"APPROVED"
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Biological and Toxicological Chemistry
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The list of questions to the final Module control 2
on Biological chemistry
for 3 year students Pharmaceutical faculty full-time education

1. The pool of free amino acids in the body: the way of receipt and use of free amino acids in the tissues. The nitrogen balance. Types of nitrogen balance. Clinical and diagnostic value of a study of residual nitrogen in the blood serum.
2. Protein digestion and absorption of amino acids in the gut. Mechanisms of activation of the inactive form of the proteolytic enzymes in the digestive tract. Pharmaceuticals for the correction of disorders of protein digestion in the digestive tract.
3. The formation of toxic products of amino acids transformation in the colon and it hepatic clearance. Quick sample.
4. Transamination of amino acids: mechanism of action of aminotransferases, biological significance. Clinical and diagnostic value of the study of liver and plasma aspartate aminotransferase.
5. Deamination of amino acids. The mechanism of indirect deamination. The biological role of glutamate in the liver and brain neurons.
6. Alpha-amino acid decarboxylation. The function of biogenic amines in the body. Neutralization of biogenic amines. Antihistamine drugs.
7. Ways of converting nitrogen-free amino acid residues. Glucogenic and ketogenic amino acids.
8. Ways of formation and neutralization of ammonia in the body. Urea biosynthesis: a sequence of enzymatic reactions of biosynthesis, the genetic abnormalities of urea cycle enzymes.
9. Biosynthesis and biological role of creatine and phosphocreatine.
10. Glutathione: structure, biosynthesis and biological functions of glutathione.
11. Specialized pathways of cyclic amino acid metabolism - phenylalanine, tyrosine and tryptophan. Hereditary enzimopatii of cyclic amino acid metabolism. Amino acids like pharmaceuticals.
12. Metabolism of porphyrins: structure of heme; scheme of biosynthesis of protoporphyrin IX and heme. Hereditary disorders of porphyrin biosynthesis, types of porphyria.
13. Hemoglobin: Structure, properties and functions in the body. Abnormal hemoglobin derivatives, the reasons for their formation. Hereditary disorders of hemoglobin synthesis. The abnormal form of hemoglobin.
14. Degradation of hemoglobin in the tissues. Bilirubin and its fractions: clinical relevance for the diagnosis of the liver disorders. The forms of jaundice.
15. Biosynthesis of purine nucleotides: scheme of reactions of IMP synthesis; biosinthesis AMP and GMP; mechanisms of regulation.
16. Biosynthesis of deoxyribonucleotides. Formation thymidylic nucleotides dTMP biosynthesis inhibitors as anticancer agents.
17. The catabolism of purine and pyrimidine nucleotides. Hereditary metabolic disorders of uric acid and pharmaceuticals correction.
18. The biosynthesis of pyrimidine nucleotides: scheme of reactions; synthesis regulation.
19. Replication, its mechanism and biological significance. Pharmaceuticals for replication control. The biological significance and mechanisms of DNA repair. Reparation of UV-induced gene mutations: xeroderma pigmentosum.
20. Transcription, its mechanism and significance. Post-transcriptional modification of the primary transcript. Pharmaceuticals - transcriptional regulators.
21. The genetic code and its properties. Transport of RNA and amino acid activation. Aminoacyl-tRNA synthetase.
22. Translation: its mechanism of protein synthesis and sequence of steps, the biological significance of the process. Post-translational modification of polypeptide chains. Pharmaceuticals - regulators of protein synthesis.
23. Regulation of prokaryotic gene expression: regulatory and structural portions of lactose (LAC-) operon (regulatory gene promoter, operator).

24. Mutations: genomic, chromosomal, gene; mutagens mechanisms of action; the role of induced mutations in causing enzimopaty and hereditary diseases in humans. Genetic Engineering: construction of recombinant DNA; gene cloning; synthesis of genetically engineered enzymes, hormones, interferons and others.
25. Understanding the mechanisms of regulatory action of hormones on the cell. Role of G-proteins and second messenger in signal transmission hormone into the cell. Hormone-sensitive protein kinase: classification, mechanism of stimulation and functions in the cell.
26. Hypothalamic-pituitary hormones: chemical nature and the biological effect.
27. Thyroid hormones: structure, biological effects of T4 and T3. Violation of metabolic processes in hypo- and hyperthyroidism.
28. Hormones of the pancreas (insulin, glucagon): mechanisms of effects on the metabolism. Insulin-dependent diabetes mellitus: changes in metabolism and drug correction.
29. Catecholamines (epinephrine, norepinephrine, dopamine): chemical nature, effect on metabolism, pharmaceutical preparations.
30. Steroid hormones of the adrenal cortex (C21-steroids) - glucocorticoids and mineralocorticoids; structure, properties. Pharmaceutical of corticosteroids and their use in medical practice.
31. Sex hormones (estrogens and androgens): control of secretion, the effect on the metabolism. The use of structural analogs of hormones as pharmaceuticals.
32. Hormonal regulation of calcium homeostasis in the body. Parathyroid hormone, calcitonin, calcitriol.
33. Eicosanoids: structure, biological and pharmacological properties. Aspirin and other nonsteroidal anti-inflammatory drugs like inhibitors of prostaglandin synthesis.
34. Vitamin B1 (thiamine): a structure, biological properties, mechanism of action, income sources, daily requirement. Medical use as pharmaceuticals.
35. Vitamin B2 (riboflavin): a structure, biological properties, mechanism of action, income sources, daily requirement. Medical use as pharmaceuticals.
36. Vitamin PP (nicotinic acid, nicotinamide): a structure, biological properties, mechanism of action, income sources, daily requirement. Medical use as pharmaceuticals.
37. Vitamin B6 (pyridoxine): a structure, biological properties, mechanism of action, income sources, daily requirement. Medical use as pharmaceuticals.
38. Vitamin B12 (cobalamin): a structure, biological properties, mechanism of action, sources of income, the daily need. Medical use as pharmaceuticals.
39. Vitamin B9 (folic acid): a structure, biological properties, mechanism of action, income sources, daily requirement. Medical use as pharmaceuticals.
40. Vitamin H (Biotin) and pantothenic acid: a structure, biological properties, mechanism of action, income sources, daily requirement. Medical use as pharmaceuticals.
41. Vitamin C (ascorbic acid) and P (flavonoids): a structure, biological properties, mechanism of action, sources of income, the daily need. Medical use as pharmaceuticals.
42. Vitamin A (retinol, retinal, retinoic acid) biological properties, mechanism of action, manifestations of deficiency, income sources, daily requirement. Medical use as pharmaceuticals.
43. Vitamin E (α-tocopherol): biological properties, mechanism of action, manifestations of deficiency, income sources, daily requirement. Medical use as pharmaceuticals.
44. Vitamin D (cholecalciferol): biological properties, mechanism of action, manifestations of deficiency, income sources, daily requirement. Medical use as pharmaceuticals.
45. Vitamin K (phylloquinone, farnohinon): biological properties, mechanism of action, manifestations of deficiency, income sources, daily requirement. Medical use as pharmaceuticals.
46. Vitamin-like compounds, their chemical structure, biological role, metabolic disorders at the failure of practical use as pharmaceuticals. Antivitamins: mechanisms of action, their use as pharmaceuticals.
47. Characteristics of blood biochemical functions. The buffer system of the blood. Violation of the acid-base balance of the body's blood as a source of medicines.
48. Overview of synthesis, functions and diagnostic value of basic proteins - components of electrophoretic fractions of blood plasma. Enzymes of blood: classification, clinical and diagnostic value of their research.
49. The kallikrein-kinin system of blood and tissue. Drugs – antagonists of kinin synthesis. Drugs that affect coagulation, anticoagulation and fibrinolytic systems of blood.
50. Non-protein organic compound of plasma. Inorganic components of blood plasma. The clinical significance of the study of non-protein components of the blood to assess of human metabolism.

51. Biochemical function of liver: carbohydrate, protein synthesis, urine synthesis, bile synthesis, regulation of blood lipids.
52. Microsomal oxidation as a phase modification of endogenous substrates and xenobiotics. Role of cytochrome P450 in the structure of the biotransformation of endogenous substrates and xenobiotics. Conjugation reaction of xenobiotics and their intermediate metabolites.
53. The biochemical composition of human urine in normal conditions and in conditions of development of pathological processes. Clinical and diagnostic value of analysis of urine composition. Effect of drugs on the change of physico-chemical properties of urine.
54. Renal renin-angiotensin system. Antihypertensive drugs - ACE inhibitors.

List of practical tasks
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. Identification of lactic acid in gastric juice. Explain the principle of the method. Under what pathological conditions in the stomach is determined the lactic acid?
2. Determination of alanine aminotransferase and aspartate aminotransferase. The principle of the method. Clinical and diagnostic value.
3. Determination of urea in the urine color reaction with diacetylmonooxim. Reactions of urea formation in the body.
4. What are supramolecular complexes form nucleic acids? Identify the main components of the nucleoprotein (protein nitrogenous base, a pentose, phosphoric acid) in its hydrolyzate. Explain principles of techniques.
5. Determination of uric acid in urine. The principle of the method. Clinical diagnostic value.
6. Fohll reaction and Biuret reaction of peptide hormones and protein (for example, insulin). Add structural fragments that identified by these reactions. The value for the pharmacy and clinic.
7. Qualitative reaction on folikulin. The principle of the method. The value for the pharmacy and clinic.
8. Qualitative reaction on adrenaline (reaction with ferric chloride). The principle of the method. The value for the pharmacy and clinic.
9. Identification of vitamin B2. The principle of the method. The value for the pharmacy and clinic.
10. Identification of vitamin B6. The principle of the method. The value for the pharmacy and clinic.
11. Identification of vitamin E (with ferric chloride). The principle of the method. The value for the pharmacy and clinic.
12. Determination of gemine group of hemoglobin. The principle of the method.
13. Determination of the content of bilirubin and its fractions in the serum. The principle of the method. Clinical and diagnostic value.
14. Identification of protein in the urine with sulfosalicylic reactions and nitric acids. The principle of the method. Clinical application of these methods.
15. Detection of glucose in urine Fehling's reaction. The principle of the method. Clinical and diagnostic value.
16. Identification of blood in the urine (benzidine test). The principle of the method. Clinical and diagnostic value.
17. Qualitative reaction for ketones in the urine. The principle of the method. Clinical and diagnostic value.
18. Detection of enzymatic activity on example of urine amylase enzyme - Wohlgemuth method. The principle of the method. Clinical and diagnostic value.

Formuls of bio-organic substances (to be able to write):
1. 20 proteinogenic alpha-L-amino acids;
2. Glucose, fructose, ribose, deoxyribose and phosphate ester;
3. Pyruvate, lactate, ketone bodies;
4. Cholesterol;
5. Higher fatty acids;
6. Triacylglycerols and phosphoglycerides;
7. Nitrogenous base;
8. Nucleosides and nucleotides
9. Uric acid

Schemes and reaction of processes (to be able to write, labeling enzymes and coenzymes, biomedical interpret the meaning):

1. The oxidative decarboxylation of pyruvate;
2. CAC.
3. Interconversion of glucose and glucose-6-phosphate;
4. Interconversion of pyruvate and lactate;
5. Activation of fatty acids;
6. The fatty acid β-oxidation (to cleave first molecule to acetyl-coenzyme A)
7. Synthesis of fatty acids (formation of malonyl-CoA biosynthesis to form butyryl-ACP scheme)
8. Synthesis and utilization of ketone bodies;
9. Synthesis of cholesterol from mevalonic acid
10. Formation glycerol-3-phosphate to glycerol;
11. Synthesis of triacylglycerols and phosphoglycerides;.
12. The oxidative deamination of glutamate;
13. Transamination of aspartate and alanine with alpha-ketoglutarate;
14. Alpha-decarboxylation of histidine, glutamate, tryptophan, lysine, ornithine;
15. Hydroxylation of phenylalanine to tyrosine;
16. Synthesis of creatine and creatinine;
17. Synthesis of glutathione;
18. Synthesis of heme to the delta-aminolevulinic acid
19. Synthesis of carbamoylphosphate;
20. Synthesis of transport forms of ammonia;
21. Synthesis of urea
22. Synthesis of IMP, AMP and GMP;
23. Synthesis of OMP, UMP, CMP, dTMP;
24. Synthesis of uric acid;
25. Synthesis of indican;
26. Synthesis of hippuric acid;
27. Synthesis of bilirubin and stercobilin.

List of Situational tasks
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1. Female 43 years - an employee paint companies - complains of general weakness, weight loss, lethargy, drowsiness. Chronic lead intoxication confirmed by laboratory - revealed hypochromic anemia. In the blood - increased levels of protoporphyrin and reduced levels of delta-aminolevulinic acid. The synthesis of substance is violated, what substance is shown?
2. Derivative pterins - aminopterin and methotrexate - is a competitive inhibitor of dihydrofolate reductase, causing them to inhibit the regeneration of tetrahydrofolic acid dihydrofolate. These drugs lead to inhibition of one-carbon groups intermolecular transport.Biosynthesis of what nucleotide is suppressed while?
3. A man is 58 years old, underwent surgery for prostate cancer. After 3 months, he had a course of radiotherapy and chemotherapy. The range of drugs included 5-ftordezoksiuridin - an inhibitor of thymidylate synthase. The synthesis of what substance is primarily locked by the action of the drug?
4. A man 46 years old went to a doctor with complaints of pain in small joints, which is exacerbated by the use of animal food. The patient was diagnosed with urolithiasis accumulation of uric acid. Allopurinol assigned to the patient, which is a competitive inhibitor of the enzyme xanthine oxidase. What's allopurinol property provides therapeutic effect in this case.
5. Orotatsidury hereditary orotic acid selection is many times higher than normal. The synthesis of some substances will be broken in this pathology?
6. The antibiotic rifampicin, which is used to treat tuberculosis, affects certain biochemical processes. Write them.
7. To treat urogenital infections using quinolones - inhibitors of DNA - gyrase enzyme. What process is broken under the action of quinolones in the first place?
8. Two year-old child was brought to the hospital. After the meal, he often vomiting. The child lags behind in weight, physical and mental development. Dark hair, but there is a gray strand. The urine sample after the addition of FeCl3 acquired a green color. Results of quantitative analysis of urine following: phenylalanine content - 7 mmol / l at a rate of 0.01; phenylpyruvate content - 4.8 mmol / l at

a rate of 0; fenillaktate content - 10.3 mmol / l at a rate of 0. The Violation of metabolic findings it's indicate? What can you recommend for the normalization of metabolism in relation to nutritional therapy in this case?
9. The patient urine has a peculiar odor of maple syrup. What biochemical defect is the cause of this disease?
10. In the blood of the patient at the age of 50 years have seen a high level of serotonin in the urine - a sharp increase in 5-oksiindolilatsetatnoy acid. Violation of any amino acid metabolism can cause such changes?
11. The patient is in a state of hypoglycemic coma. An overdose of which hormone can lead to such a situation?
12. A person is in a stressful situation. As this condition will affect on the function of the endocrine glands?
13. Inhibition of lipolysis in adipocytes of adipose tissue is caused by decrease in cAMP concentration that is required to activate the triglyceride. Indication of which hormones reduce the rate of lipolysis in adipose tissue?
14. The lifetime of most hormones in the blood is relatively small. Thus, if the animal has the radiolabeled insulin, the half of the hormone administered will be inactivated in the blood for 30 min. As constant level of hormone in the blood can be maintained under normal conditions, given its rapid inactivation?
15. Rheumatic patients assigned prednisolone. The anti-inflammatory action of this drug due to inhibition of the release of arachidonic acid. What is the previous substance of prednisolone?
16. Aspirin has anti-inflammatory effect, because inhibits cyclooxygenase. The level of which active compounds will then decline?
17. In pregnant women, there is a need for increased amounts of cholecalciferol, one of whose metabolites is a potent synergist PTH. This hormone stimulates bone resorption and release of calcium and phosphate in blood. What is its metabolite synergist?
18. On examination, the patient's 32 years have seen disproportionate growth of the skeleton, increase brow, nose, lips, tongue, jaw bones, stop. The function of which endocrine gland is broken?
19. A patient appealed for a hospital with complaining of constant thirst, general weakness, blood detected hyperglycemia (16mmol / L), polyuria, and increased content of the 17-keto steroids in urine. What disease is characterized by such indicators?
20. In a patient with Cushing's syndrome is a steady hyperglycemia and glycosuria. Synthesis and secretion of what hormone is increased in this case?
21. The patient women with low blood pressure after parenteral administration of the hormone increased blood pressure and blood glucose and lipid levels. Which hormone has been introduced?
21. The patient women with low blood pressure after parenteral administration of the hormone increased blood pressure and blood glucose and lipid levels. Which hormone has been introduced?
22. When thyrotoxicosis increased production of thyroid hormones T3 and T4, developed weight loss, tachycardia, psychic anxiety and so on. What is the effect of thyroid hormones on energy metabolism in the mitochondria of cells?
23. The doctor has appointed aspirin rheumatic patients as the anti-inflammatory agent. The synthesis of which substances are associated with inflammation, blocking the aspirin?
24. On examination, the 10-year-old child found a small increase, the disproportionate development of the body, poor mental development. Deficiency of which hormone in the body has caused these changes?
25. Patient after eating raw eggs dermatitis appeared. Vitamin deficiency of which vitamin has been developed in the patient's organism?
26. Name the vitamin, coenzyme form of which is involved in the conversion of dUMP to dTMP.
27. A girl 10 years is often sick with acute respiratory infections, after which there are numerous petechial hemorrhages in places clothing friction. Hypovitaminosis of which vitamin occurs in girls?
28. The patient complained of general weakness and bleeding from the gums. Deficiency of which vitamin can be assumed?
29. The patient has bleeding of internal organs and mucous membrane detected proline and lysine composed of collagen fibers. Due to the lack of which vitamin will violated their hydroxylation?
30. The patient has identified lack of hydroxyproline and hydroxylysine in the composition of the collagen fibers. Due to the lack of which vitamin will violated the patient's body processes of the hydroxylation of these amino acids?

31. The patient scurvy infringements hydroxylation of proline and lysine in the composition of collagen. Braking of what biochemical process is leading to the violation?
32. Patient after ectomy gallbladder suppressed processes of absorption of Ca 2+ through the intestinal wall. Appointment of what vitamin will stimulate this process?
33. A patient suffering from thromboembolic disease, artificial appointed anticoagulant - pelentan. The antagonist of what vitamin is it?
34. The patient is observed day-blindness (night blindness). Which of the following substances will have a therapeutic effect?
35. The child at the next examination revealed the termination of bone mineralization. Lack of vitamin may cause this?
36. Treatment of a child suffering from rickets, has not given a positive result. What is the most likely cause of treatment failure?

Test
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In snake venom there isa substance that causes erythrocyte hemolysis,whe nitisintroduced into ahumanorganism. Blood test revealed alarge amount of lysolecthin (lysophosphatidylcholine).What enzyme leads to accumulation of lysolecithin in blood? **A.** Phospholipase A2 **B.** Phospholipase A1 **C.** Phospholipase C **D.** Phospholipase D **E.** Neuraminidase	Enzymes are widely used as drugs in pharmacy. What is the main difference that separates enzymes from non-biological catalysts? **A.** High specificity and selectivity **B.** High universality **C.** Low universality **D.** High dispersion **E.** High homogeneity
A patient demonstrate smilky- white color of blood plasma due to high content of chylomicrons. Disintegration of triacylglycerolis disrupted. Deficiency of the following enzyme activity is observed: **A.** Lipoprotein lipase **B.** Amylase **C.** Tripsin **D.** Cholesterol esterase **E.** Lactase	What enzyme allows for synthesis of various genes from template-RNA to DNA in genetic engineering (this enzyme catalyzes the process discovered in RNA-viruses)? **A.** Reverse transcriptase **B.** Exonuclease **C.** DNA-ligase **D.** Helicase **E.** Endonuclease
Purine ring biosynthesis occurs in ribose-5-phosphate by gradual accumulation of nitrogen and carbon atoms and closing the rings.The source of ribose phosphate is the process of: **A.** Pentose phosphate cycle **B.** Glycolysis **C.** Glyconeogenesis **D.** Gluconeogenesis **E.** Glycogenolysis	Intracellular metabolism of glycerol starts with its activation. What compound is formed in the first reaction of its conversion? **A.** α-glycerolophosphate **B.** Pyruvate **C.** Lactate **D.** Choline **E.** Acetyl-coenzyme A
The second stage of detoxification involves joining certain chemical compounds with functional groups of toxines. Select one such compound: **A.** Glucuronic acid **B.** Higher fatty acids **C.** Cholesterol **D.** Glucose **E.** Pyruvate	Fatty acids arrive into mitochondria, and there their oxidation occurs. Name the vitamin-likesubstance that takes part in transportation off atty acids through mitochondrial membrane: **A.** Carnitine **B.** Choline **C.** Biotin **D.** Pantothenic acid **E.** Folicacid
A patient under goes chemotherapy with 5-fluorouracil that is a competitive inhibitor of	A patient has been receiving Theophylline (inhibitorof cyclic adenosine monophosphate

thymidilate synthase. What process is inhibited by this drug? **A.** Thymidinemonophosphate synthesis **B.** Purine nucleotidesdisintegration **C.** Adenosinetriphosphatesynthesis **D.** Purine nucleotidessalvage **E.** Glucose synthesis	phosphodiesterase) for a week. What hormone can increase its action due to such treatment and cause hyperglycemia? **A.** Glucagon **B.** Testosterone **C.** Aldosterone **D.** Insulin **E.** Estradiol
The end product of starch hydrolysis is: **A.** D-glucose **B.** D-fructose **C.** Saccharose **D.** Maltose **E.** D-galactose	Accidental ingestion of death cap mushrooms containing α-amanitin causes intoxication.What enzyme is inhibited with this toxine? **A.**RNApolymerase II **B.** DNApolymerase **C.** DNAsynthetase **D.** Peptidyltransferase **E.** Translocase
Due to prolonged taking of phenobarbital the epileptic patient has developed tolerance for this drug. What is this phenomenon based on? **A.** Biotransformation acceleration **B.** Absorption process weakening **C.** Increase of receptor sensitivity **D.** Biotransformation suppression **E.** Substance accumulation in body	Disintegration of adenosine nucleotides results in release of ammonia. What enzyme plays the key role in ammonia synthesis from these compounds? **A.** Adenosinedeaminase **B.** Alcohol dehydrogenase **C.** Lactatedehydrogenase **D.** Alaninetransaminase **E.** Amylase
Fatty acids synthesis occurs in human body. What compound is initial in this rocess? **A.** AcetylcoenzymeA **B.** Vitamin C **C.** Glycine **D.** Succinate **E.** Cholesterol	A patient has icteric skin; unconjugated bilirubin content in blood is high;conjugated bilirubin in urine is not detected.There is significant amount of urobilinin urine and stercobilin in feces. Name the pathology characterized by given symptoms: **A.** Hemolytic jaundice **B.** Obstructive jaundice **C.** Jaundiceofthenewborn **D.** Hepatocellular jaundice **E.** Atherosclerosis
The primary structure of nucleic acids is a polynucleotide chain which has a certain composition and order of the nucleotides. What bonds stabilize this structure? **A.** 3',5'-phosphodiester **B.** Peptide **C.** Glycosidic **D.** Disulfide **E.** Amide	Natural peptides can perform various functions. What bioactive peptide is a major antioxidant and performs coenzyme functions? **A.** Glutathione **B.** Bradykinin **C.** Oxytocin **D.** Liberin **E.** Anserine
A 46-year-old patient was found to have hyperactivity of creatine kinase in the blood serum. What pathology can be suspected? **A.** Myocardial infarction **B.** Acute pancreatitis **C.** Chronic hepatitis **D.** Hemolytic anemia **E.** Renal failure	Cataract (lenticular opacity) has developed in the 52-year-old female patient with pancreatic diabetes. What process intensification has caused lenticular opacity? **A.** Protein glycosylation **B.** Lipolysis **C.** Ketogenesis **D.** Protein proteolysis **E.** Gluconeogenesis
After drinking milk a 1-year-old child developed diarrhea, flatulence. The	Patients with severe depression demonstrate decreased serotonin levels in brain and

baby is likely to have the deficiency of the following enzyme: **A.** Lactase **B.** Maltase **C.** Aldolase **D.** Hexokinase **E.** Glycosidase	cerebrospinal fluid. What amino acidis a serotonin precursor? **A.** Tryptophan **B.** Threonine **C.** Tyrosine **D.** Glutamic acid **E.** Aspartic acid
Universal system of biological oxidation of nonpolar compounds (numerous drugs, toxicagents, steroid hormones, cholesterol) is microsomal oxidation. Name the cytochrome that is included in oxygenase chain of microsomes: **A.** CytochromeP-450 **B.** CytochromeC **C.** CytochromeA3 **D.** CytochromeA **E.** CytochromeC1	Chromatin contains positively charged histone proteins. What amino acidis contained in histone proteins in large amounts? **A.** Lysine **B.** Alanine **C.** Valine **D.** Threonine **E.** Serine
A man presents with signs of albinism: blonde hair, extreme photosensitivity, impai red vision. What amino acid metabolism is disrupted in the patient? **A.** Tyrosine **B.** Methionine **C.** Proline **D.** Histidine **E.** Valine	Substrate-linked phosphorylation occurs in the cycle of tricarboxylic acids. What compound takes part in this reaction? **A.** Succinyl coenzymeA **B.** α-ketoglutarate **C.** AcetylcoenzymeA **D.** Succinate **E.** Malate
Inhibition of the synthesis of bile acids from cholesterol in liver of an experimental animals has caused maldigestion of lipids. What is the role of these acids in the entera llipidic metabolism? **A.** They emulsifydietary lipids **B.** They keep balance of alkaline environment in the intestines **C.** They participate in the synthesis of lipids **D.** They are part of LDL **E.** They activate the formation of chylomicrons	In response to the administration of protein drugs, a patient developed an allergic reaction. The development of the allergic reactionis caused by the increased synthesis of the following compound: **A.** Histamine **B.** Choline **C.** Adrenaline **D.** Histidine **E.** Serotonin
Hemoglobin catabolism results in release of iron which is transported to the bone marrow by a certain transfer protein and is use dagain for the synthesis of hemoglobin. Specify this transfer protein: **A.** Transferrin(siderophilin) **B.** Transcobalamin **C.** Haptoglobin **D.** Ceruloplasmin **E.** Albumin	A patient has amental disorder due to the insufficient synthesis of gamma- aminobutyric acid in the brain. Such pathological changes might be caused by the deficiency of the following vitamin: **A.** Pyridoxine **B.** Tocopherol **C.** Cyanocobalamin **D.** Folicacid **E.** Riboflavin
A 5-year-old child presents with abdominal distension, abdominal cramps, and diarrhea occurring 1-4 hour safter drinking milk. Described symptoms are caused by the lack of enzymes that break up: **A.** Lactose **B.** Glucose **C.** Maltose **D.** Saccharose **E.** Fructose	In large intestine microorganisms synthesize vitamins that participate in organism's biochemical processes. What vitamins are mainly synthesized by microflora? **A.** *K*, *B*12 **B.** *A*, *C* **C.** *E*, *PP* **D.** *B*1, *B*2 **E.** *B*6, *E*
During gastric secretory function	Information transfer from

research decrease of hydrochloric acid concentration in gastric juice was detected. What enzyme will be less active in such a condition? **A.** Pepsin **B.** Amylase **C.** Lipase **D.** Dipeptidase **E.** Hexokinase	peptide hormones to intracellular second messengers occures involving adenylate cyclase. What reaction is catalyzed by adenylate cyclase? **A.** Cyclic adenosine monophosphate production **B.** ATP breakdown into ADP and inorganic phosphate **C.** ATP synthesis from adenosine monophosphate and pyrophosphate **D.** ADP breakdown with adenosine monophosphate and inorganic phosphate production **E.** ATP breakdown into adenosine monophosphate and pyrophosphate
When hydrogen peroxide solution is administered to bleeding wounds, it is broken up by one of the blood enzymes. Point out this enzyme. **A.** Catalase **B.** Monoamine oxidase **C.** Cytochrome oxidase **D.** Aspartate aminotransferase **E.** Lactate dehydrogenase	Catabolism of body's own tissue proteins is intensified during such diseases as thyrotoxicosis and tuberculosis. This process is attended by intensive synthesis in liver and subsequent excretion with urine of the following: **A.** Urea **B.** Glucose **C.** Acetone bodies **D.** Fatty acids **E.** Nucleotides
Milk intake has resulted in the one-year-old child having diarrhea and abdominal distension. What enzyme deficiency does the child have? **A.** Lactase **B.** Maltase **C.** Aldolase **D.** Hexokinase **E.** Glycosidase	Ketoacidosis occurs during starvation. What metabolite blood concentration increase is symptomatic of this medical condition? **A.** Acetoacetate **B.** Oxaloacetate **C.** Malonate **D.** Beta-hydroxy-beta-methylglutaryl-CoA **E.** Acetyl-CoA
The patient with myocardial infarction has been prescribed statines, cholesterol synthesis inhibitors, to prevent complications. What enzyme activity is suppressed by these medicines? **A.** Beta-GHB-reductase **B.** Hydroxylase **C.** Lecithin-cholesterol acyltransferase **D.** Esterase **E.** Oxygenase	Streptomycin and other aminoglycosides by binding with 30Ssubunit of ribosome prevents formylmethionyl-tRNA joining. What process is disrupted due to this effect? **A.** Translation initiation **B.** Translation termination **C.** Transcription initiation **D.** Transcription terminat E.Peprication
The patient has hypovitaminosis PP. What amino acid taken with meals partially compensates patient's need for vitamin PP? **A.** Tryptophan **B.** Phenylalanine **C.** Valine **D.** Arginine **E.** Methionine	During long-term carbon tetrachloride poisoning of animals significant activity drop of aminoacyl tRNA synthetase in hepatocytes was detected. What metabolic process is disrupted in this case? **A.** Protein biosynthesis **B.** DNA replication **C.** RNA transcription **D.** Post-translational modification of peptides **E.** Post-transcriptional modification of

