types of enzyme circulate in blood – P-type (produced by the pancreas) and S-type (produced by the salivary glands); under physiological conditions in the blood – 40 % is P-type, the rest – S-type; excreted in the urine mainly P-type, which is more informative about the functional state of the pancreas;* *– hyperamylasemia is observed under: acute pancreatitis (10–30 times); exacerbation of chronic pancreatitis (3–5 times), inflammatory liver disease (1.5–2.0 times); cholecystitis, etc.* *!!! During the development of total pancreatosis, tumor processes in the pancreas and chronic pancreatitis, the activity of the enzyme may not increase.* *– hyperamylasuria is observed under acute pancreatitis, exacerbation of chronic pancreatitis;* *– detection of hyperamylasemia and hyperamilasuria is an important but nonspecific marker of acute pancreatitis → for more information, the content of creatinine in blood and urine is determined at the same time → the results are calculated by the index of amylase-creatinine clearance (AMurine × CRblood) / / (AMblood × CRurine) ×100, normal: not more than 3 → increase in the index – a sign of pancreatitis;* *– results of investigation of blood and urine activity is complicated by the fact that alpha-amylase is contained in the salivary glands, as well as the colon, prostate, skeletal muscle → increasing of blood levels may also indicate diseases that have a similar picture with acute pancreatitis: acute*

	appendicitis, peritonitis, perforated ulcer of the stomach and duodenum, intestinal obstruction, etc. ***2.3. Lipase in the blood:*** *– pancreatic enzyme that hydrolyzes neutral fats;* *– the most informative indicator of acute pancreatitis than alpha-amylase;* *– increasing of activity in blood occurs in parallel with increasing of activity of amylase, but normalization occurs later than normalization of activity of amylase;* *– increase in blood activity is observed under: acute pancreatitis (growth begins in 2–6 hours after defeat of a pancreas, a maximum – in 12–30 hours, gradual decrease – within 2–4 days); chronic pancreatitis (first moderate increase, then decrease and normalization); tumor processes in the pancreas, obstruction (stone, scar) of the pancreatic duct, etc .;* *– decrease in blood activity is observed under: decrease in functions of a pancreas, a cystic fibrosis, a pancreatectomy.* *!!! The best diagnostic indicator for acute pancreatitis is a 5–10-fold increase in lipase activity, hyperamylasemia and increased amylase / creatinine clearance.* ***2.4. Chymotrypsin in feces:*** *– the main exocrine enzyme of the pancreas → activity reflects the overall exocrine function;* *– determination of the level in the stool is a more likely test to assess the function of the pancreas than the level of trypsin; this is due to the higher destruction of trypsin as it passes through the intestinal tract;* – decrease in feces is observed under: chronic inflammatory lesions of the pancreas; destruction of the exocrine parenchyma of the gland, etc. **2.5. Trypsinogen-2 (anionic trypsinogen) in the blood**: – one of the two main isoenzymes of trypsinogen; – normally the ratio of trypsinogen-1 (cationic) and trypsinogen-2 is ≈ 3.8; – a marker of acute pancreatitis – a significant increase in blood levels
3. Some pancreas tumor markers	***3.1. Glycoprotein antigen 19-9 (CA 19-9) - a marker of malignant tumors of the gastrointestinal tract:*** *– most sensitive to pancreatic cancer (≈ 80–85 % of cases), as well as tumors of the liver and biliary tract;* *– normal content in blood serum 0–37 IU/ml;* *– a significant increase in serum – pancreatic cancer, gastric cancer, tumors of the colon;*