	RNA
Nucleoproteins contain significant amount of alkaline proteins.What propteins carry out structural function in chromatin? **A.** Protamines and histones **B.** Albumines and globulines **C.** Prolamines and glutenins **D.** Hemoglobin and myoglobin **E.** Interferones and mucin	The poultry factory worker, who has been consuming 5 or more raw eggs daily, complains of weakness, drowsiness, muscle pain, loss of hair, seborrhea. What vitamin deficiency causes such condition? **A.** *H* (biotin) **B.** *C* (ascorbic acid) **C.** *A* (retinol) **D.** *B*1 (thiamine) **E.** *B*2 (riboflavin)
Oligomycin antibiotic is prescribed to the patient with tuberculosis. What mitochondrial process is slowed down by this medicine? **A.** Oxidative phosphorylation **B.** Substrate-linked phosphorylation **C.** Microsomal oxidation **D.** Lipid peroxidation **E.** Oxidative decarboxylation	Detoxication rate is 4 times lower in children than in adults.What enzyme necessary for toxic compounds conjugation has low activity in children? **A.** Glucuronosyltransferase **B.** ALAT **C.** AspAT **D.** Creatine phosphokinase **E.** LDH1
Certain drugs can stimulate liver to synthesize enzyme systems taking part in drugs and toxines metabolism. What compound stimulates drug metabolism in liver microsomes? **A.** Phenobarbital **B.** Heparin **C.** Menadione sodium bisulfite **D.** Sulfanilamide **E.** Aspirin	Barbiturates are used as soporifics. These substances, similarly to rotenone, are tissue respiration inhibitors. What complex level do these compounds suppress respiratory chain at? **A.** NADH-coenzyme Q reductase **B.** Cytochrome oxidase **C.** Cytochrome C reductase **D.** Adenosine triphosphate synthetase **E.** Succinate dehydrogenase
Inhibitors of one of the amides metabolism enzymes are used to treat depression. What enzyme inhibition has such an effect? **A.** Flavin adenine dinucleotide (FAD)-containing monoamine oxidase (MAO) **B.** Acetylcholinesterase **C.** Formylkynureninase (Arylformamidase) **D.** Kynurenine 3-hydroxylase **E.** Lactate dehydrogenase	Pathogenic microorganisms produce various enzymes in order to penetrate body tissues and spread there. Point out these enzymes among those named below. **A.** Hyaluronidase, lecithinase **B.** Lyase, ligase **C.** Transferase, nuclease **D.** Oxydase, catalase **E.** Esterase, protease
Chronic pancreatitis is accompanied by the decreased synthesis and secretion of trypsin. This impairs the hydrolysis and absorption of the following substances: **A.** Proteins **B.** Lipids **C.** Polysaccharides **D.** Nucleic acids **E.** Disaccharides	During the gastric secretion, proteolytic enzymes are secreted in form of zymogens.What enzyme is activated by hydrochloric acid? **A.** Pepsin **B.** Trypsin **C.** Amylase **D.** Lipase **E.** Chymotrypsin
A child exhibits physical and mental retardation. Urine analysis revealed high concentration of orotic acid. This disease can be addressed by the constant use of: **A.** Uridine **B.** Adenine **C.** Guanine	The intracellular metabolism of glycerol starts with its activation. What compound is formed as a result of the first reaction of its conversion? **A.** Alpha-glycerolophosphate **B.** Pyruvate **C.** Lactate

D. Glutamine **E.** Alanine	**D.** Choline **E.** Acetyl coenzyme A
Growth of some cancer cells is caused by a certain growth factor. Treatment of leukemia involves applying an enzyme that destroys this essential factor. Specify this enzyme: **A.** Asparaginase **B.** Glutaminase **C.** Succinate dehydrogenase **D.** Citrate synthase **E.** Aspartate aminotransferase	The anti-tumor preparation Methotrexate is a structural analogue of folic acid. The mechanism of its action is based on the inhibition of the following enzyme: **A.** Dihydrofolate reductase **B.** Xanthine oxidase **C.** Hexokinase **D.** Creatine kinase **E.** Lactate dehydrogenase
Addison's (bronze) disease is treated with glucocorticoids. Their effect is provided by the potentiation of the following process: **A.** Gluconeogenesis **B.** Glycolysis **C.** Pentose phosphate cycle **D.** Glycogenolysis **E.** Ornithine cycle	Apatient has developedmegaloblastic anemia on a background of alcoholic cirrhosis. The main cause of anemia in this patient is the following vitamin deficiency: **A.** Folic acid **B.** Lipoic acid **C.** Biotin **D.** Thiamin **E.** Pantothenic acid
Food rich in carbohydrates at first increases the blood sugar and then decreases its rate due to the insulin action. What process is activated by this hormone? **A.** Synthesis of glycogen **B.** Gluconeogenesis **C.** Breakdown of glycogen **D.** Breakdown of proteins **E.** Breakdown of lipids	It is known that malonyl CoA is formed from acetyl CoA and carbon dioxide under the influence of acetyl CoA carboxylase. What vitamin is a coenzyme of this enzyme? **A.** Biotin **B.** Folic acid **C.** Pantothenic acid **D.** Ascorbate **E.** Thiamine
Vitamin *B*1 deficiency has a negative effect on a number of processes. This is caused by the dysfunction of the following enzyme: **A.** Pyruvate dehydrogenase complex **B.** Aminotransferase **C.** Succinate dehydrogenase **D.** Glutamate **E.** Lactate dehydrogenase	A patient was admitted to a hospital in a state of hypoglycemic coma. It occurs at the following level of blood glucose: **A.** 2,5 mmol/l or less **B.** 4,0 mmol/l **C.** 3,3 mmol/l **D.** 4,5 mmol/l **E.** 5,5 mmol/l
Antidepressants can increase the concentartion of catecholamines in the synaptic cleft. What is the mechanism of action of these drugs? **A.** Inhibition of monoamine oxidase **B.** Activation of monoamine oxidase **C.** Inhibition of xanthine oxidase **D.** Activation of acetylcholinesterase **E.** Inhibition of acetylcholinesterase	In response to the administration of protein drugs, a patient developed an allergic reaction. The development of the allergic reaction is caused by the increased synthesis of the following compound: **A.** Histamine **B.** Choline **C.** Adrenaline **D.** Histidine **E.** Serotonin
A child with PKU has an unpleasant mouse-like odor, growth retardation, mental retardation.These symptoms are associated with the high concentration of the following substance in blood: **A.** Phenylpyruvic acid **B.** Glucose **C.** Cholesterol	A 40-year-old male presented to the endocrinology department with disproprortionate enlargement of limbs, mandible and nose. These manifestations are caused by the overproduction of the following hormone: **A.** Somatostatin

D. Adrenaline **E.** Uric acid	**B.** Corticotropin **C.** Aldosterone **D.** Adrenaline **E.** Vasopressin
Diabetes and starvation cause the excess production of ketone bodies that are used as an energy source. They are produced from the following compound: **A.** Acetyl-CoA **B.** Isocitrate **C.** Lactate **D.** Malate **E.** Ketoglutarate	A patient complains of severe abdominal pain, cramps, blurred vision. His relatives exhibit the same symptoms. The urine is of red colour. The patient has been hospitalized for acute intermittent porphyria. This disease might have been caused by the impaired synthesis of the following compound: **A.** Heme **B.** Insulin **C.** Bile acids **D.** Prostaglandins **E.** Collagen
A patient with Parkinson's disease exhibits low level of dopamine which is produced from dihydroxyphenylalanine (DOPA). What enzyme catalyzes this conversion? **A.** Decarboxylase **B.** Deaminase **C.** Hydrolase **D.** Aminotransferase **E.** Carboxypeptidase	Hemoglobin catabolism results in release of iron which is transported to the bone marrow by a certain transfer protein and used again for the synthesis of hemoglobin. Specify this transfer protein: **A.** Transferrin (siderophilin) **B.** Transcobalamin **C.** Haptoglobin **D.** Ceruloplasmin **E.** Albumin
A patient exhibits small (petechial) hemorrhages under the skin and mucous membranes, bleeding gums, tooth decay, general weakness, edemata of the lower extremities. What vitamin deficiency can be suspected? **A.** *C* **B.** *B*1 **C.** *A* **D.** *D* **E.** *E*	Amylolytic enzymes catalyze the hydrolysis of polysaccharides and oligosaccharides. They have an effect upon the following chemical bond: **A.** Glycosidic **B.** Hydrogen **C.** Peptide **D.** Amide **E.** Phosphodiester
A patient has been found to have sugar in the urine. Blood glucose is normal. Arterial pressure is normal. What is the mechanism of glycosuria development in this case? **A.** Disturbance of glucose reabsorption in the nephron tubules **B.** Insulin deficiency **C.** Hyperfunction of adrenal medulla **D.** Hyperfunction of thyroid gland **E.** Hyperfunction of adrenal cortex	Blood serum electrophoresis revealed interferon. This protein is in the following fraction: **A.** γ-globulins **B.** α1-globulins **C.** α2-globulins **D.** β-globulins **E.** Albumins
Proteolytic enzymes of gastric juice exhibit maximum activity in the medium with the following pH: **A.** pH 3,2-3,5 **B.** pH 6,5 **C.** pH 7,0 **D.** pH 9,0 **E.** pH 0,5-1,0	Urine analysis revealed a decrease in sodium ion concentration. Which hormone provides an enhanced reabsorption of sodium ions in the convoluted nephron tubules? **A.** Aldosterone **B.** Vasopressin **C.** Somatostatin **D.** Adrenaline

	E. Acetylcholine
A 40-year-old patient has developed polyuria (10-12 liters per day) and polydipsia induced by damage to the hypothalamo-hypophyseal tract. What hormone deficiency causes such disorders? **A.** Vasopressin **B.** Oxytocin **C.** Corticotropin **D.** Somatotropin **E.** Thyrotropin	Fatty degeneration of liver is prevented by lipotropic substances. Which of the following substances relates to them? **A.** Methionine **B.** Cholesterol **C.** Bilirubin **D.** Glycine **E.** Glucose
A patient has an increased concentration of hippuric acid in the urine. This acid is the product of benzoic acid detoxification in the liver of. In the human body benzoic acid is formed from the following amino acid: **A.** Phenylalanine **B.** Succinate **C.** Lactate **D.** Aspartate **E.** Malate	The intracellular metabolism of glycerol starts with its activation. What compound is formed in the first reaction of its conversion? **A.** Alpha-glycerolophosphate **B.** Pyruvate **C.** Lactate **D.** Choline **E.** Acetyl coenzyme A
A patient has obstruction of the common bile duct. Which of these substances is usually found in urine in such cases? **A.** Bilirubin **B.** Ketone bodies **C.** Uric acid **D.** Creatinine **E.** Glucose	It is known that some chemical compounds uncouple the tissue respiration and oxidative phosphorylation. Name one of these compounds: **A.** 2,4-dinitrophenol **B.** Carbon monoxide **C.** Antimycin A **D.** Lactic acid **E.** Acetyl-CoA
A 70-year-old patient has been found to have atherosclerosis of heart and brain vessels. Examination revealed the changes in the lipid profile. Pathogenesis of atherosclerosis is greatly influenced by an increase in the following lipoproteins rate: **A.** Low-density lipoprotein **B.** Very-low-density lipoproteins **C.** Intermediate-density lipoproteins **D.** High-density lipoprotein **E.** Chylomicrons	A patienth asobstruction of the common bile duct.Which of these substances is usually found in urine in such cases? **A.** Bilirubin **B.** Ketone bodies **C.** Uricacid **D.** Creatinine **E.** Glucose
Medicinal plants infected by microorganisms cannot be used in the pharmaceutical industry. Invasive properties of phytopathogenic microorganisms are due to the following enzymes: **A.** Hydrolytic **B.** Isomerase **C.** Transferase **D.** Oxidoreductase **E.** Lyase	A 28-year-old male got a burn that caused an increase in spontaneous secretion of gastric juice. It is associated with secretion of the following substance: **A.** Histamine **B.** Secretin **C.** Gastric inhibitory peptide **D.** Cholecystokinin-Pancreozymin **E.** Serotonin
Blood pressure is regulated by a number of biologically active compounds. What peptides that enter the bloodstream can affect the vascular tone?	Food rich in carbohydrates at first increases the blood glucose and then decreases its rate due to the insulin action. What process is activated by this

A. Kinins **B.** Leukotrienes **C.** Enkephalins **D.** Iodothyronines **E.** Endorphins	hormone? **A.** Synthesis of glycogen **B.** Gluconeogenesis **C.** Breakdown of glycogen **D.** Breakdown of proteins **E.** Breakdown of lipids
A patient has developed megaloblastic anemia on a background of alcoholic cirrhosis. The main cause of anemia in this patient is the following vitamin deficiency: **A.** Folic acid **B.** Lipoic acid **C.** Biotin **D.** Thiamin **E.** Pantothenic acid	A patient was found to have increased blood serum LDH-1 activity. In which organ is the pathological process localized? **A.** Heart **B.** Liver **C.** Kidneys **D.** Stomach **E.** Muscles
A male patient was found to have hypovitaminosis *PP*. What amino acid taken with food may partially compensate the vitamin *PP* deficiency? **A.** Tryptophan **B.** Phenylalanine **C.** Valine **D.** Arginine **E.** Methionine	Alkaptonuria is characterized by an excessive urinary excretion of homogentisic acid. Development of this disease is associated with disorder of the following amino acid metabolism: **A.** Tyrosine **B.** Tryptophan **C.** Alanine **D.** Methionine **E.** Asparagine
The patient uses a daily basis for several raw eggs, which contain antivitamin biotin - avidin. Violations of any phase of lipid metabolism might arise? **A.** Fatty acid biosynthesis **B.** Cholesterol biosynthesis **C.** Lipid absorption **D.** Glycerol oxidation **E.** Lipid transport in blood	Caffeine inhibits phosphodiesterase which converts cAMP to AMP. The most typical feature of caffeine intoxication is the reduced intensity of: **A.** Glycogen synthesis **B.** Protein phosphorylation **C.** Pentose phosphate pathway **D.** Glycolysis **E.** Lipolysis
Parents of a 10-year-old child have made an appointment with endocrinologist due to complaints of the child's low height.The child' sappearance is corresponding with that of a 5-year-old. What hormone causes such changes in physical development, if its secretion is disrupted? **A.** Somatotropic hormone **B.** Adrenocorticotropic hormone **C.** Thyroxin **D.** Testosterone **E.** Insulin	A patient complains of tachycardia, insomnia, weightloss, irritability,sweating.Objectively: the patient has goiter and slight exophthalmos.What gland is affected, and what functional disorder is it? **A.** Hyperthyroidism **B.** Hypothyroidism **C.** Hyperparathyroidism **D.** Hypoparathyroidism **E.** Adrenomedullaryhyperfunction
During ultra sound investigation a patient has been diagnosed with bilateral stenosis of renal artery with atherosclerotic genesis.Specify the bioactive substance that due to its excessive secretion is the key component of arterial hypertension pathogenesis in the given case: **A.** Renin **B.** Cortisol **C.** Vasopressin **D.** Noradrenaline **E.** Thyroxin	A woman complains of nausea, vomiting, skinitch. She was diagnosed with mechanical jaundice. What is the possible cause of skinitch in such a condition? **A.** Bile acids accumulating in the blood **B.** Increased blood content of indirect bilirubin **C.** Cholesterol accumulating in the blood **D.** Direct bilirubin appearing in the blood **E.** Erythrocyte disintegration products accumulating in the blood

A 48-year-old patient has been intravenously administered prednisolone solution to arrest severe attack of bronchial asthma.What group of hormonal agents does prednisolone be long to? **A.** Glucocorticoids **B.** Gestagenicdrugs **C.** Estrogenicdrugs **D.** Mineralocorticoid **E.** Anabolic steroids	Interferons are natural antiviral and antitumor agents.What is their mechanism of action? **A.** Protein synthesis depression **B.** Protein synthesis increase **C.** Replication activation **D.** Transcription activation **E.** Repair activation
The most severe and dangerous complication of diabetes mellitusis hypoglycemic coma that is characterized by loss of conscious ness and is lethal,unles sefficient emergency treatment is received by patient. What is the main pathogenetic component of hypoglycemic coma? **A.** Carbohydrate deficiency and low energy of cerebral neurons **B.** Carbohydrate deficiency and low energy of myocardium cells **C.** Blood hyperosmia **D.** Noncompensated ketoacidosis **E.** Respiratory alkalosis	A patient demonstrates symmetrical dermatit is on the palms. A docto made a diagnosisof pellagra. What vitamin deficiency can result in such symptoms? **A.** Nicotinicacid **B.** Cobalamin **C.** Ascorbic acid **D.** Folic acid **E.** Cholecalciferol
A patient with hyperproduction of thyroid hormones has been prescribed Merkazolilum. This drug inhibits the following enzyme of iodothyronine synthesis: **A.** Iodide peroxidase **B.** Aromatase **C.** Reductase **D.** Decarboxylase **E.** Aminotransferase	Removal of low-molecular impurities from colloidal systems and highmolecular compound solutions by means of semi permeable membrane diffusion is called: **A.** Dialysis **B.** Electrodialysis **C.** Ultrafiltration **D.** Decantation **E.** Compensatorydialysis
A patient with signs o fcardiac glycosides intoxication was prescribed Unithiol.What is the mechanism of drug action in this case? **A.** Reactivation of membrane _+, Na+ - adenosine triphosphatase **B.** Binding ofionized Ca2+ **C.** Increasedpermeabilityof K+ into myocardiocytes **D.** Increased Na+ content in myocardium **E.** Induction ofcardiacglycoside metabolism	A patient consulted an ophthalmologist about deterioration of twilight vision and xerophthalmus. What drug should the doctor prescribe? **A.** Retinol **B.** Pyridoxine **C.** Tocopherol **D.** Ascorbic acid **E.** Cocarboxylase
A 25-year-old woman with signs of acute morphine intoxication was administered naloxone,which rapidly improved her condition.What is the mechanism of action of this drug? **A.** Opioid receptor blockade **B.** GABA receptor blockade **C.** Serotonin receptor blockade **D.** Dopamine receptor blockade **E.** Benzodiazepine receptor blockade	Diet of an individual must contain vitamins.What vitaminis usually prescribed for treatment and prevention of pellagra? **A.** Vitamin PP **B.** Vitamin C **C.** Vitamin A **D.** Vitamin B1 **E.** Vitamin D
Contrykal is used to prevent pancreatic autolysis. This drug is the inhibitor of the following enzymes: **A.** Proteases **B.** Lipases **C.** Glycosidases	An elderly man exhibits low levels of red blood cells and hemoglobin in blood; however, his color index is 1,3. Blood smear analysis revealed megaloblasts. What type of anemia is observed in this case? **A.** B12-folic aciddeficiency

D. Nucleases **E.** Synthetases	**B.** Iron-deficiency **C.** Acquired hemolytic **D.** Hereditary hemolytic **E.** Chronic post hemorrhagic
An ophthalmologist has detected increased time of dark adaptation in a patient. What vitamin deficiency can result in such symptom? **A.** A **B.** C **C.** K **D.** B1 **E.** B6	A 70-year-old patient presents with cardiac and cerebral atherosclerosis. Examination revealed changes of blood lipid spectre. Increase of the following lipoproteins plays a significant role in atherosclerosis pathogenesis: **A.** Low-densitylipoproteins **B.** Verylow-densitylipoproteins **C.** Intermediate densitylipoproteins **D.** High-density lipoproteins **E.** Chylomicrons
A woman noticed that acuton her skin was still bleeding even after 20 minutes had passed.What vitamin deficiency causes such condition? **A.** Vitamin K **B.** Vitamin A **C.** Vitamin D **D.** Vitamin E **E.** Vitamin B12	Isoniazid is an antituberculous drug derivative from: **A.** Isonicotinic acid **B.** Nicotinicacid **C.** Picolinic acid **D.** Pyrrole-2-carboxylicacid **E.** N-aminobenzoic acid
Uric acid is a derivative of: **A.** Purine **B.** Indole **C.** Pyrazine **D.** Pyrazole **E.** Pyridine	Tryptophan amino acid is a derivative of: **A.** Indole **B.** Coumarin **C.** Pyridine **D.** Imidazole **E.** Purine
Structure of proteins includes proteinogenic aminoacids.Whatis the position of the aminogroup in the structure of these amino acids? **A.** α-position **B.** β-position **C.** γ-position **D.** δ-position **E.** _-position	Name the disaccharide with the following structure: **A.** β-lactose **B.** α-lactose **C.** β-maltose **D.** β-cellobiose **E.** Saccharose
One of the cyclic glucose forms is as follows: Name this compound: **A.** α-D-glucopyranose **B.** β-D-glucopyranose **C.** α-L-glucopyranose **D.** α-D-glucofuranose **E.** β-D-glucofuranose	A patient with atherosclerosis has been prescribed Linaetholum containing essential fatty acids.Which o fthe following acids is an essential part of the preparation? **A.** Linolenic **B.** Palmitic **C.** Crotonic **D.** Stearic **E.** Oleic
A newborn born to an Rh-negative mother (3rd pregnancy) presents with progressing jaundice, symptoms of CNS excitation, anemia. What type of jaundice is it? **A.** Hemolytic **B.** Parenchymatous **C.** Obstructive **D.** Parasitic **E.** Toxic	During calculous cholecystitis attack the patient has developed the following symptoms: saponated feces and steatorrhea. What stage of fats metabolism is disrupted according to those symptoms? **A.** Fat digestion, absorption and secretion **B.** Fat absorption **C.** Intermediary metabolism of fats **D.** Fats metabolism in adipose tissue **E.** Depositing disruption

Tetanic spasms of skeletal muscles occur under low calcium concentration in blood. What endocrine disorder can this condition be associated with? **A.** Hypofunction of parathyroid glands **B.** Hyperfunction of adrenal cortex **C.** Hypofunction of adrenal cortex **D.** Hyperthyroidism **E.** Hypothyroidism	Eicosanoids, - hormone-like compounds, - are used to stimulate labor and for contraception. What substances have such an effect? **A.** Prostaglandines **B.** Interleukines **C.** Endorphines **D.** Angiotensines **E.** Enkephalines
A newborn infant has hemolytic jaundice caused by rhesus incompatibility. What bile pigment will be concentrated highest in the blood of this infant? **A.** Unconjugated bilirubin **B.** Conjugated bilirubin **C.** Urobilinogen **D.** Stercobilinogen **E.** Bile acids	The 49-year-old female patient suffering long-term from pancreatic diabetes has developed the following symptoms after administering insulin: weakness, facial pallor, palpitation, anxiety, double vision, numbness of lips and tongue apex. Glucose molar concentration in blood was 2,5 mmol/l. What complication has developed in the patient? **A.** Hypoglycemic coma **B.** Hyperosmolar coma **C.** Hyperglycemic coma **D.** Hyperketonemic coma **E.** Uremic coma
The 55-year-old female patient has developed a case of acute pancreatitis caused by greasy food. What is the main pathogenesis step of this disorder? **A.** Premature activation af enzymes in gland ducts and cells **B.** Pancreatic juice deficiency **C.** Low bile production in liver **D.** Fats digestion disruption **E.** Acute bowel obstruction	L-DOPA and its derivatives are used in treatment of Parkinson's disease. What aminoacid is this substance made of? **A.** Tyrosine **B.** Asparagine **C.** Glutamate **D.** Tryptophan **E.** Arginine
The 56-year-old patient has developedmegaloblastic anemia in the course of alcoholic cirrhosis. What vitamin deficiency is the main cause of anemia in this patient? **A.** Folic acid **B.** Lipoic acid **C.** Biotin **D.** Thiamine **E.** Pantothenic acid	The patient with mushroom poisoning has developed the following symptoms: yellow coloring of skin and sclera, dark-colored urine. Hemolytic jaundice was diagnosed.What pigment causes such coloring of the patient's urine? **A.** Stercobilin **B.** Conjugated bilirubin **C.** Biliverdin **D.** Unconjugated bilirubin **E.** Verdohemoglobin
A patient complains of painin the small joints. High concentration of uric acid is detected in his blood plasma.What pathology causes such changes? **A.** Gout **B.** Diabetes mellitus **C.** Phenylketonuria **D.** Lesch-Nyhan syndrome **E.** Diabetes insipidus	Method consisting in removal of low-molecular impurities from colloidal systems and high-molecular compound solutions by semipermeable membrane diffusion is called: **A.** Dialysis **B.** Electrodialysis **C.** Ultrafiltration **D.** Decantation **E.** Compensatory dialysis
The patient has mucosal dryness	A patient with ischemic heart disease

and mesopic vision disorder. What vitamin deficiency causes these symptons? **A.** *A* **B.** *P* **C.** *E* **D.** *C* **E.** *D*	has been administered inosine which is an intermediate metabolite in the synthesis of: **A.** Purine nucleotides **B.** Metalloproteins **C.** Lipoproteins **D.** Glycoproteins **E.** Ketone bodies
Sulfanilamides inhibit the growth and development of bacteria. The mechanism of their action is based on the impairment of the following acid synthesis: **A.** Folic **B.** Lipoic **C.** Nicotinic **D.** Pantothenic **E.** Pangamic	Sulfanilamides are widely used as bacteriostatic agents. The mechanism of antimicrobial action of sulfanilamides is based on their structural similarity to: **A.** Para-aminobenzoic acid **B.** Glutamic acid **C.** Folic acid **D.** Nucleic acid **E.** Antibiotics
A patient was found to have a tumor of the pancreatic head, which is accompanied by the impaired patency of the common bile duct. Blood test will reveal an increase in the following substance level: **A.** Bilirubin **B.** Urea **C.** Hemoglobin **D.** Insulin **E.** Adrenaline	After an insulin injection a 45-yearold female with a long history of diabetes mellitus has developed weakness, paleness, palpitation, anxiety, double vision, numbness of lips and the tip of tongue. Blood glucose is at the rate of 2,5 mmol/l. What complication has developed in the patient? **A.** Hypoglycemic coma **B.** Hyperosmolar coma **C.** Hyperglycemic coma **D.** Hyperketonemic coma **E.** Uremic coma
A parturient woman diagnosed with uterine inertia has been delivered to the maternity ward. The doctor gave her an injection of the drug that activates the contraction of smooth muscles of the uterus. What hormone is a component of this drug? **A.** Oxytocin **B.** Gastrin **C.** Secretin **D.** Angiotensin **E.** Bradykinin	Depressive states can be treated by means of drugs inhibiting the enzyme that inactivates biogenic amines. Specify this enzyme: **A.** MAO (monoamine oxidase) **B.** LDH (lactate dehydrogenase) **C.** CPK (creatine phosphokinase) **D.** AST (aspartate aminotransferase) **E.** ALT (alanine aminotransferase)

"APPROVED"
Head of Department of Pharmaceutical,
Biological and Toxicological Chemistry
MD, Professor _____ I.V.Nizhenkovska
Protocol № 2 of 31.08.2017

The list of practical skills that a student must master to the final Module control 2 on Biological chemistry for *3rd year* students Pharmaceutical faculty full-time education

1. Assimilation of safety rules when working with chemicals and equipment;
2. To know the analytical principles and technology of biochemical research (appointment of material and technical equipment of laboratories; use of chemical reagents and laboratory utensils);
3. To know the theoretical foundations, advantages and disadvantages of photo- and spectrometric analysis methods, chromatographic methods (adsorption chromatography, distribution chromatography, high performance liquid chromatography, paper chromatography, thin-layer chromatography, ion-exchange chromatography, affinity chromatography);
4. To know the theoretical foundations of electrophoretic methods of analysis (types of electrophoresis, characteristics of carriers);
5. To know the theoretical foundations of molecular genetic research (allocation of nucleic acids from a biological material, stages of polymerase chain reaction).
6. Preparation of biological material for various types of laboratory research (homogenization, centrifugation, plasma and serum selection, etc.).
7. Work with means of measuring equipment and basic laboratory equipment (photoelectrocolorimeter, spectrophotometer, pH-meter, centrifuges, thermostat, water bath, dispensers, etc.).
8. Construction of calibration graphs, for calculating the concentration of substances in biological material
9. Detection of protein content in biological material (sulfosalicylic acid test; Geller test; birette reaction; protein separation by vine method).
10. Determination of the activity of enzymes in biological fluids (determination of activity of α-amylase urine, alanine and aspartate aminotransferases of blood serum).
11. Analysis of carbohydrate metabolism parameters: qualitative reactions on monosaccharides (Trommer's reaction, Feling's reaction); qualitative reaction to starch (iodine test); quantitative determination of glucose content in biological fluids (in urine - glucose, in blood - by glucose oxidase method);
12. Analysis of lipid metabolism indices: investigation of the content of ketone bodies in urine by reaction with sodium nitroprusside (Lange test) and ferric chloride (III Gerhard reaction), determination of cholesterol by the Ilka method (with Lieberman-Burhard reagent).
13. Determination of the main components of the nucleoprotein (protein, nitrogenous base, pentose, phosphatic acid) in its hydrolyzate.
14. Determination of the amount of urea in serum (by reaction with diacetylmiooxime).
15. Qualitative determination of phenylpyruvic acid in urine (Felling test).
16. Detection of hemoglobin hemoglobin in biological objects (reaction with benzidine).
17. Quantitative determination of serum uric acid in blood serum by the Folin method (by reaction with phosphorus-refined reagent).
18. Qualitative determination of insulin.
19. Qualitative determination of adrenaline and products of its oxidation.
20. Qualitative determination of folliculin (estrone)
21. Qualitative reactions on vitamins B2, B6 and E.
22. Quantitative determination of total bilirubin and its fractions in blood serum using the method of Yandrashek

MINISTRY OF HEALTH OF UKRAINE
BOHOMOLETS NATIONAL MEDICAL UNIVERSITY
Department of Pharmaceutical, Biological and Toxicological Chemistry

APPROVED
at the methodical meeting of the pharmaceutical, biological and toxicological chemistry department
« 31 » ___08_____2017

Protocol № 2

Head of the department, M.D, professor
_____ I.V.Nizhenkovska

GUIDELINES FOR PRACTICAL TRAINING

Academic subject	Biological chemistry
Module №	2
Topic № 1	*№ 1-11*
Year	3 year
Faculty	Pharmaceutical
Hours	2,5 hours

Kyiv 2017

Topic 1. Protein digestion in the digestive canal. General ways of amino acid metabolism.
Determination of levels of aminotransferases (ALT and AST) in serum.
The purpose of the lesson:

- study the stages of digestion of proteins in different parts of the digestive tract
- explore common ways of amino acids converting;
- be able to explain by the exchange of free amino acids;

Theoretical questions

1. The concept of nitrogen balance and causes of its failures.
2. Digestion of proteins and peptides in the stomach and small intestine, the mechanism of action of proteolytic enzymes (pepsin, renin).

3. Deamination of amino acids:
· types of deamination reactions of amino acids and their terminal products,
· the mechanism of oxidative deamination of amino acids. Glutamate dehydrogenase reaction, its value and regulation.
4. Amino acids transamination:
· substrates for transamination reactions;
· chemical structure of amine transferase;
· transamination reaction mechanism,
· biochemical importance.
5. Decarboxylation of amino acids, physiological significance. Biogenic amines as pharmaceuticals. Pharmaceuticals – amine oxidase(MAO, DAO) inhibitors.
6. Common ways of the nitrogen-free skeletons of amino acids metabolism. Glucogenic and ketogenic amino acids.

Practical work

Experiment 1. Determination of aminotransferases (ALT and AST)

The principle of the method. The result of transamination under AST is that aspartic acid turns to oxaloacetic acid, and alanine under ALT – to pyruvic acid. Oxaloacetic acid is transformed to AML. Adding acidic 2,4-dinitrophenylhydrazine (DNPH, Brady's reagent) leads to the termination of the enzymatic process and to 2,4-dinitrophenylhydrazone of pyruvic acid, which in an alkaline medium gives brownish red color, which intensity is proportional to the amount of pyruvic acid forme. The quantity of the formed pyruvate allows estimating the activity of the enzyme. The activity of aminotransferase expressed in micromoles of pyruvic acid formed by 1 ml of serum during 1 h incubation at 37^0C.

1.1. Determination of alanine aminotransferase

Progress: The work is performed in accordance with the table.

Reactant	Experiment, ml	Contol, ml
Substrate mixture (alanine and α-ketoglutarate)	0,5	0,5
Put into thermostat for 5 min at 37^0C		
Serum Blood	0,1	-
H_2O (Dist.)	-	0,1
Put into thermostat for 30 min at 37^0C		
0.1% solution of 2,4-BPG	0,5	0,5
Put into thermostat for 20 min at 37^0C		
0,4n NaOH	5	5
Note. Thoroughly mix for 10 min at 25^0C (to form color). Optical density measured on photocolorimeter at λ = 500-560 nm		

Calculation of ALT activity in serum by conducting calibration graph that shows the dependence of the optical density of pyruvic acid content.

Construction of calibration:

Preparation of the calibration solution: 11 mg sodium pyruvate dissolved in a little the amount of water transferred into a volumetric 100 ml flask of water and bring to a label: 1 ml gauge solution contains 110 mg of sodium pyruvate, corresponding to 88 mg or 1 mmol pyruvic acid.
Prepare a dilution series with calibration solution (see. Table). Conduct calibration test as well as experimental, but add diluted calibration solutions instead serum. Measure against the idle test, add water instead calibration solutions. Defining optical density build calibration graph plotting enzyme activity on the abscissa axis, and absorbance values on the axis of ordinate. Calibration curve is linear to the value of optical density 0.3.

Obtaining the calibration solutions

№ of test	Calibration sodium pyruvate solution, ml	Distilled water, ml	Piruvic acid		ALT Activity nmol / (SL)
			microgram	micromole	
1	0,05	0,55	4,4	0,05	278
2	0,10	0,50	8,8	0,10	556
3	0,15	0,45	13,2	0,15	834
4	0,20	0,40	17,6	0,20	1112

Number of pyruvic acid formed (in mg) are on the calibration graph or by the formula I:

$$X = \frac{Д}{0,09} \quad (I),$$

ALT activity is calculated by the formula II:

$$ALT = \frac{X \cdot 2 \cdot 10}{88} (II),$$

where: X – the amount of pyruvic acid, found by calibration schedule or formula I, mg;
2 – Conversion rate for 1 h incubation;
10 – Conversion rate for 1 ml serum;
88 – weight of 1 mmol pyruvic acid.
Serum ALT healthy activity determined by this method varies from 5-30 units/ml (0,1-0,7 micromoles / ml).
Conclusion.

1.2 Determination of aspartate aminotransferase

Progress: The work is performed in accordance with the table.

Reactant	Experiment, ml	Contol, ml
Substrate mixture (alanine and α-ketoglutarate)	0,5	0,5
Put into thermostat for 5 min at 37^0C		
Serum Blood	0,1	-
H_2O (Dist.)	-	0,1
Put into thermostat for 30 min at 37^0C		
0.1% solution of 2,4-BPG	0,5	0,5
Put into thermostat for 20 min at 37^0C		
0,4n NaOH	5	5
Note. Thoroughly mix for 10 min at 25^0C (to form color). Optical density measured on photocolorimeter at λ = 500-560 nm		

The enzyme activity is calculated by the formula

$$X = E \cdot 133 \text{ units/ml},$$

where X – enzyme activity;
E – extinction;
133 – conversion factor.

1 mg of pyruvic acid - 0,015 enzyme units. IS; 1 enzyme units - 133 mg of pyruvic acid, or by calibration graph. Activity expressed in standard units per 1 ml of serum. 1 unit. AST corresponds the enzyme activity able to form under these conditions 1 mg of pyruvic acid. In calculating enzyme activity one must take into account the dilution of serum:

$$X = a \cdot 10,$$

where X – a unit of the enzyme;
10 – recalculation for 1 ml;
a – a quantity of pyruvic acid determined by calibration curve, μg.

In healthy people serum, AST activity determined by this method ranges from 5 to 40 units / ml (0.1 - 0.5 m / ml). Recalculation of micromolar enzyme activity into micromoles of pyruvic acid, formed in 1 ml of serum during the incubation for 1 hour at 37^0C:

$$AST = \frac{a \cdot 10}{88},$$

where a – a quantity of pyruvic acid determined by calibration schedule in micrograms;
88 – weight of 1 mmol PMC mg;
10 – a conversion rate of 1 ml serum.

Literature

1. Yu.Gubsky Biological chemistry: textbook/edited by Yu.Gubsky. – Vinnytsia: Nova Knyga, 2017 – 488 p.
2. Lehninger Principles of Biochemistry 6th ed - David L. Nelson, Michael M. Cox -W H Freeman and Company – 2013. – 1010 p.
3. Lectures at the Dept.

Tasks for self-control

Task 1. Cytological study of gastric mucosa were found degenerative changes of the main cell. Synthesis of a substance is broken?
A. pepsinogena
B. Hydrochloric acid
pepsin C.
D. Lactic Acid
E. Tsyankobalaminu
Task 2 patients after the study of secretory activity of the stomach was diagnosed with Akhil. Explain this term.
A. Lack of HCl in gastric juice
B. Lack of HCl and pepsin in gastric juice
C. Hiperatsydnnyy state
D. Hipoatsydnyy state
A. Increase of pepsin
Task 3. To determine the activity of ALT student used a 2.4-DNFH (dynitrofenilhidrazyn). For any number of acid formed, you can judge the activity of the enzyme?
A. Lactate
B. pyruvate
C. citrate
D. Malate
E. folic acid
Task 4. In animal experiments, it was found that the transamination reactions involving enzymes aminotransferase. What a coenzyme that is part of these enzymes.
A. FAD
B. NAD
C. Tiaminpirofosfat
D. Tetrahidrofoliyevaya acid
E. piridoksalfosfat
Correct decision check by comparing them with standard answers.
Standards of answers to the challenges for self and self-control output level: Task 1 - A, Task 2 - B, Task 3 - B, Task 4 - E,
Task 5. Fill in the table based on the specificity of action of proteolytic enzymes:

Place of action	Optimum pH	Activation of proteinase			Specificity of action
		Proenzyme	Activator	Active form	

Topic 2. The ways of ammonia utilization. The metabolism of individual amino acids. Molecular pathology of metabolism of amino acids. *Quantitative determination of urea in the blood.*

The purpose of the lesson:

- To explain basic metabolize processes of transformation: explain the basic metabolic conversion of acyclic, cyclic, sulfur-containing aminoacids, branched chain aminoacids.
- To know the mechanism of glutathione and creatine formation, their biological significance.
- To estimate metabolic changes with hereditary diseases of aminoacid metabolism.
- To characterize main ways of ammonia formation and utilization in organism.
- To understand the methods of urea determination in biological fluids and interpret the results.

Theoretical questions

1. Specific cyclic pathway phenylalanine and tyrosine aminoacids, the sequence of enzymatic reactions. Hereditary enzimopatii exchange cyclic acyclic aminoacids phenylalanine and tyrosine - phenylketonuria, Alkaptonuria, albinism.
2. Exchange of tryptophan: kinureninovy and serotonin way. Hereditary enzimopatii tryptophan metabolism.
3. Exchange of sulfur-containing amino acids cysteine and methionine, and hereditary disorders (homocystinuria).
4. Features of the exchange of branched chain aminoacids. Maple syrupurine diseaseas metabolic BCAA.

5. Biosynthesis and biological role of creatine and creatine phosphate, formation of creatinine.
6. Exchange of glycine and serine; role tetrahydrofolate (H4-folate) in the transfer of one carbon fragments, dihydrofolatereductase inhibitors as anticancer agents.
7. The exchange of arginine; biological role of nitric oxide, NO-synthase.
8.The ways and sources of ammonia formation in organism, reasons and result of it's toxicity.
9. The main mechanisms of ammonia neutralization:

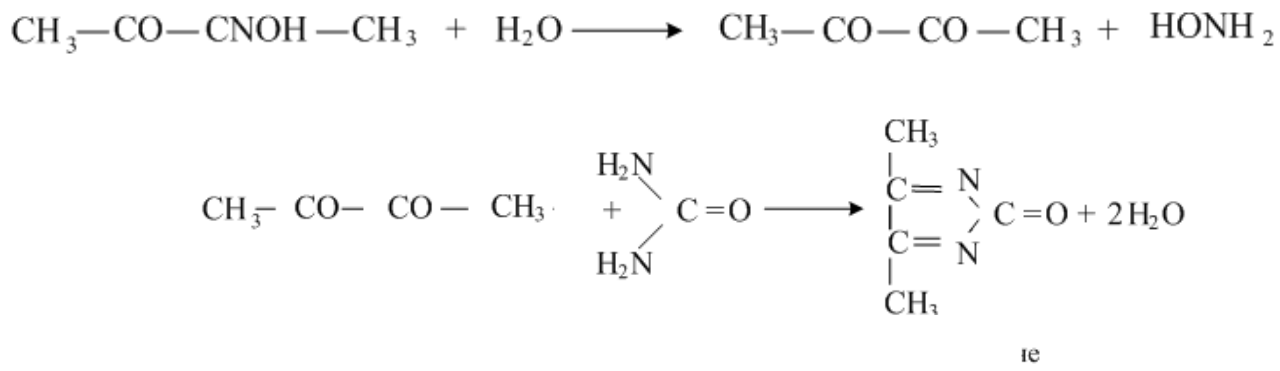
- reductive amination of a-ketoglutarate;
- formation of amides of dicarboxylic acids;
- formation of ammonia salts in the burrows;
- formation of urea in the liver.

10. Genetic abnormalities of enzymes of the ureacycle. Hyperammonemia.

Practical work

Experiment 1. Determination of urea in blood serum and urine, by reaction with diatsetilmonooxide.

Principle of the method:Urea in acidic medium in the presence of iron salts and thiosemicarbazidet form a complex compound diatsethylmonooksim, which is red color and it's optical density, at which the green color filters are (500 - 560 nm), is proportional to the urea concentration.



Proceedings. Determining the course of conduct on the table:

Reagent	Test		
	research	standart	control
Blood serum	0,02 мл	-	-
Reference urea solution (7 mmol / L).	-	0,02 мл	-
H_2O	-	-	0,02 мл
Diatsethylmonooksima solution (2.5 g / l)	2,00 мл	2,00 мл	2,00 мл
Tiosemidcarbazyd solution (2.5 g / l)	2,00 мл	2,00 мл	2,00 мл

Tubes were covered with aluminum foil, and the contents were heated under stirring in a water bath for exactly 10 minutes. At the same time treat research, standard and control samples. Then tubes should be quickly cooled under cold running water. Colorimetrate research and a standard sample against the control at a wave length of 530-560 nm (greenfilter) in a cuvette with a layer thickness of 1 cm. Optical density measurements should be carried out for no more than 15 minutes after cooling.

If, after heating the solution in the first vial is turbid, it has to be centrifuged for 5 minutes or deproteinize with threechloroacetic acid solution.

Calculation. The concentration of urea was calculated with this formula:

$$C = \frac{E_{res}}{E_{ref}} \cdot 16{,}64 \text{ mmol/l},$$

where - C – the concentration of urea;

E_{res} – optical density of research test;

$E_{эт}$ – optical density of reference test.

Notes:

1. With the content of urea over 25 mmol / L sample should be diluted with distilled water and repeat the analysis. Multiply the result by dilution.

2. Hemolytic and lipemic serum deproteinize. For this purpose, 0.1 ml of serum was mixed with 0.9 ml of threechloroacetic acid solution and centrifuged for 5 min. The same process standard. For the analysis of selected studies as deproteinization without serum. This method can be used for blood research.

Explain the result. Conclude.

The value for the pharmacy and clinic. Urea synthes is in the liver (cytosol and mitochondria) mainly from ammonia, which is formed by deamination of aminoacids, purine and pyrimidine decay nucleotides. During the day, the urine of a healthy personisal located 20 - 35 g (or 333 - 583 mmol) of urea. Normally, the content of urea in the blood serum of 3.3 - 8.3 mmol / l.

Increase of urea in the blood serum is one of the main signs of impaired renal excretory function. In addition, the increase in the level of urea in the blood serum can be extrarenal origin: loss of body fluids (vomiting, diarrhea, dehydration), increased protein breakdown (acutefatty liver). Reduction of urea can be observed in diseases of the liver (hepatocellular jaundice, cirrhosis of the liver) due to violation of its synthesis in the body.

Elevated levels of urea in urine observed when dietaryprotein deficiency, pernicious anemia, fever, intensive decomposition of protein sinthe body after ingestion of salicylates, with phosphorus poisoning. Low content of urea observed in liver cirrhosis, hepatocellular jaundice, nephritis, acidosis, uremia.

Literature

1. Yu.Gubsky Biological chemistry: textbook/edited by Yu.Gubsky. – Vinnytsia: Nova Knyga, 2017 – 488 p.
2. Lehninger Principles of Biochemistry 6th ed - David L. Nelson, Michael M. Cox -W H Freeman and Company – 2013. – 1010 p.
3. Lectures at the Dept.

Tasks for self-control

Task 1. One of the amino acids is a member of intracellular metabolism and methyl group donor. Select this amino acid.
A. Glutamate
C. Lysine
C. valine
D. Tyrosine
E. Methionine
Task 2. Experimental animals entered glycine labeled on carbon, to determine its participation in metabolic processes. Choose a synthesis in which personal involvement takes glycine.
A. Synthesis of ketone bodies
B. Cholesterol Synthesis
S. Synthesis of creatine
D. The synthesis of melanin
E. The synthesis of bile acids
Task 3 The patient, whose limbs were crushed a long time, after removing scales developed signs of hepatic coma, hyperammonemia found in the blood. What process led to an increase in the content of ammonia in the blood?
A. Reductive amination a-keto acids
B. Synthesis of Urea
C. deamination of amino acids
D. decarboxylation of amino acids
Task 4. Group on test animals was prolonged no proteins diet, so that they have moved many of the metabolic processes associated with the use of essential amino acids. Which is used as metylyuyuchoho agent in the biosynthesis of creatine?
A. valine
B. Threonine
C. Phenylalanine
D. Methionine
E. Glycine
Correct decision check by comparing them with standard answers.
Standards of answers to the challenges for self and self-control output level: Task 1 - E, Task 2 - C,

Objective 3 - C. Task 4 - D,
Task 5. Fill in the table:

Enzymopathy	Enzyme, whith activity is violetad	Amino acid, whoth synthesis is violetad

Topic №3. Metabolism of nucleotides. Pathology of metabolis: hyperuricemia, gout, orotatatsiduriya. *Quantitative determination of uric acid in serum.*

The purpose of training.

- examine the metabolic conversion of purine and pyrimidine nucleotides,
- know the mechanism of action of drugs which are used for correction of metabolic disorders of nucleotides.
- master methods determine the amount of uric acid in biological fluids, able to interpret the received data.

Theoretical questions

1. The biosynthesis of purine nucleotides: scheme of reactions of IMP synthesis; AMP and GMP formation and its regulation.
2. The biosynthesis of pyrimidine nucleotides: scheme of reactions forming reaction UMP, UDP, UTP, and CTP and its regulation.
3. Biosynthesis of deoxyribonucleotides. dTMP biosynthesis inhibitors as anticancer agents (dTMP structural analogs, derivatives pterins).
4. Purine nucleotide catabolism.
5. The catabolism of pyrimidine nucleotides.
6. Hereditary disorders of nucleotide metabolism. Gout. Lesch-Nyhan syndrome. Orotatatsiduriya.
7. The use of drugs to correct nucleotide metabolism disorders.

Practical work

Experiment 1. The quantitative determination of uric acid in serum.

The principle of the method. Uric acid restores phosphate tungstate reagent to form a compound of the blue color, the absorbance at a wavelength of 640 nm is proportional to the concentration of uric acid in serum.

Proceedings: The centrifuged tube is placed 0.5 ml of serum and 4 ml of distilled water. The contents of the tubes was stirred and 0.25 ml of 0.35 M sulfuric acid and 0.25 ml of 10% sodium digidrogenvolframatdigidrat. The contents of the tubes was stirred and after 5 minutes, centrifuged for 10 min at 3000 rev / min. Withdraw supernatant. Take three test tubes and make them according to the reactants

Reagents	Control sample, ml	Standart sample, ml	Experiment sample, ml
Supernatant	-	-	2
Standart uric acid solution	-	2	-
H2o	2	-	-
10 % NaHCO3	1	1	1
Phosphate tungstate reagent	0,5	0,5	0,5

The tubes are mixed. After 30 minutes, the optical density of standard and test samples at a wavelength of 640 nm (590 - 700 nm, a red filter) vs. a control sample cuvette of 10 mm thick. Blue color is stable for 30 minutes.

Calculation of the uric acid content of the formula is carried out:

$$C = \frac{А_{досл}}{А_{конт}} \times 30 \times 10,$$

where: C - the content of uric acid in the test sample, .mu.mol / l;
Adosl - the optical density of the test sample;
Acont - optical density of the control samples;
30 - the content of uric acid in the standard solution, mol / l;
10 - the value of serum dilution.

Explain the results. To summarize.

The value for the pharmacy and clinic. Formed as a result of the collapse of the purine bases uric acid excreted by the kidneys. In normal human urine released with 1.60 - 3.54 mg / day (270 - 600 mg / day)

uric acid. Normal levels of uric acid in the blood serum of men - 240 - 530 mmol / l (0.05 - 0.06 g / l) for women approximately 25% less - 185 - 440 mmol / l (0.04 - 0 , 05 g / l). Hyperuricemia accompanies gout - a disease that occurs in a precipitation of urate in tissues primarily in joints. Uric acid and its salts are extremely poorly soluble in water, their concentration in the body fluid in normal conditions close to the border of solubility. For the treatment of gout using drugs which inhibit the formation of uric acid (allopurinol) or stimulate its excretion by the kidneys (anturan, tsinhofen). In patients with gout, uric acid concentration in blood is almost always greater than 0.075 - 0.080 g / l, and the formation of seals gouty iiridko content is below 0.08 - 0.09 g / l.

Literature

1. Yu.Gubsky Biological chemistry: textbook/edited by Yu.Gubsky. – Vinnytsia: Nova Knyga, 2017 – 488 p.
2. Lehninger Principles of Biochemistry 6th ed - David L. Nelson, Michael M. Cox -W H Freeman and Company – 2013. – 1010 p.
3. Lectures at the Dept.

Tasks for self-control

Task 1. A woman of 40 years went to the doctor with complaints about pain in the small joints of the feet and hands. Joints enlarged, thickened nodes have the form. The serum - high content of urate. The reason is a violation of the exchange:
A. The amino acids.
B. purines.
C. carbohydrates.
D. Lipids.
E. pyrimidine.
Task 2: Patients with gout doctor prescribed allopurinol. What allopurinol property provides therapeutic effect in this case.
A. Accelerating the catabolism of pyrimidine nucleotides.
B. Increase output rate of nitrogen-containing substances.
C. Competitive inhibition of xanthine oxidase.
D. Slowdown reutilization of pyrimidine nucleotides.
E. Acceleration of the synthesis of nucleic acids
Task 3. For the treatment of malignant tumors is prescribed methotrexate - a structural analog of folic acid, which is a competitive inhibitor of dihydrofolate reductase and thus inhibits the synthesis:
A. nucleotides.
B. monosaccharides.
C. fatty acids.
D.Glycerophosphats.
E. Glycogen.
Task 4. Derivative pterins - aminopterin and methotrexate - is a competitive inhibitor of dihydrofolate reductase, causing them to inhibit the regeneration of tetrahydrofolic acid dihydrofolate. These drugs lead to inhibition of one-carbon groups intermolecular transport. nucleotide biosynthesis is suppressed while?
A. dTMP.
B. IMP.
C. UMP
D. OMP.
E. AMP.
The correctness of the decision to test, to compare with the standards of the responses.
Standards of answers to solve problems for self-examination and self-baseline: Objective 1 - B, C Task 2, Task 3 - A. Task 4 - A.
Problem 5. Fill in the table

№		Purine nucleotides	Pyrimidine nucleotides
	Structure		
	Sources for synthesis		
	The final metabolic product		
	Disorder of metabolism		

	Drugs for corrections of disorders of metadolism		

Topic 4. The biosynthesis of nucleic acids and proteins and their regulation. Inhibitors of transcription and translation. Regulation of gene expression in eukaryotes and prokariot. Molecular mechanisms of mutations. Genetic Engineering. *Determination of the main components of the nucleoprotein (protein nitrogenous base, a pentose, phosphoric acid) in its hydrolyzate.*

The purpose of the activity:

- Study the patterns of the matrix nucleic acid synthesis stages of these processes, the mechanisms of mutation, reparations, and the emergence and development of hereditary diseases.
- Examine general patterns of protein synthesis, the stages of this process, the molecular mechanisms and regulation of broadcasting.
- To know the mechanism of action of antibiotics and other inhibitors of the synthesis of nucleic acids and proteins.
- To know the principles of genetic engineering and biotechnology, its importance for developing of modern pharmaceutical science.

Theoretical questions

1. General scheme of DNA biosynthesis. Enzymes of DNA replication in prokaryotes and eukaryotes.
2. The biological significance and mechanisms of DNA repair. Smoothing UV-induced gene mutations; xeroderma pigmentosum.
3. Mutations: genomic, chromosomal, gene (point) role in the occurrence of hereditary diseases and enzimopatii person.
4. Stages and RNA synthesis enzymes. RNA polymerase prokaryotes and eukaryotes.
5. Processing, posttranscriptional modification of RNA.
6. Ribosomal protein-synthesizing system. Stages and mechanisms of translation: initiation, elongation, termination.
7. Posttranslational modificationof peptide chains.
8. Antibiotics - inhibitors of the replication, transcription and translation in prokaryotes and eukaryotes,their biomedical applications. Biochemical mechanisms of antiviral action of interferons. Blocking protein biosynthesis diphtheria toxin (ADP-ribosylation factors broadcast).
9. Genetic engineering or recombinant DNA technology: general concepts, biomedical importance.

Practical work

Experiment 1. Biuret reaction on peptides and proteins.

The principle of the method. All proteins and peptides than dipeptide with CuSO4 in an alkaline medium (NaOH) form complexes which cause the solution purple. Peptide bonds react in the enol form.

Progress. The tube is placed hydrolyzate nucleoprotein 5 drops, 10 drops of NaOH solution, 2-3 drops CuSO4 solution. The contents of the tube mixed. The solution acquires a violet color.

Experiment 2. Silver test for purine bases.

The principle of the method. Purine nitrogenous base form a precipitate upon reaction with silver nitrate.

Progress. The tube was placed 10 drops nucleoprotein hydrolyzate is neutralized with ammonia, were added 5 drops of silver nitrate solution, stirred contents of the tube. After 3-5 minutes falls loose sediment silver salts purine nitrogenous bases of light brown color.

Experiment 3. Trommer reaction to ribose and deoxyribose.