	– moderate increase – in acute and chronic pancreatitis, cholestasis, mechanical jaundice, systemic connective tissue diseases. ***3.2. Glycoprotein antigen CA 242 – a marker of gastrointestinal tract malignant tumors****; produced by cells of the gastrointestinal tract epithelium; appearance in the blood indicates the development of pancreas tumors, colon, in particular, the rectum*
4. General characteristics of biochemical parameters that characterize hepatobiliary system diseases	***4.1. Markers of hepatocyte cytolysis (disturbances of hepatocyte integrity):*** *increase in blood activity of aminotransferases (ALT, AST), glutamate dehydrogenase, γ-glutamyltranspeptidase, sorbitol dehydrogenase, lactate dehydrogenase and its isoform LDH4.* ***4.2. Markers of cholestasis (impaired bile outflow):*** *increased blood activity of alkaline phosphatase, γ-glutamyltranspeptidase, leucine aminopeptidase, 5-nucleotidase, bile acid content, bilirubin (mainly due to the direct fraction), cholesterol, phospholipids.* ***4.3. Markers of toxic hepatocyte damage*** *(under various intoxications, such as alcohol, when cytolysis is virtually absent, but toxic substances disrupt the function of hepatocyte organelles): increased blood activity of AST due to its mitochondrial isoform, γ-glutamyltranspeptidase on the background of a slight increase in alkaline phosphatase activity.* ***4.4. Markers of impaired hepatocyte protein synthesis*** *(destructive and cytolytic changes of hepatocytes with mesenchymal inflammatory reaction, manifested by impairment of most hepatocyte functions, especially protein synthesis): decrease in blood total protein and especially albumin, transferrin, cholesterol VII, cholesterol, α-lipoproteins, cholinesterase activity and increase in bilirubin due to indirect fraction.* ***4.5. Markers of biliary pigment metabolism disorders*** *(diseases associated with increased bilirubin formation when the liver and biliary tract are not involved in the pathological process; diseases associated with hepatocyte damage or congenital enzymopathy resulting in impaired ability of hepatocytes to conjugate bilirubin; diseases, associated with impaired bile flow due to obstruction of the bile ducts): change in blood levels of total bilirubin and its fractions* ***4.6. Markers of impaired liver detoxification function****: increased blood levels of ammonia, decreased hippuric acid during the test with its formation under the administration of sodium benzoate, decreased excretion of bromosulfalein during the test, based on intravenous administration bromosulfalein.*

	4.7. Markers of mesenchymal-inflammatory process*: increase in acute phase proteins blood content (especially C-reactive protein, acid-α1-glycoprotein, fibrinogen), dysproteinemia due to increased γ-globulins, etc.; changes in cellular and humoral immunity: there are antibodies to subcellular fractions of heaptocytes, rheumatoid factor, antimitochondrial and antinuclear antibodies, changes in the number and functional activity of T- and B-lymphocytes, increased levels of immunoglobulins.* ***4.8. Markers of liver fibrosis****: pooled test (ELF) for the determination of serum hyaluronic acid, N-terminal procollagen III peptide and tissue metalloproteinase-1 inhibitor.* ***4.9. A marker of tumor processes in the hepatobiliary system*** *– α-fetoprotein: has a high sensitivity in liver tumors, as an additional tumor marker – to detect malignant tumors in the bile duct and gallbladder (recommended with simultaneous determination of the level of CA 19-9)*

TASKS FOR SELF-CONTROL

1. In patients with long time alcohol consumption take place a development of liver cirrhosis, edema.

–What is the cause of edema?

– Justify the mechanism of edema under liver cirrhosis.

2. The patient complains of pain in the stomach, especially on an empty stomach ("hungry" pain). Spicy food causes the pain intensification. Examination of gastric juice revealed an increase in its total acidity.

– What causes the gastric juice acidity?

– Excessive secretion of which acid is associated with hyperacidity of gastric juice?

– What are the functions of this component of gastric juice?

– Which compound is the main protection of the stomach wall from the aggressive action of acid?

– How is the secretion of this acid regulated?

3. The activity of ALT and AST was determined in the blood of a patient who had hepatitis. Which enzyme activity increases the most and why? When answering:

– Write the reactions that catalyze these enzymes.

– Explain the importance of these reactions in amino acid metabolism.

– Name the basic principles underlying enzyme diagnostics.

4. The man complains of yellowing of the skin. The content of indirect fraction of bilirubin in the blood is increased, no direct fraction is detected in urine. Urobilin in urine and stercobilin in feces is determined in significant quantities.

– Specify the pathology for which these symptoms are typical.

– Describe the breakdown of hemoglobin with the formation of free bilirubin.

– Name the enzyme involved in the conjugation of bilirubin.

– Name the metabolites formed during the reduction of bilirubin in the intestine.

– Describe the properties of indirect bilirubin.