The principle of the method. Compounds containing an aldehyde group is reduced by heating the composition in the Cu2 + Cu (OH) 2 to Cu1 +, and thus themselves are oxidized to the corresponding carboxylic acids. The reaction is accompanied by a change in sediment color: blue Cu (OH)2 is transformed into a yellow CuOH and further heating to brick red Cu2O. Excess copper sulfate reaction masks as

Cu (OH) 2 decomposes upon heating to copper oxide CuO and black water.

Progress. The test tube was placed 5 drops nucleoprotein hydrolyzate was added 10 drops of sodium hydroxide solution, 3-5 drops of the copper sulfate solution (until turbidity which does not disappear), the contents of the tube mixed, then heated to boiling. Coloration varies. Drops brick-red precipitate Cu2O.

Experiment 4. Molybdenum test for phosphoric acid.

The principle of the method. Phosphoric acid by heating with a molybdenum reagent forms ammonium phosphomolybdate yellow.

Progress. The tube was placed 10 drops of a molybdenum reagent was added 5 drops nucleoprotein hydrolyzate is heated to boiling. Painting becomes lemon-yellow. Upon cooling a yellow crystalline precipitate falls complex compound - ammonium phosphomolybdate.

Clinical and diagnostic value.

Nucleic acids exist in cells as nucleoproteins. When complete hydrolysis of nucleoprotein formed their components: amino acids, nitrogenous bases, pentose, phosphoric acid. DNA analysis is increasingly used in the diagnosis of hereditary diseases.

Literature

1. Yu.Gubsky Biological chemistry: textbook/edited by Yu.Gubsky. – Vinnytsia: Nova Knyga, 2017 – 488 p.
2. Lehninger Principles of Biochemistry 6th ed - David L. Nelson, Michael M. Cox -W H Freeman and Company – 2013. – 1010 p.
3. Lectures at the Dept.

Tasks for self-control

Task 1. If poisoning amanitin - poison pale toadstool - blocked by RNA polymerase B (II). This stops:

A. mRNA synthesis.
B. Synthesis of tRNA.
C. Reverse transcription.
D. Synthesis of primers.
E. Maturation of mRNA.

Task 2. The antibiotic rifampicin, which is used to treat tuberculosis, affects certain biochemical processes. Call them.

A. inhibits RNA polymerase initiation step.
B. Inhibits DNA polymerase initiation step.
C inhibits DNA ligase.
D. inhibit aminoacyl-tRNA synthetase.
E. inhibitory effect of protein factors in protein synthesis.

Task 3. A child suffering from diphtheria, fibrinous growths found on the tonsils. The process inhibits the diphtheria toxin?

A. The synthesis of protein.
B. gluconeogenesis.
C. fibrinolysis.
D. β-Oxidation of fatty acids.
E. Synthesis of biogenic amines.

Task 4. All living organisms same triplets encode the same amino acid, allows E.Coli transplanted human insulin gene. As the name of this property is the genetic code?

A. Versatility.
B. degeneration.
C. Redundancy.
D.Tripletnost.
E. Continuity.

Correctness check solutions, comparing them with the standards of the responses.
Answeres: 1 - A, 2 -A, 3 – A, 4 - A.
Task 5. Fill in the table:

Antibiotics	Mechanismof the action
Inhibitors of replication	
Inhibitors of transcription	
Inhibitors of translation	

Topic 5. Biochemistry of intercellular communication. Molecular mechanisms of signal transduction of hormone. *Determination of insulin, adrenaline, folikulin.*

The purpose of the activity:

- to study the general principles of the classification of hormones;
- know the molecular mechanisms of action of hormones protein-peptide, and amino acid derivatives of biogenic amines on the target cells with signal molecules mediators.
- know the molecular mechanisms of action of steroid and thyroid hormones;
- master the method of qualitative determination of insulin, adrenaline and estrone in biological fluids.

Theoretical question

1. General characteristic of hormones, classification:
   - place of synthesis;
   - chemical nature;
   - mechanism of action.
2. Targets of hormonal action; cell types of reactions to hormone action.
3. Hormone receptor: Membrane (ionotropic, metabotropic) and cytosolic receptors.
4. Molecular and cellular mechanisms of action of protein-peptide hormones and biogenic amines.
5. Molecular mechanisms of action of steroid and thyroid hormones.
6. Eicosanoids: structure, classification (prostanoids - prostaglandins, prostacyclins, thromboxanes, leukotrienes), the path and location of the synthesis, biochemical effects. Aspirin and other nonsteroidal anti-inflammatory drugs like inhibitors of prostaglandin synthesis.

Practical work

Experiment 1. Biuret reaction (on the example of insulin).

Principe of the method: The chemical nature of insulin - a simple protein which in an alkaline medium reacts with copper sulphate with the formation of the compound colored in purple.

Proceedings: Take up to 10 drops of insulin and add 5 drops of 10% NaOH solution and drop of CuSO4. The liquid is colored purple.

Make a conclusion

Experiment 2. Qualitative reaction to adrenaline (reaction with ferric chloride).

The principle of the method: Adrenaline is easily oxidized in air to form adrenochrome that gives the emerald-green color with ferric chloride.

Proceedings: making a tube 10 drops of test solution containing epinephrine, and 1 drop of ferric chloride. Observe the green color in the presence of catechol in the molecule of adrenaline. If ammonia is added, there is a change in color to red, and then - brown. To make a conclusion.

The value for the pharmacy and clinic. In normal conditions the concentration of adrenaline in the blood plasma is 112 - 658 pg / ml; noradrenaline - less than 10 pg / ml. Increased excretion of adrenaline in hypertension, pheochromocytoma, in the acute phase of myocardial infarction, strokes, infectious diseases. Low adrenaline observed in collagenosis, acute leukemia, the defeat of the hypothalamus, myasthenia gravis, syndrome Cushing et al. Smoking, physical exertion, emotional stress cause catecholamine excretion in the urine. Increased excretion of catecholamines is observed in hepatic cirrhosis, acute gastric ulcer and 12 duodenal ulcer. Violation of excretion was observed in the pathogenesis of uremia.

Experiment 3. Quality reaction to folikulin (estrone) - the female sex hormone.

Principe of the method: Folikulin with sulfuric acid is painted in yellow color when heated becomes yellow-hot.

Proceedings: In a test tube put 0.5 ml alcohol solution of folikulinu and put it in a water bath for 10 minutes to remove the alcohol. By folikulinu remaining in the test tube, adds 6.0 ml of concentrated sulfuric acid and again put the tube in a water bath for 10 minutes. The liquid in the tube painted in yellow color and then became yellow-hot with green fluorescence after heating.

Literature

1. Yu.Gubsky Biological chemistry: textbook/edited by Yu.Gubsky. – Vinnytsia: Nova Knyga, 2017 – 488 p.
2. Lehninger Principles of Biochemistry 6th ed - David L. Nelson, Michael M. Cox -W H Freeman

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3. Lectures at the Dept.

Tasks for self-control

Task 1. Patient for the purpose of analgesia (pain relief) designated substance that mimics the effects morphine, but is synthesized in the central nervous system:

A. Somatoliberyn
B.Oxytocin
C. endorphins
D. Vasopressin
E.Prolactin

Task 2 Women in labor to induce labor appointed prostaglandin E, which is a product oxidation:

A. arachidonic acid
B. linoleic acid
C. linolenic acid
D. cholesterol
E. glycerol

Task 3. The interaction of many protein and peptide hormones and catecholamines with nature membrane receptors leads to the formation of messenger cAMP. For some substances formed this messenger?

A. ADP
B. GDP
C. ATP
D. GTP
E. UTP

Task 4. The patient with rheumatoid arthritis treated with hydrocortisone. What enzyme takes participation in the implementation of anti-inflammatory action of this hormone?

A. Phospholipase A2
B. hexokinase
C. Aminotsyl-tRNA-synthetase
D. Phosphofruktokinaze
E. lipoprotein lipase

Correct decision check by comparing them with standard answers.

Standards of answers to the challenges for self and self-control output level: Task 1 - C, Task, 2 - A, Task 3 – C, Task 4 - A,

Task 5. Fill in the table:

Name of hormone	Type of hormone receptor	Intracellular mediator

Topic 6. Biochemical basis of vitaminology. Vitamins like pharmaceuticals. *Qualitative reaction to vitamins B2, B6 and E.*

The purpose of the activity:

- to study the general principles of the classification, the functional role of vitamins and vitamin compounds.
- know the biochemical mechanisms of participation of vitamins and vitamin-like substances in the metabolic transformations
- master the methods of qualitative determination of vitamins
- master the methods of detection of vitamins B2, B6 and E in the test solutions.
- be able to assess metabolic changes in disorders due to the imbalance of vitamins in the body.

Theoretical questions

1. Vitamins as essential bioactive components of food, their classification and nomenclature, the role and importance in the metabolism.

2. Water-soluble coenzyme vitamins (B1, B2, PP, B6, B12, H, folic acid, pantothenic acid, vitamins C, P):
• the structure of biologically active forms;
• biochemical function and role in metabolism;
• sources and the daily need.
3. coenzyme liposoluble vitamins (A, D, E, K, F):
• the structure of biologically active forms;
• biochemical function and role in metabolism;
• sources and the daily need.
4. The vitamin-like substances and their biological functions.
5. antivitamin, the most important representatives, their mechanism of action.
6. The use of vitamins and antivitamin in medicine.

Practical work

Experiment 1. Identification of vitamin B2 (riboflavin)

Principle of the method: the reaction is based on the ability of vitamin B2 to oxidation and reduction. When changing from the reduced form of riboflavin in an oxidized color change from yellow solution was observed (riboflavin) to red (rodoflavin) and in the future - a colorless (leykoflavin). Conversion of the reduced form of vitamin B2 in the oxidized reaction occurs with concentrated hydrochloric acid in the presence of zinc.

Proceedings: to 1 ml of riboflavin, 0.5 ml of concentrated HCl, and a small piece of metallic zinc. The observed changes in color of the solution. Make a conclusion.

Clinical and diagnostic and practical significance. Riboflavin is a part of flavin cofactors including FMN and FAD prosthetic groups that is flavoproteins enzymes are involved in numerous oxidation reactions substances in cells: proton and electron transfer in the respiratory chain; Oxidation of pyruvate, succinate, α-ketoglutarate, α-glycerol phosphate, fatty acids into the mitochondria; oxidation of biogenic amines and aldehydes, etc.

In clinical practice using riboflavin and coenzyme preparations: flavin mononucleotide (FMN) and flavinat (FAD) in various dosage forms. They are used in giporiboflavinoze, diseases of the skin, eyes, dermatitis and ulcers that do not heal, inflammation of the cornea (keratitis), conjunctivitis (inflammation of the conjunctiva).

Experiment 2. Detection of vitamin B6 (pyridoxine)

The principle of the method: vitamin B6 by reacting with a solution of ferric chloride forms a complex salt type iron phenolate red.

Proceedings: for 5 dropwise of vitamin B6 (1% solution) was added an equal amount of 1% ferric chloride solution and stirred. The liquid is colored in red. Make a conclusion.

Clinical and diagnostic and practical significance. Main coenzyme pyridoxal-5-phosphate is a part of almost all classes of enzymes: oxidoreductases, transferases, hydrolases, lyases and isomerases. Now there are more than 20 pyridoxal enzymes that catalyze key metabolic reactions nitrogenovogo. Pyridoxal-5-phosphate is a coenzyme aminotransferase which carry amino groups of amino acids to α-keto acids, decarboxylases amino acids involved in the formation of biogenic amines, enzymes MAO and DAO which neutralize biogenic amines enzymatic non-oxidative deamination of serine and threonine residues, oxidation of tryptophan to nicotinamide in the synthesis of δ-aminolevulenovoi acid -predecessor of heme glycogenolysis process, etc.

Experiment 3. Identification of vitamin E. The reaction with iron chloride.

Principle of the method: The alcohol solution of α-tocopherol is oxidised by iron chloride (Fe + 3) in tokoferilhinon colored red.

Proceedings: dry tube poured 4-5 drops of 0.1% alcoholic solution of α-tocopherol, is added 0.5 ml of 1% ferric chloride is vigorously stirred. Contents of the tube becomes red. Make a conclusion.

Clinical and diagnostic and practical significance. Vitamin E (tocopherol) is a powerful and essential antioxidant. Its action is aimed at strengthening the tissue respiration and maintain a constant level of free radical peroxidation. Indirectly vitamin E as a cofactor involved in the transport of electrons and protons in the respiratory chain and stimulates the synthesis of ubiquinone. Tocopherol is a "trap" for free radicals - forms with them inactive forms, which terminated a free radical chain. This vitamin E prevents peroxidation of polyunsaturated fatty acids in the composition of cell membranes. Hypovitaminosis membranes accompanied by disorders in the form of peroxide hemolysis of erythrocytes, resorption of the fetus during pregnancy, muscular dystrophy, hepatic necrosis, softening of the brain atrophy simyannikiv that leads to infertility.

Literature

1. Yu.Gubsky Biological chemistry: textbook/edited by Yu.Gubsky. – Vinnytsia: Nova Knyga, 2017 – 488 p.
2. Lehninger Principles of Biochemistry 6th ed - David L. Nelson, Michael M. Cox -W H Freeman and Company – 2013. – 1010 p.
3. Lectures at the Dept.

Tasks for self-control

Task 1. Vitamin deficiency of vitamin A can cause a significant decrease in serum transaminase activity of the blood?
A. PP (nicotinamide)
B. B1 (thiamine)
C. B2 (riboflavin)
D. B6 (pyridoxine)
E. B9 (folic acid)
Task 2. The patient after eating raw eggs appeared dermatitis, characteristic dlya.avitaminoza:
A. biotin
B.Folic acid
C. pantothenic acid
D. PABA
E. inositol
Task 3: Deficiency of what vitamin leads to changes in the blood picture?
A. B12
B. C.
C. P
D. B6
E. PP
Task 4. A pregnant woman who had a history of multiple miscarriages, assigned therapy, which comprises vitamin preparations. Promotes nurturing pregnancy vitamin:
A. rutin
B. Folic Acid
C. cyanocobalaminum
D. pyridoxal phosphate
E. alpha-tocopherol
Correctness check solutions, comparing them with the standards of the responses. Standards of answers to the solution of tasks for self-examination and self-baseline: Objective 1 - D, Task 2 -A, Task 3 - A. Task 4 - E,
Task 5. Fill in the table

The name of vitamin	The structure of the biologically active form	Example enzymatic reactions involving coenzyme forms of vitamin

Topic 7. The control of mastering content modules 5,6.

Theoretical questions

1. Amino acids: classification, structure, properties (essential and nonessential; hydrophobic and hydrophilic, charged, uncharged).
2. The role of proteins in the organism. The biological value and the daily requirement of dietary protein.
3. The levels of the structural organization of the protein molecule (primary, secondary, tertiary, quaternary, domain), types of chemical bonds in protein molecules.
4. Digestion of proteins and amino acid absorption in the gut. Role of hydrochloric acid in the digestion of proteins in the stomach. Mechanisms of activation of the inactive form of the proteolytic enzymes of the digestive tract.
5. Pharmaceutical drugs for the correction of protein digestion's disorders in the digestive tract.
6. Ways of formation and retention of the pool of free amino acids in the body. Common amino path conversion in the tissues.
7. Transamination of amino acids: mechanism of action of aminotransferases, biological significance.
8. Deamination of amino acids. The mechanism of indirect deamination. The biological role of glutamate in the liver and brain neurons.

9. Alpha-amino acid decarboxylation. The function of biogenic amines in the body. Neutralization of biogenic amines. Antihistamine drugs.
10. The ways of conversion of amino acid (without nitrogen) residues. Glucogenic and ketogenic amino acids.
11. Ways of formation and neutralization of ammonia in the body. The mechanism of formation of urea (ornithine cycle).
12. The exchange of individual amino acids: phenylalanine, tyrosine, tryptophan, glycine, methionine. Synthesis and biological significance of creatine and phosphocreatine. The role of CK (CPK).
13. The pathology of amino acid metabolism and drug correction. Amino acids like pharmaceutical drugs.
14. Clinical and diagnostic value of the study of liver enzymes aspartate aminotransferase and plasma.
15. The nitrogen balance. Types of nitrogen balance. Clinical and diagnostic value of a study of residual nitrogen and urea in serum.
16. Nucleoproteins: characteristics and functions in the body.
17. Mononucleoside triphosphate cyclic mononucleotides: the structure and their function in the cell. The use of derivatives of nucleosides and nucleotides as medicaments.
18. Conversion of nucleoproteins in the gut and tissues.
19. Exchange of purine nucleotides, its violation and correction with drugs.
20. Exchange of pyrimidine nucleotides, and its violation.
21. Replication, it's mechanism and biological significance. Tooling DNA.
22. General concepts of mutation and mutagens. Genetic engineering in pharmacy.
23. Arrangement, its mechanism and significance. Post-transcriptional modification of the primary transcript.
24. The concept of the genetic code and its properties.
25. Ribosomal protein-synthesizing system components and their functions. Translation: its mechanism of protein synthesis sequence of steps, the biological significance of the process.
26. The post-translational modification of polypeptide chains.
27. Pharmaceutical - synthesis regulators nucleic acids and proteins. Mechanisms of action of drugs and toxins on a protein biosynthesis: antibiotics, interferon, antitumor drugs, diphtheria toxin and amanitin.
28. Clinical and diagnostic value of a study of uric acid in blood plasma and urine.
29. Components of the endocrine system. The concept of APUD system, APUD cell. Types of communication between cells.
30. Hormones and hormone-like substances. Classification of hormones.
31. The principles of the forward and reverse links in the mechanism of regulation of biosynthesis and secretion of hormones.
32. Understanding of the mechanisms of regulatory action of hormones on the cell.
33. Role of G-proteins and second messenger in signal transmission hormone into the cell.
34. Hormone-sensitive protein kinase: classification, mechanism of stimulation and functions in the cell.
35. Hormones of the hypothalamus: the chemical nature and the biological effect.
36. The pituitary hormones (front and rear): the chemical nature and the biological effect.
37. Thyroid hormones (iodotironiny): effects on metabolism, dysfunction of the thyroid.
38. Hormones calcitriol, calcitonin in the regulation of phosphate-calcium metabolism.
39. Hormones of the pancreas (insulin, glucagon): mechanisms of effects on the metabolism. Insulin-dependent diabetes mellitus: changes in metabolism and drug correction.
40. Hormones of the adrenal medulla (epinephrine, norepinephrine): chemical nature, effect on metabolism, pharmaceutical drugs.
41. The hormones of the adrenal cortex (glucocorticoids): secretion conditions, effect on metabolism. Pharmaceutical formulations of corticosteroids and their use in medical practice.
42. Mediators and hormones of the immune system: interleukins; interferons; protein-peptide regulation of growth factors and cell proliferation.
43. Aldosterone, renin-angiotensin system, and natriuretic peptide in the control of mineral metabolism person.
44. Eicosanoids (arachidonic acid derivatives) as tissue hormones: effects on person's metabolism. Pharmaceuticals - derived eicosanoids.
45. Sex hormones (estrogens and androgens): control of secretion, the effect on the metabolism. The use of structural analogs of hormones as pharmaceuticals.
46. The general idea about the vitamins, their classification and physico-chemical properties.

47. Features of the suction-soluble and water-soluble vitamins in the gut.
48. Pathological states: hypo-, hyper- and deficiency diseases, the causes in the human body.
49. Retinol, calciferol, naphthoquinones, tocopherols: chemical structure of their role in the metabolism and disorders in vitamin deficiency, medical use as pharmaceuticals.
50. Thiamine, riboflavin, pyridoxine, cyanocobalamin, biotin, bioflavonoids, ascorbic, folic, pantothenic acid: chemical structure of their role in the metabolism and vitamin deficiency disorders in, practical use as pharmaceuticals.
51. The vitamin-like substance - unsaturated higher fatty acids, inositol, pangamic, lipoic acid, and orotic choline metilmetioninsulfony, ubiquinone: their chemical structure, biological role, metabolic disorders at the failure of practical use as pharmaceuticals.
52. Antivitamines: mechanisms of action, their use as pharmaceutical drugs.

Situational tasks

1. Female 43 years - an employee paint companies - complains of general weakness, weight loss, lethargy, drowsiness. Chronic lead intoxication confirmed by laboratory - revealed hypochromic anemia. In the blood - increased levels of protoporphyrin and reduced levels of delta-aminolevulinic acid. The synthesis of substance is violated, what substance is shown?
2. Derivative pterins - aminopterin and methotrexate - is a competitive inhibitor of dihydrofolate reductase, causing them to inhibit the regeneration of tetrahydrofolic acid dihydrofolate. These drugs lead to inhibition of one-carbon groups intermolecular transport.Biosynthesis of what nucleotide is suppressed while?
3. A man is 58 years old, underwent surgery for prostate cancer. After 3 months, he had a course of radiotherapy and chemotherapy. The range of drugs included 5-ftordezoksiuridin - an inhibitor of thymidylate synthase. The synthesis of what substance is primarily locked by the action of the drug?
4. A man 46 years old went to a doctor with complaints of pain in small joints, which is exacerbated by the use of animal food. The patient was diagnosed with urolithiasis accumulation of uric acid. Allopurinol assigned to the patient, which is a competitive inhibitor of the enzyme xanthine oxidase. What's allopurinol property provides therapeutic effect in this case.
5. Orotatsidury hereditary orotic acid selection is many times higher than normal. The synthesis of some substances will be broken in this pathology?
6. The antibiotic rifampicin, which is used to treat tuberculosis, affects certain biochemical processes. Write them.
7. To treat urogenital infections using quinolones - inhibitors of DNA - gyrase enzyme. What process is broken under the action of quinolones in the first place?
8. Two year-old child was brought to the hospital. After the meal, he often vomiting. The child lags behind in weight, physical and mental development. Dark hair, but there is a gray strand. The urine sample after the addition of FeCl3 acquired a green color. Results of quantitative analysis of urine following: phenylalanine content - 7 mmol / l at a rate of 0.01; phenylpyruvate content - 4.8 mmol / l at a rate of 0; fenillaktate content - 10.3 mmol / l at a rate of 0. The Violation of metabolic findings it's indicate? What can you recommend for the normalization of metabolism in relation to nutritional therapy in this case?
9. The patient urine has a peculiar odor of maple syrup. What biochemical defect is the cause of this disease?
10. In the blood of the patient at the age of 50 years have seen a high level of serotonin in the urine - a sharp increase in 5-oksiindolilatsetatnoy acid. Violation of any amino acid metabolism can cause such changes?
11. The patient is in a state of hypoglycemic coma. An overdose of which hormone can lead to such a situation?
12. A person is in a stressful situation. As this condition will affect on the function of the endocrine glands?
13. Inhibition of lipolysis in adipocytes of adipose tissue is caused by decrease in cAMP concentration that is required to activate the triglyceride. Indication of which hormones reduce the rate of lipolysis in adipose tissue?
14. The lifetime of most hormones in the blood is relatively small. Thus, if the animal has the radiolabeled insulin, the half of the hormone administered will be inactivated in the blood for 30 min. As constant level of hormone in the blood can be maintained under normal conditions, given its rapid inactivation?
15. Rheumatic patients assigned prednisolone. The anti-inflammatory action of this drug due to inhibition of the release of arachidonic acid. What is the previous substance of prednisolone?

16. Aspirin has anti-inflammatory effect, because inhibits cyclooxygenase. The level of which active compounds will then decline?
17. In pregnant women, there is a need for increased amounts of cholecalciferol, one of whose metabolites is a potent synergist PTH. This hormone stimulates bone resorption and release of calcium and phosphate in blood. What is its metabolite synergist?
18. On examination, the patient's 32 years have seen disproportionate growth of the skeleton, increase brow, nose, lips, tongue, jaw bones, stop. The function of which endocrine gland is broken?
19. A patient appealed for a hospital with complaining of constant thirst, general weakness, blood detected hyperglycemia (16mmol / L), polyuria, and increased content of the 17-keto steroids in urine. What disease is characterized by such indicators?
20. In a patient with Cushing's syndrome is a steady hyperglycemia and glycosuria. Synthesis and secretion of what hormone is increased in this case?
21. The patient women with low blood pressure after parenteral administration of the hormone increased blood pressure and blood glucose and lipid levels. Which hormone has been introduced?
21. The patient women with low blood pressure after parenteral administration of the hormone increased blood pressure and blood glucose and lipid levels. Which hormone has been introduced?
22. When thyrotoxicosis increased production of thyroid hormones T3 and T4, developed weight loss, tachycardia, psychic anxiety and so on. What is the effect of thyroid hormones on energy metabolism in the mitochondria of cells?
23. The doctor has appointed aspirin rheumatic patients as the anti-inflammatory agent. The synthesis of which substances are associated with inflammation, blocking the aspirin?
24. On examination, the 10-year-old child found a small increase, the disproportionate development of the body, poor mental development. Deficiency of which hormone in the body has caused these changes?
25. Patient after eating raw eggs dermatitis appeared. Vitamin deficiency of which vitamin has been developed in the patient’s organism?
26. Name the vitamin, coenzyme form of which is involved in the conversion of dUMP to dTMP.
27. A girl 10 years is often sick with acute respiratory infections, after which there are numerous petechial hemorrhages in places clothing friction. Hypovitaminosis of which vitamin occurs in girls?
28. The patient complained of general weakness and bleeding from the gums. Deficiency of which vitamin can be assumed?
29. The patient has bleeding of internal organs and mucous membrane detected proline and lysine composed of collagen fibers. Due to the lack of which vitamin will violated their hydroxylation?
30. The patient has identified lack of hydroxyproline and hydroxylysine in the composition of the collagen fibers. Due to the lack of which vitamin will violated the patient's body processes of the hydroxylation of these amino acids?
31. The patient scurvy infringements hydroxylation of proline and lysine in the composition of collagen. Braking of what biochemical process is leading to the violation?
32. Patient after ectomy gallbladder suppressed processes of absorption of Ca 2+ through the intestinal wall. Appointment of what vitamin will stimulate this process?
33. A patient suffering from thromboembolic disease, artificial appointed anticoagulant - pelentan. The antagonist of what vitamin is it?
34. The patient is observed day-blindness (night blindness). Which of the following substances will have a therapeutic effect?
35. The child at the next examination revealed the termination of bone mineralization. Lack of vitamin may cause this?
36. Treatment of a child suffering from rickets, has not given a positive result. What is the most likely cause of treatment failure?

Literature

1. Yu.Gubsky Biological chemistry: textbook/edited by Yu.Gubsky. – Vinnytsia: Nova Knyga, 2017 – 488 p.
2. Lehninger Principles of Biochemistry 6th ed - David L. Nelson, Michael M. Cox -W H Freeman and Company – 2013. – 1010 p.
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Topic 8. Blood biochemistry. Metabolism of hemoglobin and it’s violations. Regulation of organism hemostasis. *Qualitative reaction of hemyn group of hemoglobin.*

The purpose of the activity:

- to learn chemical composition, physic-chemicals properties and functions of blood;
- to learn the mechanisms of support of major blood parameters;
- to learn the biochemical principles of coagulative, anticoagulative and fibrinolytic systems;
- to take the method of determining of hemyn group of hemoglobin with benzidine reaction.

Theoretical questions

1. Chemical composition and physic-chemical properties of the blood of a healthy person. Residual nitrogen levels. Types of azotemia.
2. Hemoglobin: structure, types, biosynthesis, pathology synthesis.
3. The main group of plasma proteins; their composition and content in normal and pathological conditions.
4. Plasma Enzymes: own (secretory) and excretory Indicator (tissue) enzymes.
5. Buffer systems of blood, their types, functions of hydrocarbonate, phosphate, hemoglobin and protein buffer systems in the body.
6. Blood coagulation system:

• clotting factors;
• mechanism of activation of blood coagulation;
• operation of the cascade of blood coagulation in the coagulation system and its features;
• internal way of coagulation;
• appearance by coagulation;
• The role of vitamin K in reactions of the coagulation cascade (carboxylation of glutamic acid in -karboksyhlutamin acid role in the binding of calcium).

7. Anticoagulative blood system:

• anticoagulants: antithrombin, 1-proteinase inhibitor, 2-macroglobulin, heparin, coumarin, prostacyclin citrate;
• mechanism of action of anticoagulants.

8. Fibrinolytic system of blood. Stages of fibrinolysis:

• Stage 1 - convert plasminogen to plasmin;
• Stage 2 - splitting fibrin.

9. The components of blood as pharmaceutical drugs.

Practical work

Experiment 1. Determining of hemyn group of hemoglobin with benzidine reaction.

The principle of method. For determining of hemyn group we use benzydyn test, which is based on catalytic properties of oxyhemoglobin and karboksyhemohlobyna. The product of oxidation of benzidine has blue color, which can gradually turns into red. The test is very sensitive.

The process. The tube is made of dilute 5 drops of blood solution were added 5 drops of benzidine and 2-3 drops of hydrogen peroxide. Watch for changes in color.

Clinical and diagnostic value. The concentration of hemoglobin in the blood of women of 120-140 g / l, at men- 130-140g / l. Reducing the concentration of hemoglobin is the main laboratory symptoms of anemia. Reducing the level of hemoglobin in blood depends on the form of anemia.

Literature

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2. Lehninger Principles of Biochemistry 6th ed - David L. Nelson, Michael M. Cox -W H Freeman and Company – 2013. – 1010 p.
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Tasks for self-control

Task 1. In diabetes as a result of the activation of fatty acid oxidation occurs ketosis. Which violations of the acid-alkaline balance can result in excessive
the accumulation of ketone bodies in the blood?

A. Metabolic acidosis
B. Metabolic alkalosis
C. Changes do not occur
D. Respiratory acidosis
E. Respiratory alkalosis

Task 2. The patient rapidly developing edema. Reducing any serum proteins leads to their emergence?
A. fibrinogen
B. Alpha-1-globulin
C. alpha-2-globulin
D. beta globulins
E. albumin
Task 3. Patient 27 years revealed pathological changes in the liver and brain. In blood plasma, a sharp decline in the urine and increase copper content. Diagnosed -Diseases Wilson. The activity of the enzyme in the serum should be investigated to confirm the diagnosis?
A. alcohol
B. carbonic anhydrase
C. xanthine oxidase
D. leucine aminopeptidase
E. ceruloplasmin
Task 4. Prolonged effect of some antibiotics and sulfonamides due to the fact that they circulate in the blood for a long time, in combination with:
A. haptoglobin
B. transferrin
C. hemoglobin
D. albumin
E. hemopexin
Correctness check solutions, comparing them with the standards of the responses. Standards of answers to the solution of tasks for self-examination and self-baseline: Objective 1 - A, Task 2 - E, Task 3 - EN Task 4 - the D.
Task 5. Fill in the table:

Nitrogen – free organic and inorganic compounds in blood	It's metabolic origin	Clinical – diagnostic value and it's determining
Carbohydrates - -		
Lipids - -		
Organic acids - -		
Vitamines - -		
Hormones - -		
Inorganic compounds - -		

Topic 9. Biochemical liver function. The role of the liver in the biotransformation of xenobiotics and endogenous toxins. *Quantitative determination of total bilirubin in the blood.*

The purpose of the activity:

- learn basic biochemical functions of the liver in the metabolism of carbohydrates, lipids, simple and complex proteins;
- znatybiohimichni mechanisms detoxification function of the liver;
- master the method of determination of bilirubin in the blood serum, to be able to interpret the results of determination of bilirubin in serum.

Teoretical question

1. The role of the liver in the metabolism of carbohydrates (glycogen synthesis and degradation, gluconeogenesis, etc.).

2. The role of the liver in lipid metabolism (synthesis and degradation of fatty acids, acetone bodies metabolism and cholesterol).
3. The role of the liver in the metabolism of proteins and amino acids, ammonia detoxification.
4. Liver function of bile producing. The biochemical composition of bile.
5. Pigment liver function. Pathobiochemistry jaundice, hemolytic, parenchymal (liver), obstructive. Enzymatic jaundice.
6. Detoxification function of the liver:
• microsomal oxidation reaction (catalytic cycle operation cytochrome P-450, genetic polymorphism of cytochrome P-450).
• Conjugation reactions in hepatocytes (glucuronidation reactions involving UDP-glucuronic acid reactions involving sulfatuvannya 3-fosfoadenozyn-5-fosfosulfatu; methylation reactions involving S-adenozylmetioninu; acetylation reaction involving acetyl-S-CoA, reaction glycine conjugation.).
7. The origin and nature of the development of tolerance to medicines

Practical work

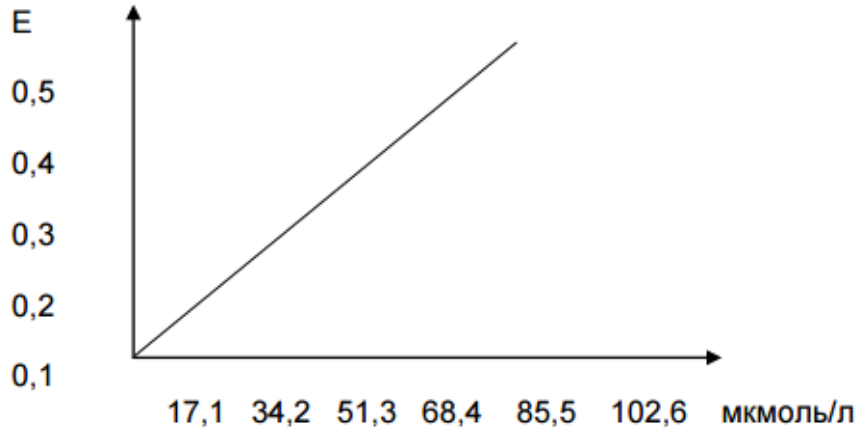
Experiment 1. Quantitative determination of the total, direct and indirect bilirubin in blood serum (the method of Iyendrasheka)

The principle of the method: diazoreagent gives direct (bound) bilirubin pink color. The intensity of the color (azobilirubin) is proportional to the concentration of direct bilirubin and can be determined photometrically. Indirect (free) bilirubin can be translated into a soluble state by adding to the reagent serum caffeine, which increases the solubility of the pigment and determined by diazo - reaction. The total content of both forms of bilirubin is total bilirubin. The difference between the number of total and direct bilirubin determining the level of indirect bilirubin.

The process: serum diluted 1: 1 solution of 0.9% NaCl. Test tubes filled under the table.

The number of the test - tube	1	2	3
Reagent	Total bilirubin	Direct bilirubin	Control
Serum, ml	0,5	0,5	-
Caffeine reagent, ml	1,75	-	1,75
NaCl, 0,9%, мл	-	1,75	0,5
Diazo – mix, ml	0,25	0,25	0,25

Mix and leave №2 tube for 10 minutes and tube №1 for 20 minutes. Fotometry: the green optical filter (530 nm) in 5 mm cuvette to control. Find content direct and total bilirubin calibration schedule for the difference .. In total and direct bilirubin content is calculated indirectly.



Clinical and diagnostic meaning: The norm for total bilirubin content in blood serum is 8,5-20,5 mmol / l, indirect - 1,7-17,1 mmol / l, direct - 0.86 - 5.1 mmol / l. The blood of newborn has a higher content of bilirubin (23.1 mmol / L). The accumulation of bilirubin in the blood is above 27,36-34,20 mmol / l leads to delay in its tissues, jaundice. In hemolytic jaundice the liver does not manage to connect a large number of indirect (free) bilirubin that is formed as a result of enhanced haemolysis of red blood cells. As a result, plasma levels observed an increased content of indirect bilirubinu. The liver jaundice occurs hepatitis (viral, toxic), cirrhosis of the liver. Because of the damage to the membranes of hepatocytes direct bilirubin part falls back into the blood. In addition, the reduced ability of the liver to neutralize indirect bilirubin. As a result, at liver jaundice observed varying degrees bilirubinemia both by fractions direct and indirect bilirubin. During obstructive jaundice due to obstruction (stones, tumors) of bile - ways duct bile overwhelms them and into the bloodstream. Therefore, it is pronounced hyperbilirubinemia (up to 170-700 mmol / l) mainly due to the direct bilirubin fraction/

Literature

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Tasks for self-control

Task 1.We know that when endogenous intoxication that accompanies hyperthyroidism, purulent inflammatory diseases, burns, etc. threat of drug lesions body. By what process is it possible?

A. The inhibition of mitochondrial oxidation
B. increased activity of microsomal oxidation
S. inhibition of peroxidation
D. increased activity peroxidation
E. inhibition of microsomal oxidation

Task 2 For the treatment of jaundice shown in the appointment of barbiturates, which induce synthesis UDP-glucuronosyltransferase. The therapeutic effect with due form:

A. protoporphyrin
B. indirect (unconjugated) bilirubin
C. Biliverdyn
D. Direct (conjugated) bilirubin
E. Gem

Task 3 The patient after blood transfusion observed yellow color of the skin and mucous membranes in the blood - increased levels of total bilirubin by indirect bilirubin in urine - high content urobilin and in feces - increased content stercobilin. What type of jaundice in the patient?

A. obstructive
B. Hemolytic
C. parenchymal
D. Jaundice newborns
E. Hereditary

Task 4. The dry cleaning worker found fatty liver. Violations by synthesis substances in the liver can lead to this pathology?

A. Phosphotydylholin
B. Threestearyn
C. Urea
D. Phosphatydic acid
E. cholic acid

Correct decision check by comparing them with standard answers.

Standards of answers to the challenges for self and self-control output level: Task 1 - E, Task 2 - D, Task 3 - B. Task 4 - A,

Task 5. Fill in the table:

jaundice type	Indicators				
	blood bilirubin		urine		feces
	direct	indirect	bilirubin	urobilin	stercobilin
hemolytic					
parenchymal					
posthepatic					

Topic 10. Biochemistry of the kidneys. Normal and pathological components of urine. The regulation of water and mineral metabolism. *Physico-chemical properties of urine.*

The purpose of the activity:

• learn the basic biochemical functions of the kidneys and the mechanisms of their regulation

• know the physical and chemical properties, basic biochemical indicators of normal and pathological urine components and ways of their penetration into the urine.

• master the methods of analysis of physical-chemical properties of the urine, and be able to interpret results

Theoretical questions

1. Features of metabolism in the kidneys
2. Biochemical mechanisms of urine synthesis
3. Physical and chemical properties of urine: urine volume, pH, clarity, odor, relative density.
4. Organic normal urine components: urea, uric acid, creatinine, amino acids, pigments, lactate, pyruvate.
5. Pathological components of urine: glucose, protein, ketone bodies, bilirubin, creatinine, hemoglobin.
6. The influence of drugs on renal function and physico-chemical properties of urine
7. Renin-angiotensin in the regulation of blood pressure, salt and water metabolism in humans.

Practical work

Experiment 1 Analysis of physico-chemical properties of urine.

A. Definition of the daily volume of urine (diuresis).

Progress. The daily amount of urine is measured using a graduated cylinder of 1 or 2 liters.

Clinical and diagnostic and practical significance. Normally, the daily urine volume averaged 1500 mL in men and 1200 mL in women. Urine volume more than 2200 mL and less than 500 mL per day indicates pathology. The amount of urine can be reduced (oliguria), increased (polyuria) and possibly complete cessation of discharge of urine (anuria).

B. Determination of the relative density of urine.

Progress. The small cylinder with a diameter that urometr freely floating in it, is poured into the wall (to prevent the formation of foam, but if it is still formed, it put off with filter paper), research urine and dipped gently it urometr graduated 1,00 to 1,030 g / l. Carry count, given that line urometra on the scale which corresponds to the lower meniscus of the liquid. In the case of high relative density of urine for the research taking second type urometra (from 1,030 to 1,060). All determinations were carried out usually at a temperature of 15 ° C, as urometr calibrated in accordance with this temperature.

If the urine has a different temperature and bring it up to 15 ° C is not possible, then for every 3 ° C above this temperature must be added, and for each 3 ° C below, subtract 0,001 urometra index scale.

Clinical and diagnostic and practical significance. Relative density depends on the amount of soluble substances in the urine, and is closely related to the amount of urine. Normally it (measured at 15 ° C) ranges from 1,010-1,025, but is generally 1,017-1,020. Inconsistency of the relative density and the amount of urine is observed in diabetes, when the relative density it is still high, despite the large amount of urine.

Relative density varies in various pathological conditions. The sharp decline is observed for her diabetes insipidus. Determination of the relative density of urine is performed using special small hydrometer called urometr.

C. Characteristics of the color of urine.

Progress. The color of urine is assessed visually.

Clinical and diagnostic and practical significance. Normally, it is straw-yellow and is caused by the presence of pigments: urochrome (dark yellow), urobilin (pale pink), uroeritrinu (red). Eating certain foods (in particular sugar beet) and the reception of various drugs (amidopirina, antipyrine) provide urine pink-red color.

If urine are blood pigments, it is colored in pink or brown color in the presence of bile pigments - in the green or yellow-brown color in the presence of pus, urine neopalestsiruyuschy, black color is observed at homogentisuria and depends on the presence of dark pigments (such melanins) in alkaline urine, which are products of transformation homogentisic acid. Green-blue color observed in bacterial contamination of urine with excess content in it indican, which turns into blue indigo.

D. Evaluation of urine transparency.

Progress. Transparency of the urine determined in the glass of a colorless glass after shaking.

Clinical and diagnostic and practical significance. Normally, urine is clear. When standing deposited loose mucous mass, which consists of a deflated epithelium of the urinary tract and mucous cells. Blood, pus, protein cause the appearance of turbidity, indicating that the pathological processes in the kidneys and urinary tract.

E. Determination of the smell of urine.

Clinical and diagnostic and practical significance. Normally, fresh urine has a peculiar smell of volatile substances it contains. With the decay of urine becomes unpleasant acrid smell of ammonia in the decay of the cells in the urinary tract urine becomes putrid odor, in the presence of a large amount

of acetone body-fruit scent (diabetes). Strong-smelling food substances or drugs can have a urine smell peculiar to them.

F. Determination of acidity (pH) of urine.

Progress. A strip of the universal indicator paper is dipped into test urine, removed it and determine the pH value on the color scale. By a change in color of colored strips coincides with the test strip color, determine the pH of urine

Clinical and diagnostic and practical significance. Normally, urine pH ranges from 5.0 to 7.0. The shift to the acid side there is the allocation of acetone bodies (diabetes, fasting) or severe renal insufficiency. Urine pH shift toward the alkaline environment is marked with the consumption of food bicarbonates, alkaline mineral water, dairy products and plant them, inflammation of the bladder mucosa after prolonged emesis.

Literature

1. Yu.Gubsky Biological chemistry: textbook/edited by Yu.Gubsky. – Vinnytsia: Nova Knyga, 2017 – 488 p.
2. Lehninger Principles of Biochemistry 6th ed - David L. Nelson, Michael M. Cox -W H Freeman and Company – 2013. – 1010 p.
3. Lectures at the Dept.

Tasks for self-control

Task 1. A patient 55 years appealed to the doctor with complaints of frequent seizures. It was found that for a long time he worked in the hot shop at high temperatures and low humidity. Violation of any type of exchange has led to this state?

A. vitamin
B. saline water
C. lipid
D. protein
E. carbohydrate

Task 2. The patient complains 45 irrepressible thirst, consumption of large quantities of liquid (5 liters), the allocation of a significant amount of urine (up to 6 liters per day). Blood glucose concentration of 4.4 mmol / l, the level of ketone bodies are not increased. Urine stained, specific gravity 1.002; sugar in the urine is not determined. Deficiency of what hormone can lead to such changes?

A. vasopressin
B. aldosterone
C. insulin
D. glucagon
E. ACTH

Task 3. After standing in air baby urine is dark due to the presence in it homogentisic acid, that characteristic of the disease:

A. cystinuria
B. homogentisuria
S. tyrosinemia
D. «maple syrup"
E. cystinosis

Task 4. The patient complains of bloating, diarrhea after consuming protein. Doctor
suspected violations of protein digestion in the stomach and strengthen the processes of decay in the gut. Confirm the diagnosis can detect in urine:

A. creatine
B. creatinine
C. animal indican
D. urea
E. alcapton

Correctness check solutions, comparing them with the standards of the responses.

Standards of answers to the solution of tasks for self-examination and self-baseline: Task 1 - B, Task 2 - Task 3 A - B. Task 4 - C

Task 5 Fill in the table

Urine component	Origin	Diagnostic value	
		Increase	Decrease

Topic 11. The control of mastering content modules

Theoretical questions

1. Complex proteins: definition, classification, a brief description of the individual classes.
2. Hemoglobin: Structure, properties and functions in the body.
3. Digestion of hemoglobin in the gut.
4. Types and hemoglobin compound. Abnormal hemoglobin derivatives, the reasons for their formation
5. The catabolism of hemoglobin in the tissues. The formation of bile pigment: intermediate metabolites final products.
6. Bilirubin and its fractions: clinical relevance for the diagnosis of disorders of the liver. Jaundices.
7. Scheme of the biosynthesis of hemoglobin and its regulation factors
8. Hereditary disorders of hemoglobin synthesis. The abnormal form of hemoglobin.
9. The chemical composition and physico-chemical properties of the blood. The blood, plasma, serum.
10. Characteristics of blood biochemical functions. Basic physical and chemical constants of blood, their regulation. The clinical significance of the study of non-protein components of the blood to assess the sharing of human substances.
11. The chemical composition of blood: protein (physiological and pathological), a non-protein nitrogen, residual blood, its clinical significance, organic nitrogen-free blood components, blood electrolyte composition.
12. Overview of the site of synthesis, functions and diagnostic value of major protein - electrophoretic components of blood plasma fractions
13. Blood Enzymes: classification, clinical and diagnostic value of their research.
14. Immunoglobulins; biochemical characteristics of individual classes of human imunoglobulins.
15. The complement system; biochemical components of the complement system of the person; classic and alternative activation pathway.
16. The blood coagulation characteristics of individual factors; mechanisms of blood clotting cascade system functioning. The role of vitamin K in the coagulation reactions; drugs - agonists and antagonists of vitamin K.
17. Anticoagulant blood system, characteristic of anticoagulants. Hereditary disorders of blood coagulation.
18. Fibrinolytic blood system. Drugs that affect the processes of fibrinolysis.
19. The blood as a source of drugs
20. Biochemical liver function carbohydrate, protein synthesis, uriniparous.
21. Biliary liver, regulation of blood lipid composition role in the metabolism of vitamins and minerals, amino acids and nucleic acids.
22. The role of the liver in protein metabolism, hepatoprotectors. Biochemical indicators of protein metabolism.
23. Detoxification function of the liver, types of reactions of biotransformation of xenobiotics and endogenous toxins.
24. Routes of xenobiotics in the body. Transport xenobiotics through cell membranes. Features of their metabolism depending on the structure and administration routes. metabolic phase
25. Reactions of microsomal oxidation. Cytochrome P450; electron-transport chain in the endoplasmic reticulum membranes of hepatocytes.
26. Conjugation reactions in hepatocytes: biochemical mechanisms functional significance
27. The role of the liver in the metabolism of bile pigments. Pathobiochemistry of jaundice; Types of jaundice; hereditary (enzyme) jaundice.
28. Clinical and biochemical indicators of violations of the functional state of the liver.
29. Water and salt exchange in the body. Intracellular and extracellular water; exchange of water, sodium, potassium.
30. The structure and function of the kidneys. Clearance.
31. Role in renal regulation of volume, electrolyte composition and pH of the body fluids. Biochemical mechanisms of uriniparous renal function.
32. Mechanisms of primary and secondary urine impact of pharmaceuticals on these processes.
33. Chemical composition and physico-chemical properties of healthy human urine.
34. Abnormal urine components.
35. Renal renin-angiotensin system. Antihypertensive drugs - angiotensin-converting enzyme.

36. Effect of drugs on the change of physico-chemical properties of urine.

Literature

1. Yu.Gubsky Biological chemistry: textbook/edited by Yu.Gubsky. – Vinnytsia: Nova Knyga, 2017 – 488 p.
2. Lehninger Principles of Biochemistry 6th ed - David L. Nelson, Michael M. Cox -W H Freeman and Company – 2013. – 1010 p.
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MINISTRY OF HEALTH OF UKRAINE
NATIONAL MEDICAL UNIVERSITY

Department of pharmaceutical, biological and toxycological chemistry

"APPROVED"
Head of pharmaceutical, biological and toxicological chemistry Departmnet
PhD in Medicine, Professor _____ I.V.Nizhenkovska
protocol number 2 on August 31, 2017

GUIDELINES
FOR INDEPENDENT STUDENTS WORK
WHILE PREPARING FOR THE PRACTICAL LESSON

Academic discipline	Biological chemistry
module number	module 2
module	**Module 5: Exchange of simple and complex proteins.** Biochemical aspects of molecular biology and genetics.
Subject lesson number 1	Digestion of proteins in the gastrointestinal tract. General ways of amino acids exchange. *Determination of aminotransferases (ALT and AST) in serum.*
Course	3 year
Faculty	Pharmaceutical
Number of hours	2,5

Kyiv 2017

Prepared by Associate Professor PhD O.V. Kuznetsova

1.Topic actuallity

Food proteins for humans is a source of essential amino acids, lack of income of which leads to violations not only of protein metabolism, and metabolic and other substances. The daily adult requirement of protein is 80-100 g protein metabolism important step is the process of digestion in the stomach and small intestine involving proteolytic enzymes. Violation activity gastric, pancreatic and intestinal peptidases proteins causing indigestion, accompanied by activation of putrefaction in the colon. In this form toxic products that require disposal.

The proteins in the body are in a dynamic state, constantly updated and destroyed. The dynamic state of protein metabolism in the body show the balans. Dynamic balance of protein metabolism provides a pool of amino acids - all free amino acids in the body (300-500h). Amino acids used for the synthesis of proteins, neurotransmitters, hormones and other biologically active substances. During the intermediate exchange amino acids may lose its carboxyl group (decarboxylation) and amino group (deamination and trans). In reactions decarboxylation of amino acids formed mainly biogenic amines. Transamination provides reversible conversion of amino acids in α-ketoacids and is replaceable by synthesis of amino acids. Coenzyme both processes are active form of pyridoxine - piridoksalfosfat.

Knowledge and understanding of the common ways to change the amino acids and their metabolites and determine the activity of enzymes involved in these transformations are the criteria for the evaluation of protein metabolism. During the exchange of amino acid metabolites are formed, as defined in the blood and urine can be used to apply pharmaceuticals.

2.Specific objectives:

- To know the concept of nitrogen balance and its role to assess the dynamic state of proteins;
- Explain biochemical mechanism of protein digestion in the digestive canal;
- Knowing the causes and mechanism of protein putrefaction in the colon, the role of cathepsin updating tissue proteins.
- analyze ways to use free amino acids in the body.
- interpret the processes of transamination, deamination, decarboxylation of amino acids.
- determine serum aminotransferase activity and interpret the results

3. Basic knowledge, skills necessary for studying the subject (interdisciplinary integration)

The names of previous disciplines	Experience
Physical methods of analysis and metrology	To master the techniques of laboratory research tools
Biology with genetics	To classify the structure of biopolymers.
Organic chemistry	1. Identify the types of chemical reactions 2. Describe the chemical reaction of 3.Pysaty structural formula of amino acids
Physiology	To explain the mechanism of protein digestion and absorption of amino acids
Pathological physiology	To explain the basic mechanisms of metabolism of proteins in the body

4.Tasks for independent work during preparation for the classes.

4.1. The list of key terms, parameters, characteristics which the student is to assimilate while preparing for classes

Term	Definition
Nitrogen balance	Nitrogen balance - the difference between the amount of nitrogen that enters the body, and the amount of nitrogen excreted.
Biogenic amines	Biogenic amines - products decarboxylation of amino acids that have a high biological activity.
Indirect deamination	Indirect deamination – deamination linkes with transamination.

Transamination	Transamination (transamination) - α amino transfer reaction of amino acids in α carbon atom α ketoacids - acceptor amino groups (mostly - α ketohlutarat).

4.2 Theoretical questions for the class.

1. The concept of nitrogen balance and causes of failures.
2. Digestion of proteins and peptides in the stomach and small intestine, the mechanism of action of proteolytic enzymes.
3. The mechanism of oxidative deamination of glutamic acid. Value and regulation hlutamatdehidrohenaze reaction.
4. The mechanism of transamination reaction. Localization of enzymes in tissues and organs, methods and diagnostic value of determination.
5. The mechanism of indirect deamination of amino acids.
6. Decarboxylation of amino acids, physiological significance. Biogenic amines as pharmaceuticals. Pharmaceuticals - aminooksydaze inhibitors (MAO, DAO).
7. General metabolism of nitrogen-free ways skeleton of amino acids in the body. Glycogenic and ketogenic amino acids.

4.3. Practical work in class.

Experiment 1. Determination of aminotransferases (ALT and AST)

The principle of the method: in a result of amination under aspartate aminotransferase (AST) aspartic acid is converted into oxalic acid, and alanine under alanine aminotransferase (ALT) - in pyruvic acid (PMC). Oxalic acid capable in the enzyme reaction is converted into AML. Adding acid 2,4-dynitrofenilhidrazic (2,4-BPG) enzymatic process stops, and formed dynitrofenilhidrazon pyruvic acid, which in an alkaline medium gives a brownish-red color, whose intensity is proportional to the amount of pyruvic acid formed. Number of educated AML allows to conclude that the activity of the enzyme. Aminotransferase activity expressed in micromoles of pyruvic acid formed by 1 ml serum for 1 h incubation at 370S.

1.1. Determination of alanine aminotransferase

Progress: The work is performed in accordance with the table.

Reagent	Research sample, ml	Control sample, ml
Substrate mix (alanin and alpha-ketoglutarate)	0,5	0,5
In the thermostat for 5 minutes at 37^0C		
Blood serum	0,1	-
H_2O (distilate)	-	0,1
In the thermostat for 30 minutes at 37^0C		
0,1% solution 2,4-DPG	0,5	0,5
In the thermostat for 20 minutes at 25^0C		
0,4n NaOH	5	5
Note. Thoroughly mix; 10 min at 250 (to form color). Optical density measured on FEKu at λ = 500-560 nm (green filter versus control cuvettes with a layer thickness of 10 mm) compared with the control sample		

Calculation of ALT activity in serum by conducting calibration graph showing the dependence of the optical density of pyruvic acid content.

Construction of calibration graph:

Preparation of the calibration solution: 11 mg sodium pyruvate dissolved in a little water, transfer to a volumetric flask of 100 ml of water and bring to a label: 1 ml calibration solution contains 110 mg of sodium pyruvate, corresponding to 88 mg or 1 mmol pyruvic acid.

With calibration solution prepared dilution series (see. Table.). Calibration tests carried out as well as research, but instead add sera diluted calibration solutions. Measured against the idle test, which instead calibration solutions add water. After determining the optical density build calibration graph plotting on axle abscissa enzyme activity, and the axis of ordinate - absorbance values. Linear calibration curve to the value of the optical density of 0.3.

Getting calibration solutions

№ of sample	Calibration solution of sodium pyruvate, ml	Distilled water, ml	pyruvic acid		The activity of AlAT, nmol
			mkg	mkmol	

1	0,05	0,55	4,4	0,05	278
2	0,10	0,50	8,8	0,10	556
3	0,15	0,45	13,2	0,15	834
4	0,20	0,40	17,6	0,20	1112

Number of formation of pyruvic acid (mcg) are on the calibration schedule or formula I:

$$X = \frac{Д}{0,09} \quad (I),$$

The activity of ALT count with formula II:

$$\boxed{\text{ALT}} \quad \frac{X \times 2 \times 10}{88} \quad (II),$$

where: X - The amount of pyruvic acid, found by calibration schedule or formula I mg; 2 – conversion factor for 1 h incubation;
10 – Conversion rate 1 ml serum;
88 – 1 mmol weight of pyruvic acid.

Serum ALT healthy activity determined by this method varies from 5-30. / Ml (0,1-0,7 m / ml). Conclude.

1.2 Determination of aspartate aminotransferase

Progress: The work is performed in accordance with the table.