5. In a patient with liver disease, the urea content in the blood is 2.0 mmol/l, 120 mmol was excreted in the urine per day.
– *Which liver function disturbance could be suspected?*
– *What enzymes should be determined to prove assumption.*
6. Explain why a patient suffering from intestinal atony and liver dysfunction is not recommended to eat foods rich in protein?
– *What process is disrupted in the intestine under disturbance of protein digestion?*
– *What is indole and skatole? What are the features of their metabolism? What is the end product of their metabolism?*
7. The patient has no hydrochloric acid in gastric juice.
– *How will it affect on digestion?*
– *Describe the functions of hydrochloric acid in the stomach.*
– *What is the origin of hydrochloric acid in gastric juice?*
8. The newborn was diagnosed with jaundice immediately after birth. Total bilirubin in the blood – 60 mmol/l, indirect – 53 mmol/l.
– *What kind of jaundice can be assumed?*
– *What types of bilirubin do you know?*
– *How are their differences from each other?*
– *What types of jaundice do you know?*
9. A biochemical study in the patient's blood revealed a sharp increase in the activity of AST and ALT. The de Ritis coefficient is 4.25.
– *What disease can be assumed in the patient?*
– *What other enzymes will increase in the patient's serum?*
10. The patient has jaundice of the sclera, mucous membranes, skin, dark urine, discolored feces. The content of direct and indirect bilirubin in the blood plasma is increased. Direct bilirubin is determined in urine, urobilinogen is absent.
– *Which pathology is characterized by these symptoms?*
– *What are the sources of direct and indirect bilirubin in blood plasma?*
– *Which pigment provides the color of feces and why does their discoloration occur under this disease?*
– *Why is bilirubin a toxic compound?*
– *Which fraction of bilirubin is higher in this jaundice? Why?*
11. The patient has a hepatitis in anamnesis. Examination revealed an increase in the liver, a change in its ultrasound structure. Diagnosed with fatty liver infiltration.
– *What does fatty infiltration of the liver indicate?*
– *Specify the mechanism of this pathology?*
– *Name the common metabolites of the synthesis of TAG and glycerophospholipids.*
× *Why do lipotropic factors slow down steatosis?*
× *What substances can be attributed to lipotropic factors?*
12. In women with hypertensive physique in the analysis of bile was determined high cholesterol content, and in the analysis of blood – increased alkaline phosphatase activity.
– *In which disease is the elevated cholesterol content in the bile and the activity of alkaline phosphatase in the blood?*

– *What causes of excessive cholesterol secretion with bile?*
– *What metabolites excreted in bile are formed in the liver from cholesterol?*
– *What reaction is catalyzed by alkaline phosphatase?*
– *What hormones regulate cholesterol synthesis?*
– *In what other diseases are there an increase in alkaline phosphatase activity is observed?*

13. With severe viral hepatitis, patients may develop hepatic coma due, in particular, to the toxic effects of ammonia on brain cells.
– *What is the reason for such a significant accumulation of ammonia in the blood?*
– *What happens to ammonia in the liver in a healthy person?*
– *Write a diagram of this process.*

14. The patient worked in a leather factory, which uses carbon tetrachloride for 10 years. On examination, the doctor found an increase in the size of the liver, biliary dyskinesia. There were complaints of weakness, nausea, dizziness.
– *What disease can be assumed in a patient?*
– *What biochemical tests should a doctor prescribe to make a correct diagnosis?*

15. A patient with chronic hepatitis was subjected to sodium benzoate administration to study the state of liver neutralizing function.
– *Excretion of what compound in the urine indicates a detoxification liver function?*
– *Reproduce the scheme of its formation in the body.*

16. A patient suffering from chronic hepatitis complains of hypersensitivity to barbiturates, which she previously tolerated without symptoms of intoxication.
– *Which liver function disturbance could provoke this state?*
– *Describe the biochemical parameters of this function.*

17. The patient complained of acute pain in the right hypochondrium. During the examination, the doctor noticed that the patient's sclera was yellow. Laboratory studies showed increased ALT activity in the blood and a negative reaction to stercobilin in the feces.
– *Which disease is characterized by such symptoms?*
– *What other biochemical indicators of the liver functional state should be examined in the patient's blood?*
– *Describe the possible causes of the disease.*

18. A patient with hepatitis was prescribed choline to prevent liver damage.
– *What is its therapeutic effect related to?*

19. A patient suffering from viral hepatitis in the second week of the disease developed sleep disorders, headache, aggression, unbearable itching of the skin. Objectively: lower blood pressure, blood clotting rate, reflex activity, bradycardia.
– *What are the possible reasons for these changes?*
– *What biochemical parameters need to be investigated in biological material?*

20. Caffeine increases the secretion of hydrochloric acid by the parietal cells of the gastric mucosa.
– *What is the biological role of HCl?*