Reagent	Research sample, ml	Control sample, ml
Substrate mix (alanin and alpha-ketoglutarate)	0,5	0,5
In the thermostat for 5 minutes at 37^0C		
Blood serum	0,1	-
H_2O (distilate)	-	0,1
In the thermostat for 30 minutes at 37^0C		
0,1% solution 2,4-DPG	0,5	0,5
In the thermostat for 20 minutes at 25^0C		
0,4n NaOH	5	5
Note. Thoroughly mix; 10 min at 250 (to form color). Optical density measured on FEKu at λ = 500-560 nm (green filter versus control cuvettes with a layer thickness of 10 mm) compared with the control sample		

The enzyme activity is calculated by the formula
X = E? 133 U / ml,
where - X - enzyme activity;
E - extinction;
133 - conversion factor.
1 mg AHC - 0,015 units. IS; 1 unit. E - 133 mg PVK, or calibration schedule. The activity is expressed in arbitrary units per 1 ml of serum. 1 unit. AST meets this enzyme activity that is able to form under these conditions 1 mg of pyruvic acid. In calculating enzyme activity must take into account dilution of serum:

$$X = a \cdot 10,$$

where X - a unit of the enzyme;
10 - UAH 1 ml;
and - the number of PMC determined calibration schedule, pg.
In healthy people serum AST activity determined by this method ranges from 5 to 40 units. / Ml (0.1 - 0.5 m / ml). Translation micromolar enzyme activity in AML, which formed during the incubation 1 ml serum for 1 hour at 370S, spend the formula

$$AST = \frac{a \cdot 10}{88}$$

where a- number PMC determined calibration schedule micrograms;
88 - weight of 1 mmol PMC mg;
10 - Conversion rate 1 ml serum;

Clinical and diagnostic value:

Laboratory standards: for AST: 0.1 0.5 mkM AHC 1 ml serum for 1 hour incubation for ALT: 0,1-0,7 mM AHC 1 ml serum for 1 hour incubation. Normally, serum AST activity is 0.1 - 0.45 mm / h · ml; ALT - 0.1 - 0.68 mm / h · ml. Diagnostic important simultaneous determination of ALT and AST activity and where Ritisa Calculation - AST / ALT, which normally is about 1.3. When infectious hepatitis is lower standards, myocardial infarction - the highest standards.

AST and ALT are the most sensitive indicators of damage to the liver parenchyma (especially ALT). ALT activity that more than 10 times the upper limit of normal, observed in acute hepatitis (viral and toxic); increase enzyme activity is 5-10 times characteristic of acute (viral, alcoholic, drug) hepatitis exacerbation of chronic active hepatitis and liver tumors. The indicators above normal in 1,5-5 times observed in all of the above diseases, and in the first week of acute obstruction of the common bile duct. AST activity changes like ALT, but with less potential. Determination of aminotransferase activity in serum is important for diagnosis of heart disease. Myocardial infarction AST activity increased 10-100 times compared with the norm. The activity of AST in the blood increases after 4-6 hours. after myocardial infarction and usually returns to normal in 3-7 days. When angina AST is normal. Reducing the normal range of aminotransferase in plasma may be in vitamin B6 deficiency and renal failure. In the initial period of myocardial infarction in 24 - 36 hours it is clearly marked and only 3-7 day normal enzyme activity. Changes ALT while small.

4.4. Content topics

Proteins - it biopolymers, monomers which are α-amino acids linked by a peptide (-CO-NH-) bond. Elemental composition of proteins: C - 50-55% O -21-24%, N -15-17%; (≈ 16%) - nitrogen is labeled protein. (In determining nitrogen content of protein in the test object), H -6-8%, S -0-2%.

Amino acids of proteins and their characteristics. The structure of proteins are 20 so-called "standard amino acids". Their inclusion in the protein molecule encoded by the genetic level. All amino acids, except glycine, contain an asymmetric carbon atom and relate to α- row, they have optical activity. Racemization of amino acids - unauthorized mutual transformation of L - and D - form, which leads to changes in optical activity. This phenomenon is used in forensic medicine to determine a person's age by the number of D - isomer of aspartic acid in dentin, where there is no exchange of proteins. Speed retsemizatsiyi L- aspartate to D-aspartate equal to 0.1% per annum (1% per decade, and 5% for 50 years, etc.)

Of great importance is characteristic of amino acids in R - group. These groups can be either hydrophilic or hydrophobic (nonpolar), which is essential for the structure and functioning of the protein. Proteins that contain large amounts of non-polar amino acids (eg α - keratin hair) insoluble in water, albumin blood contains large amounts of amino acids with polar R - groups and therefore easily soluble in water. In the α-keratin hydrophobic groups on the surface fibrils and to albumin, which is also hydrophobic groups are mostly hidden within the molecule and the surface hydrophilic molecules prevail, that provide high solubility of albumin.

Non-standard amino acids - those that occur after protein synthesis. For example, proline is oxidized to oxyproline.

The value of proteins to the body. In the body there is a constant decay and synthesis of tissue proteins. One day an adult is destroyed and formed about 400 grams of protein. Protein synthesis na70-75% provided endogenous amino acids (ie, amino acids that were formed by the decay of its own proteins), the rest is provided by the exogenous amino acids formed during digestion of food proteins. Among exogenous amino acids are those that are not synthesized in the human body as food proteins is an essential factor in the diet. During prolonged absence of disease proteins occurs "protein deficiency" that occurs in children especially hard, entitled -kvashyorkor.

The most common indicator of protein metabolism is a "nitrogen balance". A positive nitrogen balance - the excess of revenues over its nitrogen excretion, and sometimes in children during growth, pregnant women, after stopping the hunger strike, during recovery and t.d.Nehatyvnyy nitrogen balance occurs when the total or protein deficiency, severe diseases, etc. .d. Nitrous Health typical adult healthy people.

Proteins full and defective. Fully called protein containing all the essential amino acids in sufficient quantities, defective proteins - do not contain all the essential amino acids, or in insufficient quantity. Fully considered animal proteins, as well as legumes and potato, other vegetable proteins

defective. The biological value proteins determined by their digestibility and amino acid composition of proteins matched person. For breast milk proteins is close to 100% for beef - 93%, bread - 30%.

Essential and nonessential amino acids. Essential - those that are not synthesized in the body, their 8 - Valine (VAL), leucine (Leu), isoleucine (ILEY), threonine (TPE), methionine (MET), lysine (Liz), phenylalanine (hair dryer), tryptophan (THREE); conditionally essential (essential for children) - arginine (ARG), and histidine (GIS) - are synthesized in inadequate amounts. Other amino acid replacement. Unlike fat and carbohydrates in the body protein reserves there. Relative reserves are considered blood proteins (albumin), skin, liver and muscles.

The protein content in foods: bread -8-10%; cheese -20-35% peas - 26%; meat - 22%; potatoes -1-2%. Soy protein contains up to 36%, but crude soy protein contains trypsin inhibitors as soybeans are heat treated.

Digestion of proteins

Table 1 number of proteolytic enzymes and their action

№ з/п	ORGAN	Enzyme	The mechanism
1	Glands of gaster	I Pepsinogen	Pepsin hydrolyzes peptide bonds formed by amine groups of aromatic amino acids and leucine and arginine.
		Hastryksyn (II pepsinogen, pepsin C)	Pepsyn enzyme. pH 3.0-3.5 action. Hydrolyze peptide bonds dicarboxylic amino acids.
		Renin (Chymosin, pepsin D)	Zvurdzhuye milk in the presence of Ca2 +. Present in the stomach infants.
		Zhelatynaza (Parapepsyn, pepsin B)	Break down connective tissue proteins. At pH 5.6 inhibited the action of the enzyme.
2	Glands of small intestine	Aminopeptydaze	Catalyzes the cleavage of amino acids of the polypeptide chain of the N-terminus (residues except proline).
		Dypeptydaze	Only cleaves dipeptides.
		Dypeptydaze	Only cleaves tripeptides.
		Enterokinase	Glycoproteins. Activates trypsinogen to trypsin.
3	Pancreas	Trypsinogen	Endopeptydaza. Trypsin hydrolyzes peptide bonds formed by carboxyl groups diaminomonokarbonovyh acids (arginine, lysine).
		Himotrypsynohen	Endopeptydaza. Chymotrypsin hydro lysing peptide bonds formed by carboxyl groups of aromatic amino acids (tyrosine, tryptophan, phenylalanine).
		Proelastaza	Endopeptydaza. Elastase hydrolyze peptide bonds formed by neutral amino acids; most active against elastin.
		A Prokarboksypeptydaza	A carboxypeptidase breaks peptide bonds formed mainly end-aromatic amino acids.
		In Prokarboksypeptydaza	Ekzopeptydaza. Carboxypeptidase B cleaves arginine and lysine from the C-terminus of the polypeptide chain.

The absorption of amino acids. As a result of all of proteolytic enzymes from food proteins produced amino acids, which are absorbed by specific transport systems that use a common transport of Na + ions (secondary active transport) or Na + -independent facilitate diffusion. One of the specific amino acid transport systems that function in the gut, kidneys and brain, called gamma hlutamilnyy cycle. In a series of six enzymes involved, one of which is embedded in the cell membrane, others are in the cytoplasm. Membrane-associated enzyme gamma-glutamyltransferase, is a glycoprotein, catalyzes the transfer of gamma hlutamilnoho remainder of tripeptide glutathione (gamma hlutamiltsisteinilhlitsina) or other gamma hlutamilnoho peptide to amino acid and subsequent transfer of modified amino acids in the cell. After transferring through the membrane gamma hlutamilaminokysloty under the action of the enzyme gamma-gamma hlutamiltsyklotransferazy detached hlutamilnyy balance. Tsisteinilhlitsin dipeptide is hydrolyzed under dypeptydazy to cysteine and glycine. As a result of these three reactions is the transfer of amino acids into the cell. The following three reactions necessary for the regeneration of glutathione to repeatedly cycle could be repeated.

Rotting proteins in the colon. The cause putrefaction of proteins - the activity of microorganisms that break down amino acids in products that are not produced in tissues under normal conditions, ammonia (NH3), methane (CH4), H2S, mercaptans, indole, skatole, cresol, phenol, cadaverine, putrescine. Diamine (putrescine and kadaverin) neutralized diaminoksydazoyu intestine and liver. Neutralization other products decay occurs in the liver by kon`yuhatsiyi. Benzoic acid zv`yazuyetsya with glycine to form hipurovoyi acid. Determination of the number hipurovoyi acid in urine (after the introduction of benzoic acid) to evaluate antitoxic liver function. Decay product of tryptophan from indole kon`yuhuye sulfate and converted into indican (kalieva salt indoksylsirchanoyi acid). In terms indican urine can determine the intensity of decay in the gut. After absorption in the gut amino acids entering the liver and then raznosyatsya throughout the body. Exogenous amino acids and amino acids formed by the decay of their own proteins to form a pool of amino acids. Common uses of amino acids in organs and tissues. Amino acids are used:

1. For the synthesis of proteins own body.
2. For the synthesis of other substances:

a) biologically active substances (epinephrine, histamine and others.)

b) synthesis of heme, purine nucleotides, pyrimidine nucleotides, choline, taurine, etc .;

a) synthesis of the carbon skeleton of essential amino-acids and converted into carbohydrates (hlyukoplastychni amino acids) and lipid.

3. Amino acids can be used as an energy source
4. Tryptophan is used in the synthesis of nicotinic acid (vitamin PP).
5. 1-2% amino unchanged excreted with urine.

Intermediate metabolism of amino acids. This set of reactions of metabolism of amino acids, leading to the formation of the end products of metabolism or the conversion of amino acids to other substances (heme, DNA bases, etc.). The main processes include intermediary metabolism of amino acids, decarboxylation, deamination and transamination.

1. decarboxylation of amino acids - is the cleavage of the carboxyl group of the amino acids in the form of CO2. As a result of decarboxylation of amino acids formed biogenic amines.

Noradrenaline and adrenaline - formed by hydroxylation and subsequent decarboxylation of tyrosine. They constrict blood vessels and raise blood pressure; increase the frequency and strength of contractions of muscles; increase glucose and fatty acids in the blood (reinforcement decay of glycogen in the liver and muscles and fat tissues collapse. Dopamine is a neurotransmitter.

Histamine - narrows the bronchus, causing choking with asthma, peryfiric expands blood vessels and reduces the system pressure (collapse), increases the secretion of gastric juice.

Serotonin - narrowing of the bronchi (sinerhist histamine) but reduces periferichni vessels (histamine antagonist). Acetylation and methylation of serotonin leads to the formation of melatonin - the hormone of the pineal gland, which regulates circadian rhythms and has a hypnotic effect.

gamma-Aminobutyric acid - inhibitory neurotransmitter of the nervous system, formed by the decarboxylation of glutamic acid. To the reaction requires the presence of vitamin B6, so children with deficiency of this vitamin may have seizures due nevrivnovazhennosti of excitation / inhibition.

Inactivation of nutrients deamination of amines is their participation FAD-dependent monoamine oxidase (MAO). If the quantity of dopamine parkinsonism, and depression - norepinephrine levels, so increasing their concentration in the brain using medication reaction inhibitor of MAO. Polyamines synthesis reaction inhibitor is used to inhibit the growth of tumors.

2.Dezaminuvannya amino acids - amino group of a separation of amino acids in form of ammonia. There are 4 types of deamination, oxidative (usually this deamination be glutamic acid); hydrolytic (eg deamination of AMP, glutamine); intramolecular (histidine deamination to urokainovoyi acid); restorative (eg deamination GMP);

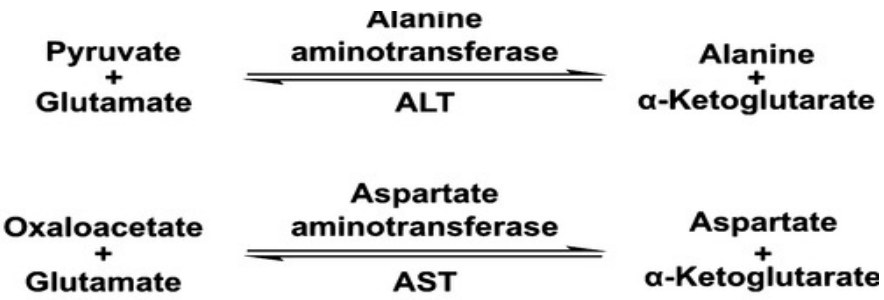
Oxidative deamination of glutamate. This is one of the important ways the formation of ammonia in the body, since glutamic acid is the transport form of ammonia. Deamination takes place in two stages (enzymatic and non-enzymatic). Originally formed α-iminohlutaratza uchastiNAD-zalezhnoyihlutamatdehidrohenazy, and further non-enzymatic hydrolysis leads to utvorennyaα-ketohlutaratui ammonia.

Or transamination transamination. This transfer α-amino group of the amino acids in α-keto acids to form new α-amino and α-ketokyslot.Protses catalyzed by aminotransferases (transaminases) which is used as a coenzyme - piridoksalfosfat (PALF) - a derivative of vitamin B6.

The biological role pereaminirovaniya:

a) synthesis of ammonia forms of transport;

b) the synthesis of essential amino-acids. The most active are alaninaminotransferase (ALT) and aspartate aminotransferase (AST). Pereaminirovaniya is the scheme:



The mechanism: The process takes place in two stages and is reversible. The first phase is transferred to the amino the amino acid aminotransferase coenzyme PALF of utvorennyamα-ketokyslotyta pirydoksaminfosfatu. The second phase is transferred to the amino pirydoksaminfosfatu inshuα-ketokyslotuz formation of new amino acids and release PALF (coenzyme can again participate in catalysis). The amino acid that entered the reaction is converted into vidpovidnuα-ketokyslotu.Naybilsh often as amino acceptor in the body vykorystovuyetsyaα-ketoglutarate, which turns into hlutaminovuyu acid.

The clinical significance of determining aminotransferase activity, in the heart muscle and liver ALT and ACT are very high. When hepatitis or myocardial infarction enzymes destroyed kletyn out of the blood in an amount that is proportional to the degree of lesion of these organs. Diagnostic value ratio has ACT / ALT as myocardial infarction mainly increases the activity of AST, while liver damage - ALT.

The fate of α-keto acids. α-keto acids formed during pereaminirovaniya may be subject

1) decarboxylation (with pyruvate, and α-ketohlutaratdehidrohenazy and other enzymes) with utvorennyamatsetyl-CoA which possible synthesis of ketone bodies or fat (ketohenni amino acids), or the formation of metabolites that can be switched in gluconeogenesis or completely break down into the water and CO2;

2) subject reaminuvannyu and converted to the corresponding amino acids.

5.Materials for self-control.

A. Tasks for self-control.

1. The patient operated on gastric ulcer after some time found a significant reduction in gastric acidity. Indigestion which substances should be expected? How to change the activity of proteolytic enzymes stomach under these conditions? What proteolytic enzymes and stomach optimal conditions for their actions.

2. Patient '45 complaining of general weakness, fatigue. In the analysis of blood found reduced activity of aminotransferases and amino acid decarboxylase. Lack of a substance can cause symptoms in the patient?

3. Blood patient age of 50 years have seen high levels of serotonin in the urine - a sharp increase 5 oksiindolilatsetatnoyi acid. Amino acid metabolism which can cause such changes?

4.

Choose substances produced in the gut with microorganisms in the decay of amino acids: 1. tyrosine 2. tryptophan 3. ornithine 4. lysine	A. putrescine B. cadaverine C. Krezol D. Phenol E. skatole F. indoles

	G. Indican H. quinones

5. With food the body has received 80 grams of complete protein. Since urine separated 16 g of nitrogen. What is the nitrogen balance in humans and what it shows?

B. Tests for self-control

1. Some biogenic amines are potent vasodilator agents, which in high concentrations can cause a sudden drop in blood pressure. Add this compound.
A. Histamine
* B. Adrenalin
C. Glycine
D. putrescine
E. Norepinephrine

2. In a man who suffers from chronic intestinal obstruction, increased decay of proteins in the colon. How toxic is formed in this case with tryptophan:
A lactate.
B Bilirubin.
* C indoles.
D Creatine.
E Glucose.

3. Digestion of proteins in the digestive canal - the complex process of hydrolysis to free amino acids and peptides. What are enzymes that break down proteins in the duodenum?
A enterokinase, lipase.
* B Trypsin, chymotrypsin.
C amylase.
D Pepsin, hastryksyn.
E phospholipase.

4. The patient reduced transport of amino acids in the intestine enterocytes. What is the substance involved in the process:
* A Glutathione.
B alanine.
C Anseryn.
D Ornithine.
E Glucose.

5. An important substrate of gluconeogenesis in the liver is alanine. What reaction, during which he produced in skeletal muscle of pyruvate.
* A. Transamination
B. Decarboxylation
C. dehydrogenation
D. isomerization
E. Phosphorylation

6. In the study of the secretory function of the stomach vyyaleno reduce the concentration of hydrochloric acid in gastric juice. The activity of the enzyme which in this case will go down?
A lipase
B Amylase
* C Pepsin
D Dypeptydazy
E hexokinase

7. decay products of amino acids in the intestine belongs compound cadaverine, which is famous for its unpleasant odor. It is composed of amino acids:
* A. lysine
B. glycine
C. alanine
D. Valin
E. serine

8. colon dekarboksylyuyutsya some amino acids to form toxic substances. Specify that a compound formed from ornithine?
* A. putrescine
B. indoles

C. Phenol
D. Lysine
E. Arginine
9. The patient dental surgeon warned that the application of pain medication can cause allergic shock. Increasing the number of levels of biogenic amines which may be the cause of this condition?
* A histamine.
GABA B.
C serotonin.
D dopamine.
E tryptamine.
10. For the treatment of depressive states prescribe drugs - inhibitors of enzyme inactivating biogenic amines. What enzyme present:
* A MAO (monoamine oxidase).
B LDH (lactate dehydrogenase).
C CPK (creatine phosphokinase).
D AST (aspartataminotransferase).
E ALT (alaninaminotransferase)

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5. Lehninger Principles of Biochemistry 6th ed - David L. Nelson, Michael M. Cox -W H Freeman and Company – 2013. – 1010 p.
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MINISTRY OF HEALTH OF UKRAINE
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Department of pharmaceutical, biological and toxycological chemistry

"APPROVED"
Head of pharmaceutical, biological and toxicological chemistry Departmnet
PhD in Medicine, Professor _____ I.V.Nizhenkovska
protocol number 2 on August 31, 2017

GUIDELINES
FOR INDEPENDENT STUDENTS WORK
WHILE PREPARING FOR THE PRACTICAL LESSON

Academicdiscipline	Biological chemistry

Module number	module 2
module	**Module 5: Exchange of simple and complex proteins.** Biochemical aspects of molecular biology and genetics.
Subject lesson number 2	Ways of formation and disposal of ammonia in the body. The exchange of individual amino acids. Molecular pathology of metabolism of amino acids. *Quantitative determination of urea in the blood.*
Course	3 year
Faculty	Pharmaceutical
Number of hours	2,5

Kyiv 2017

Prepared by Associate Professor PhD O.V. Kuznetsova

1. **Topic actuality**

The result of deamination processes and catabolism of amino acids, nucleotides, biogenic amines are ammonia formation. In addition, a large amount of ammonia formed in the gut in the decay of proteins, as well as enhanced skeletal muscle during exercise. Ammonia - a toxic substance in the body because there are special ways to detox.

Formed in the brain, myocardium, muscle and other tissues ammonia binds with certain alpha-amino keto acids and (pre-neutralization) and their composition is transported to the liver and kidneys, which undergoes final disposal.80-90% ammonia is converted to in hepatocytes urea (in Ornithine cycle), and the rest - in the ammonium salt in the kidney. Violation urea formation process leading to accumulation of ammonia in the blood plasma (hyperammonemia) that damages nerve cells and can cause death

For future pharmacists to exchange knowledge ammonia and urea formation as its main product disposal are important for understanding the causes and consequences of hyperammonemia.

The result of conversion of free amino acids is the formation of a large number of different biologically important compounds. Amino acids are the precursors of the synthesis of hormones (catecholamines and thyroid), biogenic amines, nucleotides, creatine, etc. melanin. Therefore there is considerable interest in the study of amino acids as sources of physiologically active compounds with medical and biological significance. Knowledge of these metabolic changes is essential basic knowledge of future pharmacists.

2. **Specific objectives:**

- treat metabolic patterns of formation and removal of ammonia, circulatory transport ammonia, urea biosynthesis.
- Explain scheme metabolic transformation of certain amino acids.
- explain the peculiarities of the specialized cyclical changes, sulfur and branched chain amino acids;
- characterize major metabolic changes in hereditary diseases of metabolism of amino acids (homocystinuria, cystinosis and Fanconi syndrome, maple syrup and Hartnupadiseasea, phenylketonuria, alkaptonuria, albinism, histydynemia).

- characterize the chemistry synthesis and cleavage of creatine.
- Master by quantitative determination of urea in serum and be able to interpret the results in serum.

3. Basic knowledge, skills necessary for studying the subject (interdisciplinary integration)

Names of previous disciplines	Obtained skills
Physical methods of analysis and metrology	Master the techniques of laboratory research tools
Biology with the basics of genetics	To classify the structure of biopolymers.
Organic chemistry	1. Identify the types of chemical reactions 2. Describe the chemical reaction 3. Write structural formula of amino acids, urea.
Pathological physiology	Explain the basic mechanisms of hereditary disorders of amino acid metabolism.

4. Task for independent work during preparation for the classes.

4.1. The list of key terms, parameters, characteristics which the student is to assimilate while preparing for classes

Term	**Definition**
Hyperammonemia	Hyperammonemia - a rise in ammonia levels due to disruption of its disposal in severe parenchymal liver disease (acute liver failure, cirrhosis portal terminal stage).
Glutathione.	Glutathione (Eng. GSH) - a tripeptideγ-hlutamiltsisteinilhlitsin.
Creatine	Creatine - a nitrogen-containing carboxylic acid is an amino acid essential contained in human muscle and is necessary for energy metabolism in the body and perform different movements.
Transportation form of ammonia	With transport form of ammonia in the body are alanine, glutamic and aspartic acids and amides of dicarboxylic acids: aspartic and glutamic - glutamine and asparagine.

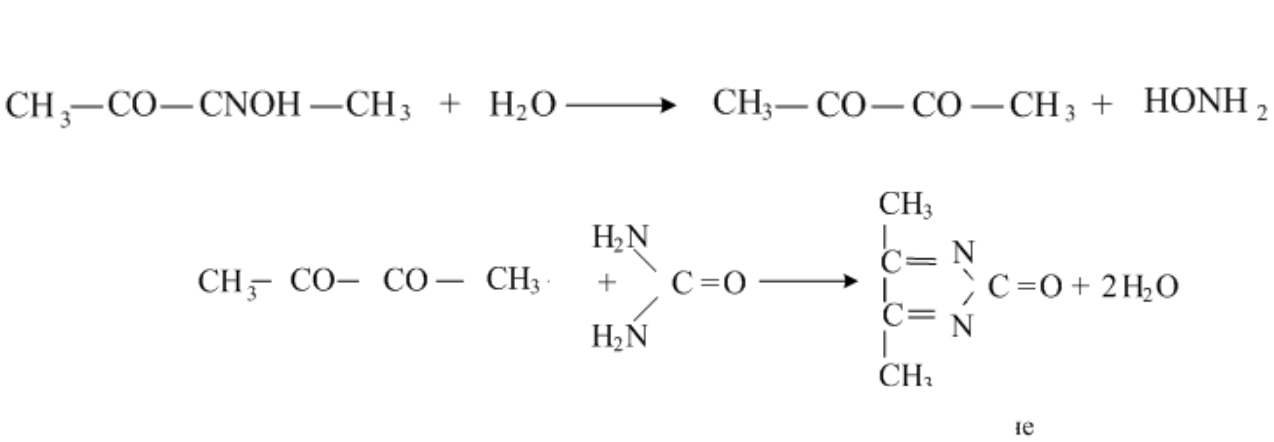
4.2 Theoretical questions for the class.

1. Specific cyclic pathway phenylalanine and tyrosine aminoacids, the sequence of enzymatic reactions. Hereditary enzimopatii exchange cyclic acyclic aminoacids phenylalanine and tyrosine - phenylketonuria, Alkaptonuria, albinism.
2. Exchange of tryptophan: kinureninovy and serotonin way. Hereditary enzimopatii tryptophan metabolism.
3. Exchange of sulfur-containing amino acids cysteine and methionine, and hereditary disorders (homocystinuria).
4. Features of the exchange of branched chain aminoacids. Maple syrupurine diseaseas metabolic BCAA.
5. Biosynthesis and biological role of creatine and creatine phosphate, formation of creatinine.
6. Exchange of glycine and serine; role tetrahydrofolate (H4-folate) in the transfer of one carbon fragments, dihydrofolatereductase inhibitors as anticancer agents.
7. The exchange of arginine; biological role of nitric oxide, NO-synthase.
8. The ways and sources of ammonia formation in organism, reasons and result of it's toxicity.
9. The main mechanisms of ammonia neutralization:
   - reductive amination of a-ketoglutarate;
   - formation of amides of dicarboxylic acids;
   - formation of ammonia salts in the burrows;
   - formation of urea in the liver.
10. Genetic abnormalities of enzymes of the ureacycle. Hyperammonemia.

4.3. Practical work in class.

Experiment 1. Determination of urea in blood serum and urine, by reaction with diatsetilmonooxide.

Principle of the method:Urea in acidic medium in the presence of iron salts and thiosemicarbazidet form a complex compound diatsethylmonooksim, which is red color and it's optical density, at which the green color filters are (500 - 560 nm), is proportional to the urea concentration.



Proceedings. Determining the course of conduct on the table:

Reagent	Test		
	research	standart	control
Blood serum	0,02 мл	-	-
Reference urea solution (7 mmol / L).	-	0,02 мл	-
H_2O	-	-	0,02 мл
Diatsethylmonooksima solution (2.5 g / l)	2,00 мл	2,00 мл	2,00 мл
Tiosemidcarbazyd solution (2.5 g / l)	2,00 мл	2,00 мл	2,00 мл

Tubes were covered with aluminum foil, and the contents were heated under stirring in a water bath for exactly 10 minutes. At the same time treat research, standard and control samples. Then tubes should be quickly cooled under cold running water. Colorimetrate research and a standard sample against the control at a wave length of 530-560 nm (greenfilter) in a cuvette with a layer thickness of 1 cm. Optical density measurements should be carried out for no more than 15 minutes after cooling.

If, after heating the solution in the first vial is turbid, it has to be centrifuged for 5 minutes or deproteinize with threechloroacetic acid solution.

Calculation. The concentration of urea was calculated with this formula:

$$C = \frac{E_{res}}{E_{ref}} \cdot 16{,}64 \text{ mmol/l},$$

where - C – the concentration of urea;

E_{res} – optical density of research test;

$E_{эт}$ – optical density of reference test.

Notes:

1. With the content of urea over 25 mmol / L sample should be diluted with distilled water and repeat the analysis. Multiply the result by dilution.

2. Hemolytic and lipemic serum deproteinize. For this purpose, 0.1 ml of serum was mixed with 0.9 ml of threechloroacetic acid solution and centrifuged for 5 min. The same process standard. For the analysis of selected studies as deproteinization without serum. This method can be used for blood research.