– Where do the ions for the formation of HCl in the stomach cells come from?
– How is HCl synthesis regulated?
– What is the mechanism of signal transmission that activates HCl synthesis?
21. What biochemical parameters confirm the cholestasis syndrome: *a) dysproteinemia, changes in thymol and sulema tests; b) increased levels of bilirubin, alkaline phosphatase, hypercholesterolemia; c) increasing the activity of ALT, AcAT, LDG4, LDG5; d) increasing the activity of amylase.*
22. What process in the intestine is disturbed in a patient with chronic hepatitis, who also showed a significant decrease in the synthesis and secretion of bile acids?
23. A patient with low acidity of gastric juice takes acetic acid instead of hydrochloric acid recommended by a doctor.
– Is such a replacement acceptable?
– What can lead to a decrease in the acidity of gastric juice?
– What are the normal values of total acidity and free hydrochloric acid in gastric juice?
24. Examination of employees of a chemical enterprise revealed an increase in the activity of ALT in the blood by 5.7 times, and AST – by 1.5 times. One doctor suggested that this was the result of increased consumption of meat products the day before, and there was no cause for concern. Another doctor suggested that the worker should be hospitalized, assuming he had liver damage with organic solvents.
– Which doctor's assumption is correct? Why?
– What reactions are catalyzed by aminotransferases? Write these reactions.
– What is the diagnostic value of determining the activity of aminotransferases in serum?
25. The patient complains of belching with the smell of rotten eggs, pain in the epigastrium. Examination of gastric juice revealed: total acidity 15 mmol/l, other types of acidity are absent, the digestive ability of the stomach is not detected.
– What pathology can be assumed?
– Recall the value of the total acidity of gastric juice in the norm.
– What types of acidity do you know?
– Why is there no digestive capacity of the stomach in this case?
– Recall the functions of hydrochloric acid in digestion.
26. In humans, the absorption of fat hydrolysis products is impaired.
– Deficiency of which components in a small bowel cavity can be the reason for this?
– Reproduce the scheme of digestion of fats in the gastrointestinal tract.
27. One of the mechanisms of steatosis development is to reduce the utilization of neutral fat by VLDL.
– What lipotropic substances prevent the development of this condition?
28. The patient after a blood transfusion appeared yellowish color of the skin and mucous membranes.
– What kind of jaundice can be assumed?

– How will the indicators of pigment metabolism in the blood and urine change?

29. The patient was admitted to the surgical department with a diagnosis of acute pancreatitis. Conservative treatment has been started.

– Which drugs are pathogenetically justified?

– What are the biochemical markers of this pathology?

30. Clinical examination of the patient allowed to establish a preliminary diagnosis – gastric cancer. Lactic acid is found in gastric juice.

– In what metabolic process is lactate formed?

– Which enzyme is involved in the formation of lactate?

– What are the consequences of lactate accumulation in tumor cells?

31. When prescribing a diet to patients with liver cirrhosis with symptoms of liver failure, first of all, should be limited to: *a) protein; b) fat; c) carbohydrates; d) liquid.*

32. Signs of intrasecretory insufficiency of the pancreas under chronic pancreatitis include: *a) deficiency of fat-soluble vitamins; b) steatorrhea; c) hyperglycemia; d) weight loss.*

33. Gastric secretion is stimulated by*: a) secretin; b) serotonin; c) cholecystokinin; d) gastrin.*

34. The development of liver cancer on the background of cirrhosis can be suspected with an increase in blood*: a) cholinesterase; b) alpha-fetoprotein; c) immunoglobulin A; d) AST.*

35. The indicator that characterizes the activity of chronic hepatitis are: *a) alkaline phosphatase; b) ALT; c) albumin; d) cholesterol.*

36. The biochemical indicator of the early stage of acute liver failure is*: a) prothrombin index; b) ALT activity; c) the level of bilirubin in the blood; d) the level of total protein in the blood.*

37. Cytolysis of liver cells in viral hepatitis reflects the following biochemical test: *a) the level of total protein and protein fractions; b) thymol sample; c) the level of ALT and AST; d) cholesterol levels.*

38. Laboratory signs of decreased synthetic liver function are*: a) hypertriacylglycerolemia; b) haptoglobulinemia; c) hypoenzymemia; d) hypoprothrombinemia.*

39. Chronic hepatitis is characterized by*: a) the predominance of ALT over AST; b) the predominance of AST over ALT; c) isolated increase in ALT; d) isolated increase in AST.*

40. The risk of developing acute pancreatitis is significant with a significant increase in blood plasma*: a) HDL; b) LDL; c) HDL; d) VLDL.*

41. Alkaline phosphatase and γ-glutamyltranspeptidase are sharply increased in: *a) Konovalov-Wilson disease; b) hemochromatosis; c) pancreatitis; d) chronic hepatitis with symptoms of cholestasis and liver cirrhosis.*