Explain the result. Conclude.

The value for the pharmacy and clinic. Urea synthes is in the liver (cytosol and mitochondria) mainly from ammonia, which is formed by deamination of aminoacids, purine and pyrimidine decay nucleotides. During the day, the urine of a healthy personisal located 20 - 35 g (or 333 - 583 mmol) of urea. Normally, the content of urea in the blood serum of 3.3 - 8.3 mmol / l.

Increase of urea in the blood serum is one of the main signs of impaired renal excretory function. In addition, the increase in the level of urea in the blood serum can be extrarenal origin: loss of body fluids (vomiting, diarrhea, dehydration), increased protein breakdown (acutefatty liver). Reduction of urea can be observed in diseases of the liver (hepatocellular jaundice, cirrhosis of the liver) due to violation of its synthesis in the body.

Elevated levels of urea in urine observed when dietaryprotein deficiency, pernicious anemia, fever, intensive decomposition of protein sinthe body after ingestion of salicylates, with phosphorus

poisoning. Low content of urea observed in liver cirrhosis, hepatocellular jaundice, nephritis, acidosis, uremia.

4.4. Content topics

The final products of decay amino acids are H_2O, CO_2 and NH_3. Ammonia in humans excreted as urea and creatinine. With human urine excreted per day: 25-35 g of urea, 0.3-1.2 g ammonium salts and uric acid; 0.5-2.0 g creatinine and a small number of amino acids (1.2 g), indican, pigments (urobilin and others), vitamins and hormones and their metabolites.

Ammonia - a key process deamination product has high toxicity. He is able to disrupt the Krebs cycle (maintain contacts ketohlutarovat α-glutamic acid) is penalized for transport of neurotransmitters. Normal levels of ammonia in krovi20-40mkmol / l, death occurs with increasing ammonia levels above 3 mg / dL. Ammonia formed in the following processes:

1) deamination of amino acids;
2) rot amino acids in the intestine;
3) The collapse of the foundations of nucleic acids aminosugar and vitamins.

Ways disposal ammonia:

1. First way (temporary disposal - the synthesis of ammonia forms of transport.
2. The final disposal of the way:

• synthesis of urea in the liver (providing utilization of 90% ammonia);
• synthesis of ammonium salts in the kidneys (this way provides the output to 8% ammonia).

Temporary disposal of ammonia (ammonia synthesis forms of transport):

1. Formation of glutamate from α-ketohlutarat way direct amination or transamination.
2. Formation of aspartic acid oxalic-acetic acid often occurs through transamination (eg involving ACT).
3. Formation alanine from pyruvic acid by transamination (this reaction is realized in a series alanine or glucose-alanine cycle). With this reaction ammonia preferably disposed in the muscles.
4. Formation amides - glutamine and asparagine (these processes are important for the central nervous system, which produce a significant amount of ammonia in the deamination of AMP). Such forms of transport ammonia ensure its temporary binding and transport the bodies in which it will be subject to final disposal (liver and kidney).

The final disposal of ammonia:

In the liver and kidneys under the influence of enzymes released ammonia. Kidney ammonia neutralisationanions of inorganic and organic acids and excreted in the urine in the form of ammonium salts. In the liver neutralized to form ammonia urea.

Urea cycle. First, ammonia molecule reacts with CO_2 to form and 2ATF karbamoyilfosfatus which reacts with ornithine to form citrulline. More citrulline reacts with aspartic acid to form argyninsuccynat, which is divided into arginine and fumaric acid. Arhinyn destroyed under the influence of arginase to urea and ornithine, wrong substance from which began the synthesis of urea. For the operation cycle of regeneration and aspartic acid.

Convert fumaric acid aspartic occurs in a cycle of fumaric acid. First fumaric acid in apple hidratuyetsya acid (malate), which is further oxidized to oksaloatsetat who converted to aspartic acid (amino received) during transamination of glutamic acid. This provides resynthesis aspartate and including the second nitrogen atom in the molecule of urea.

During the day the body synthesis to 25-35 g urea. Urea - a non-toxic substance, readily soluble in water, excreted in the urine by the kidneys.

Violation of the urea cycle education havenature origin and is a result of reduced activity of one of the enzymes of this cycle. The most common genetic defects in carbamoyilfosfatsynthesys and ornithyncarbamoyilfosfattransferaz. These diseases are manifested increasing concentration of ammonia in the blood, poisoning symptoms and reduction in ammonia urea.

The exchange of individual amino acids biological significance of amino acids. Amino acids are used:

a) for the synthesis of proteins;
b) as a source of energy;
c) the carbon skeleton of amino acids can serve as a source for the synthesis of glucose (glycogen amino acids) or synthesis of ketone bodies and fatty acids; d) each amino acid can be used in the synthesis of biologically active substances such as biogenic amines, glutathione, etc.

Glycine. Glycine - Replacement glycogen amino acid that is synthesized from serine or threonine. Glycine is used:

1) for the synthesis of glutathione;

2) to form a pair of bile acids (glycolic, and glycodezoxyholyc etc.).
3) the synthesis of heme;
4) for the synthesis of creatine;
5) for the synthesis of purine nucleotides;
6) for choline synthesis;
7) forconverting benzoic acid into hipur;
8) glycine in significant amounts (30%) part of the collagen.

Serine. Replacement amino acid 1) is used for protein synthesis and is part of the active centers of many enzymes - trypsin, chymotrypsin, acetylcholinesterase; 2) Regulation of the majority of protein phosphorylation by protein kinases is made serine residues. Extremely toxic organophosphorus poisons block serine residues in proteins and eliminate their function; 3) serine - donor single-carbon fragments (metilentetrahidrofolat); 4) serine is used for the synthesis of cysteine. 5) serine - hlyukohenna amino acid; 6) serine is used for the synthesis hlitserofosfolipidiv.

Cysteine. Replacement aminoacid.U proteins of this amino acid is in the form of cysteine and its disulfide - cystine. The latter is formed by oxidation of two cysteine molecules.
The biological significance. 1) Cysteine stabilizes the tertiary structure of the protein; 2) part of the active centers carboxypeptidase, apoptosis protease, papain, in large quantities it is part of the skin and hair keratins; 3) important source of sulfate, which is used for the synthesis of glycosaminoglycans and conjugation of xenobiotics; 4) amino glycohen 5) source of taurine synthesis paired bile acids (tauroholic, taurodezoksyholic) for the development and functioning of the brain, retina, heart (mediator); 5) glutathione precursor.

Methionine. Essential amino acid in the human body is not synthesized. Used for protein synthesis. Glycogen amino acid, the main source of methyl groups for the synthesis of adrenaline, creatineanseryn, choline, phosphatidylcholine.

Glutamic acid.Glutamine.Replaceable hlyukohenni amino acids. Glutamate formed by transaminuvanniα-ketoglutarate and glutamine - glutamate at amidation.
Value glutamate. 1) is used for protein synthesis, a source of negatively charged groups in the protein molecule; 2) Balances glutamate proteins in blood coagulation and bone are exposed to vitamin K-carbocsyl process to form carbocsyhlutaminic acid (it has an additional carboxyl group), which provides proteins ability to bind Ca2 + ions; 3) glutamate and glutamine - transport form of ammonia; 4) formed at the decarboxylation of glutamate GABA - inhibitory neurotransmitter; 5) glutamate - the main excitatory neurotransmitter. At high concentrations, glutamate acts toxic, causing calcium accumulation and death of neurons. In the brain, there are many types of glutamate receptors that differ in sensitivity doN-methyl-D-aspartic acid.Z dysfunction of these receptors bind diseases such as epilepsy, schizophrenia; 6) glutamine is involved in the synthesis of purine and pyrimidine nucleotides; 7) glutamate formed histidine, proline, ornithine, arginine; 8) glutamate required for the synthesis of glutathione metabolism and folic acid (tissue formed polyhlutamat folic acid);

Aspartic acid.Asparagine.Replaceable glycogen and amino acids. Aspartate formed by transamination oksaloacetate (oxalic-acetic acid) and asparagine - aspartic acid by amidation
Meaning: 1) is used for protein synthesis, a source of negatively charged groups in the molecule; 2) aspartate and asparagine - transport form of ammonia; 3) the decarboxylation aspartate carboxyl groups on the first formed β-alanine, and last -α-alanine, 4) aspartate is used for the synthesis of purine nucleotides and pirymydyn; 5) member aspartate cycle of urea synthesis; 6) aspartate, N-acetylaspartat neurotransmitters in the brain; 7) tumors need high amounts of asparagine, but the poorly synthesized it with aspartate. Therefore, for the treatment of tumors using asparaginase enzyme that breaks down asparagine and deprives them of asparagine.

Arginine.Essential amino-acids for adults, children synthesized in insufficient quantities (partly indispensable).

Value arginine: 1) is used for protein synthesis, a source of positively charged groups in the molecule. Nuclear proteins - histones and protamine contain a lot of arginine
to basic protein; 2) Arginine is involved in the formation of the urea cycle; 3) together with the glycine form huanidynatsetat arginine - precursor of creatine; 4) Ornithine (product of arginine metabolism) in the decarboxylation gives putrescine - spermine and spermidine predecessor - regulators of cell proliferation; 5) in the form of arginine decarboxylation agmatine - a neurotransmitter with analgesic effect; 6) Arginine - a source of nitric oxide. Nitric oxide - the main factor of relaxation of blood vessels, mediator of inflammation, platelet aggregation inhibitor, regulator of mitochondrial function.

Lysine. Essential amino acids used for protein synthesis, a source of positively charged groups in the protein molecule. A large number of histone lysine contained in

iprotamine, fibrinogen. Lysine residues in collagen hydroxylation exposed to form oksylizyn, which is important for the maturation of collagen.

Phenylalanine and tyrosine. Phenylalanine - an essential amino acid, is synthesized from tyrosine phenylalanine. Phenylalanine and tyrosine are involved in the formation of protein molecules and by their aromatic cycles give it hydrophobic properties.

1) tyrosine formed catecholamines - dopamine, norepinephrine and epinephrine; 2) Tyrosine - the predecessor of skin pigment melanin; 3) after iodized tyrosine is converted into thyroid hormones thyroxine and -tryyodtyronin.

The main way of phenylalanine catabolism is its hydroxylation of tyrosine to fenilalaninhydroksylaz and secondary - in transamination to fenilpiruvat. If the genetic defect fenilalaninhidroksylaz (disease fenilpyruvic mental retardation) violated convert phenylalanine to tyrosine. This leads to accumulation of phenylalanine which excess toxic effect on the brain of the child. As a result of lack of education disrupted tyrosine neyromediator (dopamine and norepinephrine). Developed dementia. One way to eliminate excess phenylalanine at phenylketonuria is strengthening its transamination to fenilpiruvat. Therefore, in the urine of children with phenylketonuriafenilpurivic out large amounts of acid. The treatment is the use of a diet low in phenylalanine in proteins.

There are genetic defects and tyrosine metabolism. In alkaptonuria (deficit oxidase homogentisic acid) in the urine excreted much homogentisic acid oxidation products which provide urine black. In albinism (lack of tyrosinase) disrupted the formation of the pigment melanin.

Tryptophan.Essential amino acid. 1) tryptophan produced neurotransmitter serotonin and the hormone epiphysis melanotonin; 2) Tryptophan is converted into vitamin PP (B5).

Histidine. Conditionally essential amino acid 1) part of the active sites of enzymes (chymotrypsin, thrombin, cholinesterase, ribonuclease, phospholipase) by histidine bind hemeprotein hemoglobin; 2) When decarboxylation of histidine formed histamine, a mediator of inflammation and allergies. Histamine - a stimulant of gastric juice.

Proline. Replacement and glycogen amino acid.Proline is a part of all proteins, but especially the much collagen. Maturation of collagen requires the hydroxylation of proline to hydroxyproline (reaction catalise ascorbic acid).

5.Material for self-control.

A. Tasks for self-control.

1. newborn baby sucking a decrease in intensity, frequent vomiting, hypotension. Urine and blood significantly increased concentration of citrulline. What disturbed metabolic process? Hepatocyte enzyme deficiency which can assume? What will change the content of ammonia and urea in plasma under these conditions?

2. The child age 10 month whose parents Brunette, has blonde hair, very light skin and blue eyes. At birth had a normal appearance, but for the past 3 months observed violations cerebral circulation, the lag in mental development, seizures. As low content of blood catecholamines. When added to fresh urine a few drops

3. $FeCl_3$ violet color appears. For what the pathology of metabolism of amino acids characteristic of this change? What metabolite gives urine violet color in the presence of iron ions? Why is light color hair and eyes of a child under these conditions?

4. In hypertensive patients in vessels decreased synthesis of vasodilator nitric oxide.

Which amino acid is synthesized nitrous oxide? In the process which produced this amino acid in the body? For the synthesis of substances that still need it?

5.The patient has a urine odor of maple syrup. What biochemical defect is the cause of this disease?

B. Tests for self-control

1. Ammonia, which is produced in the body during deamination of a toxic substance especially for cells of the central nervous system. Who is the substance that causes the neutralization of ammonia in the tissue.

A Norepinephrine.

B Buffer systems.

C Arginine.

* D glutamic acid.

E Histamine.

2. Ammonia produced in different tissues and organs and neutralized in the liver, turning into urea. Which amino acid carries it from skeletal muscle to the liver:

* A alanine.

B histidine.
C Glycine.
D serine.
E Valine.
3. After suffering a viral disease of the liver showing signs of ammonia poisoning: loss of consciousness, seizures, blood - hyperammonemia. Violation of any process takes place?
A. * urea synthesis
B. Citric acid cycle
C. Rotting proteins in the gut
D. decarboxylation
E. glycolysis
4. Patients with fatty liver appointed aminoacids donating methyl groups for the synthesis of choline, what connects its lipotropic effect. Add this amino acid.
* A Methionine.
B Cysteine.
Alanine C.
D Valine.
E Glycine.
5. In albinism in the body there is no formation of the pigment melanin. On the violation of which amino acids metabolism associated emergence of this disease?
* A phenylalanine.
B methionine.
C alanine.
D glutamine.
E asparagine.
6. During the decarboxylation of 5-hydroxytryptophan formed biogenic amine having constrictor action. What are biogenic amines present.
* A serotonin.
B histamine.
C gamma-aminobutyric acid.
D putrescine.
E cadaverine.
7.for epilepsy for glutamic acid. What is a compound formed from glutamate, able to adjust manifestations of epilepsy?
A. * Gamma-aminobutyric acid
B. Serotonin
C. Histamine
D. asparagine
E. Dopamine
8. The doctor asked the patient complained of sunburn, reduced visual acuity. Hair, skin and eye pigmentation have. The diagnosis - albinism. Which enzyme deficiency occurs?
A Histydyndecarboksylaz.
B arginase.
C carbonic anhydrase.
* D tyrosinase.
E hexokinase.
9. A man found vitamin E vitamin deficiencies. The use of amino acids whose food partially offset the needs of the patient vitamin PP?
A methionine
B phenylalanine
C valine
D arginine
* E Tryptophan
10. Parkinson's disease disrupted the synthesis of dopamine in the brain. For the treatment used his immediate predecessor, which easily penetrates the blood-brain barrier, namely:
A. * DOPA
B. Tryptophan
C. GABA

D. Norepinephrine
E. Adrenaline

Literature

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"APPROVED"
Head of pharmaceutical, biological and toxicological chemistry Departmnet
PhD in Medicine, Professor _____ I.V.Nizhenkovska
protocol number 2 on August 31, 2017

GUIDELINES
FOR INDEPENDENT STUDENTS WORK
WHILE PREPARING FOR THE PRACTICAL LESSON

Academic discipline	Biological chemistry
module number	module 2
module	**Module 5: Exchange of simple and complex proteins.**
Subject lesson number 3	Metabolism of nucleotides. Pathology nucleotide metabolism, hyperuricemia, gout, orotatatsyduriya. *Assay of uric acid in the blood serum.*
Course	3 year
Faculty	Pharmaceutical
Number of hours	2,5

Kyiv 2017

Prepared by Associate Professor PhD O.V. Kuznetsova

1. Topic actuality

In the cells of the body nucleotides are structural components of nucleic acids (DNA and RNA) and are in a free state and taking part in a series of metabolic transformations: energy metabolism (ATP, ADP, AMP), transmission of hormonal signals into the cell (cAMP and cAMP) functioning of enzymes (coenzyme form of NAD, FAD), activating molecules in the synthesis (UDP-glucose, CDP-choline) and others. Therefore, knowledge of the metabolism of purine and pyrimidine nucleotides are basic in the training of future pharmacists. Disruption of biosynthesis and catabolism of purine and pyrimidine nitrogenous bases and nucleotides can lead to the development of diseases such as Lesch-Nyhan syndrome, gout, orotatsyduriya.

2.Concrete goals:

- analyze sequence of reactions of biosynthesis and catabolism of purine nucleotides abuse uric acid synthesis and biochemical basis of gout.
- analyze sequence of reactions of biosynthesis and catabolism of pyrimidine nucleotides.
- characterize the chemistry synthesis of deoxyribonucleotides.
- quantify the uric acid in biological fluids, be able to interpret the results.

3. Basic knowledge, skills necessary for studying the subject (interdisciplinary integration)

The names of previous sciences	Experience
Physic methods of analysis and metrology	Master the techniques of laboratory research tools
Biolofy with genetics	Classify the structure of DNA and RNA
Organic chemistry	1. Identify the types of chemical reactions 2. Describe the chemical reactions 3.Write the formulas of nitrogenous bases, nucleosides and nucleotides.

4.Tasks for independent work during preparation for the classes.

4.1. The list of key terms, parameters, characteristics which the student is to assimilate while preparing for classes.

Term	Definition
Hyperuricemia	increasing the concentration of uric acid in the blood
Nucleoside	consists of a nitrogenous base and pentose (ribose or deoxyribose), which joins the N-glycoside bond to a nitrogenous base.
nucleotide	consisting of nucleotide residues 1-3 and phosphoric acid.
Nucleic acids	biopolymers, monomers which are mononucleotides.
nucleoprotein	this complex proteins, not protein which is part of the nucleic acid
Gout	metabolic disease characterized by the deposition in various tissues urate crystals in the form of monosodium urate or uric acid

4.2 Theoretical questions.

1. The biosynthesis of purine nucleotides: scheme of reactions of IMP synthesis; AMP and GMP formation and its regulation.
2. biosynthesis of pyrimidine nucleotides: scheme of reactions, the reaction of UMF, UDP, UTP and TSTF and its regulation.
3. Biosynthesis of deoxyribonucleotides. DTMP biosynthesis inhibitors as anticancer agents (dTMP structural analogs, derivatives pterine).
4. Catabolism of purine nucleotides.
5. Catabolism of pyrimidine nucleotides.

6. Hereditary nucleotide metabolism. Gout. Lesch-Nyhan syndrome. Orotatatsyduriya.
7. The use of pharmaceuticals for metabolic correction nucleotides.

4.3. Practical work

Experiment 1. Assay of uric acid in the blood serum.

The principle of method. Uric acid restores fosfatvolframatnyy reagent to form a compound of blue, whose optical density at 640 nm wavelength is proportional to the concentration of uric acid in the blood serum.

The process: In a centrifuge tube containing 0.5 ml of serum and 4 ml of distilled water. The contents of the tube mixed and added 0.25 ml of 0.35 M sulfuric acid and 0.25 ml of 10% sodium dyhidrohenvolframatdyhidratu. The contents of the tube mixed and centrifuged 5 minutes for 10 minutes at a speed of 3000 rev / min. Selected supernatant. Take three tubes and reagents make them according to the table:

Reagents	Control sample, ml	Standart sample, ml	Research sample, ml
Supernatant	-	-	2
Standart solution of uric acid	-	2	-
Distilled water	2	-	-
10 % sodium carbonate	1	1	1
Phosphatevolframate reagent	0,5	0,5	0,5

The contents of the tubes mixed. After 30 minutes determine the optical density of the standard and test sample for the wavelength of 640 nm (590 - 700 nm red filter) compared with the control sample in the cell thickness of 10 mm. The blue color is stable for 30 minutes.

$$C = \frac{A\ res}{A\ cont} \times 30 \times 10$$

Calculation of uric acid is carried out as follows:
where: C – the content of uric acid in the tested sample mmol / l;
A res- optical density of test sample;
A cont- optical density of control sample;
30 - uric acid standard solution mmol / l;
10 - value dilution of serum.
Explain the results. Conclude.

Pharmaceutical and clinical meaning. Formed as a result of the collapse of purine bases uric acid excreted by the kidneys. Normally a person with urine excreted 1.60 - 3.54 mg / day (270 - 600 mg / day) of uric acid. The normal concentration of uric acid in the blood serum of men - 240 - 530 mmol / L (0.05 - 0.06 g / L) for women approximately 25% less - 185 - 440 mmol / L (0.04 - 0 , 05 g / l). Hiperurikemiya - increase the concentration of uric acid in the blood, hiperurykuriya (hiperuraturiya) - increase of uric acid in the urine. Hyperuricemia accompanies gout - a disease that occurs in conditions of precipitation of urate in the tissues, especially in joints. Uric acid and its salts are extremely poorly soluble in water, their concentration in body fluids under conditions close to mezhirozchynnosti rules. For the treatment of gout using drugs that inhibit the formation of uric acid (allopurinol) or stimulate the excretion of kidneys (anturan, cinchophen). In patients with gout uric acid concentration in the blood is almost always higher than the 0.075 - 0.080 g / l, and during the formation of gouty seals it rarely content below 0.08 - 0.09 g / l.

4.4. The context of topic

Nomenclature

Nitrogenous bases	Nucleotides	Nucleotides
Purina		
adenine	adenosine	Adenosine monophosphate (AMP) ;
guanine	guanosine	guanosine monophosphate (GMP).
Pirymidiny		
uracil	uridine	uridine monophosphate (UMF).

cytosine	cytidine	cytidine monophosphate (CMF).
thymine	thymidine	thymidine monophosphate (TMF).

* - If pentose - deoxyribose, the name - dezoksyadenozyn, etc. (c) corp.

The biological role of nucleotides:

- universal source of energy in the cell (ATP, GTP);
- activators and vectors monomers (eg, UDP-glucose, CDP-choline);
- allosteryc regulators enzyme activity;
- members of the nucleotides (NAD +, NADP +, FAD, KoASH);
- cyclic mononucleotides (cAMP, cGMP) mediators are secondary effects of hormones and other signals in the cell;
- monomers are composed of nucleic acids.

The biosynthesis of purine nucleotides takes place in the cytoplasm of all tissues, but the highest activity observed in the liver.

The Features of synthesis of purine nucleotides:

1.Puryne nucleotides de novo synthesized not in erythrocytes and polymorphonuclear leukocytes because they can not synthesize 5- fosforybozylamin.

2.Syntez purine nucleotides begins with ribose-5-phosphate, which is the source pentose phosphate cycle in which the synthesis and purine ring by successive additions of substances that are donors of carbon atoms and nitrogen purine ring.

3. The precursor synthesis of AMP and GMP are inozynova acid (IMP). Directly from inozynmonofosfatu involving glutamine and aspartate are formed according AMP and GMP.

Sources atoms purine ring in the synthesis de novo

Sources of carbon atoms:
-glycine (source 2 C atoms);
-meteiltetrahidrofolat;
-carbon dioxide.
Sources of nitrogen atoms:
-glycine;
-amide group of glutamine (source 2 atoms of N);
-aspartate.

Catabolism of purine nucleotides occurs mainly in the liver. In humans, the end product of purine nucleotides metabolism is uric acid. The fact that humans are the end product of uric acid is adaptive effect to prevent excessive loss of water from the body as uric acid - sparingly soluble compounds. Organism uric acid performs antioxidant functions. Most uric acid and its salts (urate) excreted by tubular secretion and lesser extent excreted in the digestive tract, where the impact of microbes degraded to CO2 and NH3 (urykoliz).

Types of hyperuricemia:

I.Produktsiyna (increased formation of uric acid).

1.First (congenital):

-Lesch-Nyhan syndrome: the effect of the enzyme hypoxanthine-guanine-fosforybozyltrnsferazy. According hypoxanthine guanine and not used for re-synthesis of AMP and GMP, and all turn into uric acid, which causes severe hyperuricemia. This syndrome is inherited as a recessive, sex-linked X chromosome, boys manifested signs of gout, paralysis, impaired intepektu

2.Second (acquired)

-increased penetration of purines yizhoyu (a large number of them found in liver, kidney);

-increased decay purines (prolonged fasting, malignancy, seriously ill (in which tissue hypoxia and increased decay ATP).

II.Retential (reducing the excretion of uric acid)

Reasons:

- kidney disease;

-diabetes, where there is ketoacidosis, which reduces tubular secretion.

Gout - a disease that is more common in men and is a manifestation of hyperuricemia. Since, uric acid is sparingly soluble compounds in water, it causes an increase urate deposition in the sediment. Urate crystals deposited in joints, particularly of small and cause the island, as well as the formation of kidney stone disease. Strengthened urate deposition in the sediment in an acidic environment.

Treatment of gout:

1.Obmezhennya consumption of foods high in purines

2.Alopurynol - competitive inhibitor of xanthine oxidase, which causes a decrease in the formation of uric acid.

The biosynthesis of pyrimidine nucleotides

Biosynthesis takes place in the cytoplasm of all tissues, but the highest activity observed in the liver.

Features synthesis of pyrimidine nucleotides:

1.Firstly synthesized pyrimidine ring, and then joins ribose-5-phosphate.

2.Previous compound of the synthesis is orotic acid (or vitamin B13 OMF), which stimulates protein synthesis, cell division and imunopoez. With orotic acid is formed first pyrimidine nucleotides - UMF (urydynmonofosfat)

3.Utvorenyy UMF is a precursor in the synthesis of other pyrimidine nucleotides.

Sources of carbon atoms and nitrogen pyrimidine ring

-karbomoyilfosfat, which is formed from carbon dioxide and ammonia

-aspartic acid

Formation of cytidyl nucleotides. With UMF, which is twice phosphorylated involving two molecules of ATP, UTP formed. Last by amination (amino donor is glutamine) is converted to TSTF.

Synthesis of deoxyribonucleotides

1.Vidbuvayetsya of di- or tryfosfatnukleozydiv.

2.B synthesis involved rybonukleotydreduktaznyy complex consisting of:

- rybonukleotidereduktaze that restores ribose. Direct donor for hydrogen recovery are low molecular weight protein tioredoksyn containing 2 SH-groups.Vin gives two hydrogen atoms that take oxygen vidON group, located at the second carbon atom of ribose. Consequently, the latter converted to deoxyribose;

- tioredoksynreduktaza which catalyzes recovery tioredoksynu oxidized using NADPH.

Formation of thymidine nucleotides. The precursor is UMF, which initially phosphorylated (under the influence of ATP) to form UDP, and involving complex rybonukleotydreduktaznoho converted into dUDF (dezoksyurydynmonofosfat). Last defosforyluyetsya to form dUMF and then under the influence metylentetrahidrofolate converted into dTMF.

Inhibitors of the synthesis of deoxyribonucleotides

1.Structure of dTMF analogs (5-fluorouracil, which the body turns na5-fluoro-dTMF)

The mechanism of antitumor action: blocking an enzyme synthesis dezoksyTMF - tymidylatsyntazu. This leads to inhibition of DNA synthesis and separation cells. They are used to treat malignant tumors,

2. Derivatives of purine (aminopteryn and methotrexate)

The mechanism of antitumor action: blocking dihydrofolate reductase, which normally provides a synthesis THFK that donating methyl groups for the synthesis of dUMF - dTMF. According purine derivatives inhibit the proper synthesis dTMF and therefore DNA and cell division. Preparations of the above groups are used as chemotherapy tumors.

Catabolism of pyrimidine nucleotides occur mainly in the liver. The final products of metabolism of pyrimidine nucleotides are:

- β-alanine used for synthesis of CoA, carnosine and anzerynu (the latter increases the amplitude of muscular contractions, increase ATP synthesis in the muscles and clear lactate, inhibit the aging process, reduce the synthesis of NO)

- CO2 derived from air

- NH3 largely neutralized by the formation of urea and ammonium salts

- β-aminoizobutyratvyvodytsya urine. The increase in its urinary excretion indicates intensification collapse pyrimidine nucleotides that is often observed in malignant diseases.

5.Materialy for self-control.