CONTROL QUESTIONS

1. Clinical biochemistry as a science. Subject, tasks, modern directions of development.
2. Biochemical research methods and their characteristics.
3. Typical disorders of carbohydrate metabolism.
4. Hypo- and hyperglycemia: types, mechanisms of development.
5. Typical disorders of lipid metabolism.
6. Typical disorders of protein metabolism.
7. Metabolic disorders of phenylalanine, tyrosine, methionine, tryptophan: clinical symptoms, criteria and diagnostic methods.
8. Disturbances of the blood plasma protein composition (hypo-, hyper-, para- and dysproteinemia).
9. Disorders mechanisms of carbohydrate, lipid and protein metabolism under diabetes mellitus.
10. Typical disorders of nucleotide metabolism: gout, hereditary orotaciduria.
11. Typical disorders of porphyrin metabolism: porphyria, jaundice.
12. Clinical and diagnostic value of determination in biological fluids of total protein and protein fractions.
13. Clinical and diagnostic value of determination of certain specific proteins in blood (haptoglobin, C-reactive protein, ceruloplasmin, α1-antitrypsin, antistreptolysin, orozomucoid, transferrin).
14. Clinical and diagnostic value of determination in the blood of total nitrogen, urea, creatine and creatinine, uric acid.
15. Clinical and diagnostic value of determining in the blood indicators of carbohydrate metabolism: glucose, pyruvic acid, lactic acid, fructose and galactose, carbohydrate-containing proteins and their components (seroglycosides, glycated hemoglobin, fructosamine, sialic acids), enzyme activity.
16. Clinical and laboratory diagnosis and monitoring of diabetes mellitus.
17. Clinical and diagnostic value of determination of blood lipid profile: cholesterol, triacylglycerols, lipoproteins, atherogenic factor – ketone bodies, apolipoproteins.
18. Clinical and diagnostic value of determination in the blood of pigment metabolism indicators: total bilirubin and its fractions.
19. Clinical and diagnostic value of determining in the blood indicators of blood acid-base status and gas composition.
20. Clinical and diagnostic value of determining in the blood of mineral metabolism indicators.
21. The value of the hormone content study for the diagnosis of the endocrine system disorders.
22. Clinical and diagnostic value of determining the activity of enzymes in blood and urine (aminotransferases, γ-glutamyltranspeptidase, glutamate dehydrogenase, alkaline and acid phosphatase, creatine kinase, lactate dehydrogenase, amylase, lipase, cholinesicaminase).

23. Cardiovascular diseases: types, risk factors, classification. Classification of biochemical markers of cardiovascular pathology.
24. Changes in biochemical parameters of metabolism under atherosclerosis, their assessment, ways of correction.
25. Changes in biochemical parameters at different stages of hypertension, evaluation of laboratory results.
26. Biochemical markers of myocardial damage.
27. Kidney disease: types, risk factors, classification.
28. General analysis of urine at examination of patients with kidneys and urinary tracts diseases.
29. Clinical and biochemical analysis of blood in the diagnosis of renal pathology.
30. Functional tests in pathology of the kidneys. Endogenous creatinine clearance.
31. Biochemical tests to assess renal pathology.
32. Biochemical markers of acute and chronic renal failure.
33. Changes in biochemical parameters of blood and urine under glomerulonephritis and pyelonephritis, their assessment and diagnostic value.
34. Changes in biochemical parameters of blood and urine under nephrolithiasis, amyloidosis, nephrotic syndrome, their assessment and diagnostic value.
35. Diseases of the digestive system: types, risk factors, classification.
36. Biochemical markers of stomach diseases: blood gastrin; pepsinogen I, pepsinogen II in the blood; analysis of gastric juice.
37. Assessment of pancreas endocrine insufficiency: determination in the blood of C-peptide, insulin, glucose, insulin resistance index HOMA-IR.
38. Assessment of pancreas exocrine insufficiency by determination activity of pancreatic enzymes in the blood and feces.
39. General characteristics of biochemical parameters that characterize diseases of the hepatobiliary system.
40. Enzyme diagnosis of liver diseases.
41. Changes in biochemical parameters under chronic hepatitis, their assessment and diagnostic value.
42. Changes in biochemical parameters under cirrhosis, their assessment and diagnostic value.
43. Changes in biochemical parameters under gallstone disease, their assessment and diagnostic value.
44. Changes in biochemical parameters under fatty infiltration of the liver (steatosis), their assessment and diagnostic value.
45. Clinical and diagnostic value of indican in urine.

Навчальне видання

КЛІНІЧНА БІОХІМІЯ (ЕЛЕКТИВНИЙ КУРС)

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