A Tasks for self-control.

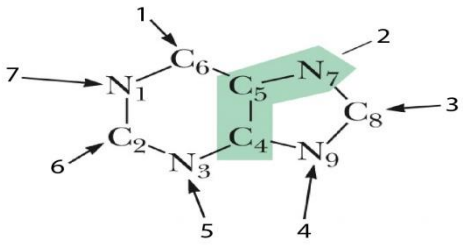
1. Fill the table "Nomenclature major nitrogenous bases, nucleosides and nucleotides"

Nitrogenous bases	nucleoside (Nitrogenous base + pentose)	nucleotides (Nitrogenous base + pentose + phosphate acid)	Abbreviation nucleotides	code nucleotides (Eng. / Ukr.)

to DNA				
Adenine			5’- dAMP	
Guanine		d-Guanosine-5’-monophosphate		
Cytosine	Desoxycitidine			
Thymine				T/T
to RNA				
Adenine	Adenisine			
Guanine				G/ Г
Cytosine			5’- CMP	
Uracil		Uridin-5’-monophosphate		

2. Using the diagram indicate the origin of carbon and nitrogen atoms that make up the purine ring.

1 – ?
2 – ?
3 – ?
4 – ?
5 – ?
6 – ?
7 – ?
8 – ?



3. The original uridine, fluorouracil, turns the cell on ftordezoksiurydylat - strong irreversible inhibitor tymidylatcyntazy. How to explain the fact of oppression fluorouracil rapid division of cancer cells in experimental animals?

4. Present the biosynthesis of deoxyribonucleotides scheme and explain the mechanism for converting rybonukleotydiv deoxyribonucleotides.

5.Opysaty structure and properties of xanthine oxidase.

B. Tests for self - control

1. Derivatives pterine - aminopteryn and methotrexate - are competitive inhibitors dihidrofolatreduktazy, so that they inhibit regeneration tetrahidrofoliyevoyi acid dyhidrofolate. These drugs lead to inhibition of intermolecular single-carbon transport groups. The biosynthesis of the polymer is thus suppressed?

A * DNA
B protein
C Homopolisaharydy
D ganglioside
E Glycosaminoglycans

2. Patient '45 turned to the doctor complaining of pain and swelling of the joints of the foot, which increases the eve of weather changes. If a blood test revealed a significant increase in uric acid. What is the name of this pathology?

* A Gout.
B Stomatitis.
Hepatitis C.
D Palahra.
E Rickets.

3 .In the child has mental stunting development. With a large amount of urine orotic acid. For the treatment of this disease should always use:

A Guanine
B adenine
* C uridine
D glutamine
E alanine

4.Joints patient increased in size, look like deformed thickened nodes. When blood analysis revealed elevated uric acid and its salts. Exchange violation substances which are the cause of this condition?
A Porfyryna.
B Pyrymydynov.
* C purines.
D cholesterol.
E phospholipids.
5. The collapse of the adenosine nucleotide causes the release of ammonia. What enzyme plays a key role in the formation of ammonia from these compounds?
* A.Aadenozindezaminazy
B. alcohol
C. Lactate dehydrogenase
D. Alanintransaminazy
E. Amylase
6.Patient with coronary heart disease intended riboksin (inosine), which is an intermediate metabolite synthesis:
* A purine nucleotides
B metalloprotein
C Lipoprotein
D glycoprotein
E Ketonovihtil
7. Disease patient hostrere designed sulfonamides structural analogs paraaminobenzoynoi acid (PAB) required for the synthesis of growth factors microorganisms - folic acid. Specify the synthesis of compounds which inhibited thus:
A purine nucleotides
* B pyrimidine nucleotides
C arginine
D tryptophan
E histidine
8.Patient with malignant tumor cytotoxic chemotherapy appointed. The mechanism of action of these drugs?
* A Depressing timidinmonofosfata synthesis.
B blocks the action of MAO
C Inhibirueproteolitichnifermenty.
D Inhibirueferменty on alosterichnomumehanizmu.
E Viklikaedenaturatsiyufermentiv.
9. Gout develops in the metabolism of purine nucleotides. The doctor assigned to the patient pharmaceuticals allopurinol, which is a competitive inhibitor:
A. succinate
* B. xanthine oxidase
C. alcohol
D. Lactate dehydrogenase
E. hexokinase
10. We know that the delay cell division of malignant tumors is influenced by 5-fluorouracil, which inhibits timidilatsintazu. Education substance thus inhibited?
A. guanylic acid
B. adenyl acid
* C. thymidine acid
D. tsytidilovoi acid
E. urydylovyy acid

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MINISTRY OF HEALTH OF UKRAINE
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"APPROVED"

Head of pharmaceutical, biological and
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PhD in Medicine, Professor _____ I.V.Nizhenkovska
protocol number 2 on August 31, 2017

GUIDELINES
FOR INDEPENDENT STUDENTS WORK
WHILE PREPARING FOR THE PRACTICAL LESSON

Academic discipline	Biological chemistry
Module number	module 2
module	**Module 5: Exchange of simple and complex proteins.**
Study subject number 4	Biosynthesis of nucleic acids and proteins. Inhibitors of transcription and translation. Regulation of gene expression in eukaryotes and prokaryots. Molecular mechanisms of mutations. Genetic engineering. *Determination of the main components of nucleoprotein (protein nitrogenous base, pentose, phosphoric acid) in its hydrolyzate.*
Course	3 year
Faculty	Pharmaceutical
Number of hours	2,5

Kyiv 2017

Prepared by Assistant V.P. Narokha

1.Topic actuality

For all living organisms characteristic biochemical individuality, which is determined genetically programmed specific set of a characteristic protein molecules. The site of the DNA molecule that carries complete information about the structure of a protein molecule, called a gene. Information about the structure of individual proteins encoded in the DNA of an organism with a genetic code and passed a number of generations. At the heart of conservation, transmission and sale of genetic information underlying mechanisms of replication and transcription.The final phase of genetic information - a protein biosynthesis, which includes three stages - the activation of amino acids, the actual broadcast (protein biosynthesis on ribosomes on the mRNA matrix) and post-translational modification. The activity of all stages of protein synthesis is regulated and depends on various factors. Regulation of gene expression in prokaryotes is at the transcription, whereas in eukaryotes regulation is much more complex and multilevel (occurs at the level of structural organization of the genome, transcription and translation). Knowledge of the molecular mechanisms that underlie the regulation of gene expression,

can affect the process of protein synthesis in eukaryotes and prokaryotes, which is very important for the development of new pharmaceuticals and treatment of infectious diseases, inherited diseases, cancer and others. Yes, some antiviral, antibacterial and anticancer drugs sell their therapeutic effect by influencing certain stages of translation.

Violation of the structure of proteins that may arise from errors synthesis in the body lead to the development of pathological conditions (Molecular Medicine). The cause of molecular diseases are mutations that cause a change in the transfer and implementation of genetic information. The cells are protective mechanisms that ensure accurate storage and transmission of genetic information - a system of DNA repair. Understanding the processes of transmission and realization of genetic information can extend the approaches to diagnosis, creation of new therapies and correction of metabolic changes are caused by the disruption of the genetic apparatus of the cell.

2.Specific objectives:

- interpret the molecular patterns of storage and transfer of genetic information
- characterize the mechanisms of DNA replication: basic principles enzymatic system.
- explain the mechanisms of RNA transcription: steps, functioning enzymes.
- To analyze the effects of genomic, chromosomal and gene mutations, the most common mechanisms of action of mutagens, biological significance and mechanisms of DNA repair (repair of UV-induced gene mutations).
- explain the mechanisms of protein-synthesis system by enzymes activating amino acids, initiation, elongation and termination biosynthesis polypeptide chains.
- Explain the biochemical processes of posttranslational modification of peptide chains.
- explain the mechanisms of gene expression in prokaryotes example lac-operon.
- explain biochemical and molecular principles of genetic engineering, recombinant DNA, gene transplantation and hybrid DNA molecules.

3. Basic knowledge, skills necessary for studying the subject (interdisciplinary integration)

Names of previous disciplines	Obtained skills
Physical methods of analysis and metrology	Master the techniques of laboratory research tools
Biology with the basics of genetics	1. Characterize the organization of information flow in the cell. 2. Interpret the concept of genetic code. 3.Analyze sequence of regulation of gene expression
Organic chemistry	Describe chemical reaction.Write structure
Pathological physiology	1. Explain main causes and conditions of hereditary diseases. 2. Explain concept mutation and mutagens.

4. Task for independent work during preparation for the classes.

4.1. The list of key terms, parameters, characteristics which the student is to assimilate while preparing for classes

Term	Definition
Amplification of genes	Amplification of genes - is the formation of additional copies of sections of chromosomal DNA, usually contain certain genes or segments of structural heterochromatin
The genetic (biological) code	The genetic code (biological) code - a combination of 3 mononucleotides in the DNA molecule that is responsible for the inclusion of certain amino acids in the polypeptide chain.
Genetic engineering	Genetic engineering - a biotechnological method aimed at constructing recombinant DNA molecules from DNA taken from different sources.
Exon	Exon - stretch of DNA within a gene is translated into a mature molecule of messenger RNA (mRNA) during transcription and splicing.
Gene expression	Gene expression - the process by which the genetic information of genes (Nucleotide sequence) used for the synthesis functional product, protein or RNA.
Intron	Intron - stretch of DNA that is part of the gene, but unlike exons, contains information about the amino acid sequence of the protein.
Mutations	Mutations - a quantitative or qualitative changes in the genotype of the organism.
nucleosomes	Nucleosomes - the block of chromatin formed plot threads DNA on the main core histone proteins.

Processing	Processing, co-transcriptional modification, post-transcriptional modification –synthesized anew maturation of RNA molecules to its functionally active form.
Primer	Primer - short nucleic acid fragment or a related molecule that is the starting point for DNA replication.
Ribosomes	Ribosomes - a nemembranna cell organelle composed of rRNA and ribosomal proteins (proteins) and protein biosynthesis provides broadcasting of mRNA polypeptide chain.
Splicing	Splicing - a process of "cutting" newly synthesized messenger RNA (mRNA) during RNA processing.
Topoisomerase	Topoisomerase - a group of key enzymes that catalyze change topological state of DNA (relaxation) in the processes of replication, repair, and others.

4.2 Theoretical questions for the class.

1. The mechanism of DNA replication. Enzymes DNA replication in prokaryotes and eukaryotes.
2. The biological significance and mechanisms of DNA repair. Reparation of UV-induced gene mutations; xerodermapigmentosum.
3. Mutations: genomic, chromosomal, gene (point); their role in causing hereditary diseases.
4. Stages enzymes and RNA synthesis. RNA polymerase of prokaryotes and eukaryotes. Regulation of gene expression in eukaryotes and prokaryotes.
5. Processing - posttranscriptional modification of RNA.
6. ribosomal protein synthesis system. Stages and mechanisms of translation: initiation, elongation, termination. Molecular mechanisms controlling broadcast on the example of the biosynthesis of hemoglobin.
7. posttranslational modification of peptide chains.
8. Antibiotics – inhibitors of replication, transcription and translation in prokaryotes and eukaryotes, their biomedical applications. Biochemical mechanisms of antiviral action of interferons. Blocking protein biosynthesis diphtheriatoxin (ADP-ribosylation factors broadcasts).
9. Genetic engineering or recombinant DNA technology, general concepts, biomedical importance.

4.3. Practical work that is done in class.

Experiment 1. Biuret reaction to peptides and proteins.

The principle of the method. All proteins and peptides, except dipeptides with CuSO4 in an alkaline medium (NaOH) form complex compounds that cause the color purple. Peptide ties reacting enol form.
Progress. In a test tube containing 5 drops of hydrolyzate nucleoprotein, 10 drops of NaOH, 2-3 drops of CuSO4. The contents of the tube mixed. The solution becomes violet.

Experiment 2. Silver test for purine bases.

The principle of the method. Purine nitrogen bases form a precipitate in the reaction with silver nitrate.
Progress. In a test tube containing 10 drops of hydrolyzate nucleoprotein, neutralize ammonia solution, add 5 drops of silver nitrate, the contents of the tube mixed. After 3-5 minutes falls loose sediment silver salts of nitrogen bases purine light brown.

Experiment 3. Trommer reaction to ribose and deoxyribose.

The principle of the method. Compounds containing the aldehyde group is reduced by heating Cu2 + consisting of Cu (OH) 2 to Su1 + and they would oxidized to the corresponding carboxylic acids. The reaction is accompanied by a color change of sediment: blue Cu (OH) 2 is transformed into yellow CuOH and further heated in brick red Cu2O. Excess copper sulfate masking reaction as Cu (OH) 2 when heated decomposes into copper oxide CuO and black water.
Progress. In a test tube containing 5 drops of hydrolyzate nucleoprotein, add 10 drops of sodium hydroxide solution, 3-5 drops of copper sulphate (before clouding, which disappears), the contents of the tube mixed, then heated to boiling. The color change. Drops brick-red precipitate Cu2O.

Experiment 4. Molybdenum test for phosphoric acid.

The principle of the method. Phosphoric acid when heated with molybdenum reagent forms fosfomolibdat ammonium yellow.
Progress. In a test tube containing 10 drops of reagent molybdenum, add 5 drops of hydrolyzate nucleoprotein, heat to boiling. The color is lemon-yellow. When cooled-down yellow crystalline precipitate of complex compounds - fosfomolibdatu ammonium.
Clinical and diagnostic value.

Nucleic acids are the cells in the form of nucleoprotein. When complete hydrolysis of nucleoprotein formed their constituents: amino acids, nitrogenous bases, pentose, phosphoric acid. DNA analysis is increasingly used in the diagnosis of hereditary diseases.

4.4. Content topics

The structure and function of DNA (deoxyribonucleic acid). The structure of DNA consists of four types of nitrogenous bases: adenine (A), thymine (T), guanine (G), cytosine (C) and pentose deoxyribose. Under the primary structure of DNA understand the sequence of nucleotides in a polynucleotide chain. Communication between nucleotides in DNA is formed with the participation of the 3'-OH group of ribose of one nucleotide and the 5 'acid remainder fosforimore. Thus the primary structure is strengthened 3'-5 'phosphodiester bond. Secondary structure of DNA - a double helix right twisted polynucleotide chain is strengthened mainly by hydrogen bonds formed between oppositely arranged complementary DNA bases (adenine complementary thymine, guanine - cytosine). Tertiary structure of DNA - the spatial arrangement vsho polynucleotide chain. At the core of the DNA molecule is composed of chromatin. The latter consists of protein (histone and nehistonovyh) which wound double-stranded DNA.

The functions of DNA storage, playback and transmission of inherited genetic material, gene expression.

Structure and function of RNA (ribonucleic acid). Unlike the DNA is single-circuit, containing uracil instead of thymine and deoxyribose on the town - ribose. RNA is of several types - and (m) RNA (information or matrix), rRNA (ribosomal), tRNA (transport) hyaRNA (heterogeneous nuclear) myaRNA (small nuclear). Secondary structure contains both twisted and not twisted area. In the tRNA molecule secondary structure resembles the shape "leaf clover" is different functional areas:

- anticodon (for binding to the mRNA codon);
- acceptor site for a combination of amino acids;
- psevdourydylovu to form links with the ribosome;
- dyhidrourydylovu branch need to recognize a specific RNA enzyme aminoacyl-tRNA synthetase.

Basic functions of RNA:

- m (i) RNA - contains information about the amino acid sequence of a protein and therefore is a template for protein synthesis.
- tRNA - carries the amino acids from the cytoplasm to the ribosomes for protein synthesis.
- RNA - forms the ribosome

The basic tenet of molecular biology (Crick postulate). The direction of transfer of genetic information is:

1.Replication DNA - DNA doubling.

2.Transcription- the matrix synthesis of DNA molecules of RNA.

3. In cells infected with RNA viruses involving reverse transcriptase (revertazy) is reverse transcription, ie, DNA synthesis on RNA matrix.

4. In cells infected by viruses can undergo replication of RNA synthesis is a subsidiary of RNA in maternal RNA matrix.

5.Translation - a transfer of information from language to language nucleic acids of amino acids (protein synthesis in ribosomes).

Replication - the process of doubling the DNA (synthesis subsidiaries to parent DNA matrix). Passes BS-phase (synthetic) cell cycle.

Location: mostly in the nucleus and in mitochondria moderately.

Value replication: creation uniform among the daughter cells, transfer of genetic information during cell division.

The mechanism of replication

1.Replication - a matrix process, ie, DNA synthesis occurs in the matrix DNA. The value matrix synthesis:

- has a higher rate;
- provides high accuracy.

2. Straight replication mechanism - Semiconservative, ie the matrix DNA double helix unwinds and each DNA chain completes 2-chain to the entire DNA molecule. That is, each daughter DNA molecule has one chain from the mother, and the second circuit completed by the principle of complementarity.

Enzymes and factors of DNA replication in eukaryotes

1.DNA matrix.

2.Substraty and energy for the synthesis DNAdezoxsyrybonuclkotydthreefosfatus(dATF, dHTF, dTTF, dTsTF).
3.DNAtopoizomeraza twisted DNA.
4.DNAhelikaza pushes a strand of DNA.
5.SSBbilok, binds to DNA chains promoted and prevents them twisted.
6.DNA-polimerazaα-zabezpechuyesyntez primer.
7.DNApolimeraza β - cleaves primer and fills voids newly synthesized deoxyribonucleotides.
8.DNApolimeraza δ - continuing an existing olihorybonukleotyd (primer) on the lead circuit.
9.DNApolimeraza α and ε extend an existing olihorybonukleotyd (primer) on lagging chain.
10.DNAlihaza - stitches Okazaki fragments.
11.Zn2 + -, Mg2 +.

Stages of DNA replication in eukaryotes

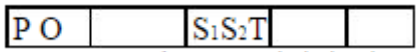
1.Initsiatsiya: the chains of DNA sequence joined:
- DNA topoizomeraza- despiralizuye DNA.
- DNKhelikaza - rozdvyhaye chain DNA.
- polimerazaα DNA, which is the leading chain forms a primer - olihorybonukleotyd (prblyzno consists of 10 rybonukleotydiv), and the behind - some primers.

Plot promoted DNA which is complementary chain synthesis subsidiary called replicative fork.
2.Elonhatsiya: in this process great importance antiparallelism DNA chains. Since DNAantyparalelni chains, aDNA polimerazyzdat lead-synthesis in napryamku5'-3 ', the elongation of both mechanisms antiparallel chains are different. Namely synthesis leading chain starting from the corresponding primer goes away in napryamku5'-3'.Syntez also lagging behind chain is fragmented. It starts from one primer and ends before reaching the other, thus forming Okazaki fragments. Besides synthesis in eukaryotes is the leading chain involving DNApolimerazy δ, and lagging behind DNA polymerases α and ε. Synthesis subsidiaries circuits based on the principle of complementarity.
3.Terminatsiya: DNApolimeraza β - cleaves primer and fills voids again
synthesized deoxyribonucleotides. With the participation of DNA fragments Okazaki lihaz combination. Then formed and DNA twisting supertwisted.

Transcription - a synthesis of RNA to DNA matrix (copying of information from DNA language the language of RNA).

Structural transcription unit is transkrypton - a stretch of DNA from the promoter to the terminator.

The structure of prokaryotic transkryptona (operon):



P - promoter, summoned connecting transcription initiation factors and RNA polymerase.
O - operator, bind him transcription regulators.
S1, S2 - structural genes: have information about the amino acid sequence of a polypeptide
T - Terminator carries information about the termination of pre-synthesis of RNA.
In eukaryotic transcription unlike prokaryotic operator instead isolated area acceptor (A), which connects regulators of transcription.
Eukaryotic transcription factors:
DNA matrix;
 substrates and energy sources is a transcription of ATP, GTP, UTP, TSTF;
 RNA polimerazy. Distinguished:
• RNA polymerase I - is the nucleolus is involved in the synthesis of pre-rRNA;
• RNA polymerase II - contained in the nucleoplasm, synthesizes pre-mRNA;
• RNA polymerase III - located in the nucleoplasm provides syntezpre-tRNA;
 σ (memb) - part of the RNA polimerazyta initiates transcription;
 TATA factor binds to the TATA site (boxing Prybnova) on the DNA molecule and directs RNA polimerazudo starting point of RNA synthesis;
 Zn2 +, Mg2 +, Mn2 +.
The mechanism of transcription in eukaryotes
1.Initsiatsiya transcription
σ -factorRNA - polymerase finds naDNA-lantsyuhupromotor and is associated with it. After TATA-factor interacts corresponding site on the DNA, stimulating movement to the starting point RNApolimerazy DNA synthesis (start site). During his way RNA-polimeraza spins DNA chain.
2.Elonhation of transcription.

Since the start site of RNA polimerazyza principle of complementary towards the 5'-3 'builds a chain of RNA in DNA matrix.
3. transcription termination.
RNA-RNA polimeraza builds chain until she DNA molecule not see a nucleotide sequence that read the same in both directions. These sequences are called palindromes. The synthesized RNA in eukaryotes is functionally immature and inactive, which requires modification.

Posttranscriptional modification of RNA (processing, maturation). This formation of mature, functionally active RNA. Mature RNA is not completely complementary DNA matrix. They formed in the core, and then sent to the cytoplasm.
Posttranscriptional modifications include:
1.Kepuvannya - is joining do5'-kintsyapre-mRNA7-metylhuanozyn.Prohodyt only when ripe m.RNA. Meaning cap initiation of translation m.RNK and protects it from splitting RNA-basics.
2.Poliadeniling - is joining to 3'-kintsyapre-sequence mRNApoliadenil
(AAAA ...). It takes only m.RNA when ripe.
Value: polyadenylic piece m.RNA required for movement of the nucleus to the cytoplasm, and protects from m.RNA splitting RNA-basics.
3.Splicing - is often useless cutting sections (introns) and cross-linking exons. Cut introns is the participation of small nuclear RNA (mya.RNA), which recognizes inrony, cutting them by rozscheplennya3'-5'-fosfodiefiric connections on the verge of exon and intron, and connecting exons. RNA splicing is in all kinds of RNA. As a result of this process preRNA becomes shorter (eg mRNA shorts 4 times).
4.Metyling - addition of methyl groups to the RNA. Held at maturity only
rRNA and t.RNA.

Inhibitors of transcription (inhibit or completely block the transcription)
1. Antibiotics:
-antituberculosis (rifampicin, inhibits RNA transcription initiation stage polimeraz)
-antifungal (antymitsyn D, olihomitsyn - inhibit transcription elongation, as bind guanine and therefore counteract the formation of complementary pre-RNA).
2.Alkaloids - anticancer agents (vincristine, vinblastine - posttranscriptional modification inhibit pre-mRNA transport into the cytoplasm of a mature m.RNA).
3. toxins (α-amanityn- pale toadstool poison that inhibition RNA-polimerazII).
Translation - a translation of information from the language of nucleotides in mRNA amino acid sequence in the polypeptide chain (protein biosynthesis on ribosomes). Factors broadcast
1.Rybosom - a cell organelle composed of protein and RNA. They contain two subunits: small and large. Cubodynytsi ribosomes can be in a dissociated state - which is inactive and associates (active) state.
A large ribosomal subunit contains two centers (sites):
- aminoatsylnyy (A) - with him zvyazuyetsya aminoacyl - tRNA;
- peptydylnyy (L or R) - it formed peptides.
2.20 acids.
3. Do not fewer than 20 tRNAs, as only 20 amino acids and no more than 61 t.RNK, as all 61 codons of content.
4.mRNA (mRNA) - called matrix because there is a template for DNA synthesis and information, because it contains information about the amino acid sequence of the protein in the future.
5.Aminoatsyl-tRNA-amino syntetazaaktyvuye and ensure their connection to the acceptor site of tRNA.
6.Peptydyltransferaza - an enzyme that forms petydni ties.
7. Protein initiation factors, eukaryotic initsiatorni factor - eIF (known eight).
8. Protein elongation factors, eukaryotic elonhatsiyni factors: eEF (three known).
9. Protein termination factors: eukaryotic releasing factor: eRF.
10.ATF, GTP - energy.
11.Mg2 + - stabilizes the structure of ribosomes.

Mechanisms broadcast
- Broadcasting is a matrix process, which ensures high accuracy and speed of the process.
- Reading the information is in the direction 5'-3 '.
- The basis of the process is the principle of complementarity.
Stages of protein synthesis:
I. Activation of amino acids (takes place in the cytoplasm). For the enzyme aminoacyl-tRNA-synthetase is activated amino acids (it connects AMP), and a combination of tRNA.

II. Actually broadcast (held in the ribosome)
1.Initiation broadcast. There are 3 stages:
- formation initiator complex: to the small ribosome subunit connects GTP, initiation factor and initiator aminoacyl-tRNA (which is formilmetionintRNA in prokaryotes and eukaryotes in -metionin-tRNA).
- connecting mRNA to the small ribosome subunit its 5 'end (Cap section). There is a way that kept the complementarity between the mRNA codon and antikodon corresponding tRNA with an amino acid initiator.
- joining the large subunit (GTP spent energy) so that the tRNA with an amino acid located in the R-rybosomy.
2.Elongation broadcast. There are 3 stages:
- accession aa-t.RNAdo ribosome. Free A-center takes new-t.RNK (such as valine) that its anticodon has to be complementary m.RNA next codon. The process requires energy GTP.
- peptide bond formation. Methionine residue from meth-tRNA comes on aminohrupuval-tRNA, thus formed dypeptydyl (meth shaft) - t.RNA all-trybosom. There peptide bond formation involving peptydyltransferaz. This t.RNA methionine passes into the cytoplasm. On the inclusion of one amino acid in the polypeptide required 2 ATP energy (for activation of amino acids) and 2 GTP (for zv'yazuvannyaaa-t.RNAz ribosome)
- stage translocation. To attach the following aa t.RNApotribno-to-release A center.Rybosom moves one codon relative to m.RNA 3 '. This is called translocation. Because this is-center empty, and the m.RNA there is a new codon which will interact novaaa-t.RNA, which anticodon complementary codon m.RNA.
The process is repeated until all the synthesized polypeptide chain.
3.Termination broadcast
Extension of the polypeptide chain will continue until the mRNA does not appear terminating triplets UAA, UAG, CAA. In the area of triplets, involving termination of factors, hydrolytic cleavage is between connections polypeptide and tRNA and the polypeptide is released separately and RNA in the cytoplasm.
III. Postranslation modification polpeptyd - a set of processes that ensure the maturation of polypeptides formed in the broadcast. These include:
- formation of secondary, tertiary and quaternary structures - called folding, carried out with the participation of protein chaperones;
- partial proteolysis - a cleavage inhibitory polypeptide center the active enzyme is inactive enzyme in active (eg, conversion of pepsinogen to pepsin, trypsinogen in trypsin);
- modification of amino acids:
• cutting initiation amino acids (methionine or formilmetioninu);
• carboksyling (provides vitamin K);
• fosforylying;
• iodization;
• hidroksyling (provides vitamin C);
• acylation;
• glycosylation (accession oligosaccharides, vitamin A contributes to this);
• joining lipid metals.
- joining sihnal protein peptides that facilitate transport of proteins to their destination.

Inhibitors of translation (inhibit or completely block protein synthesis)

1. Antibiotics:
- bind to the 50S ribosome subunit prokaryote (microorganism) and therefore block peptydyltransferaz reactions and processes translocation.
These include:
-macrolids (erythromycin, clarithromycin, azithromycin);
-levomitsetyn, lincomycin.
- bind to the 30S subunit of the ribosome and block prokaryotic translation initiation
They include:
-tetratsyclin (Tetracycline, Doxycycline);
-aminohlicozid (strepromitsyn, kanamycin, gentamicin).
2.Protyvirusni preparations:
For example, interferon, activates ts.AMF-proteyinkinazui according inaktyvuyeIF-2ta inhibits the synthesis of viral proteins.
3. Toxins:

For example, diphtheria toxin ADP-accession provides rybozyd translation elongation factor (eEF-2) and its inactivation. This causes inhibition of protein synthesis in human cells.

Regulation of gene expression in prokaryotes

Implemented at the level of transcription. There are two types of regulation:

I. For such induction. Consider on example lactose operon, whose work fairly well studied in E.soli French scientists Jacob and Monod in 1961

The structure of the lactose operon areas are: a promoter, operator, and structural genes terminator. Assign each of the areas addressed in the transcription.

Before promoter is a gene regulator.

Given the presence of glucose in the medium E.soli gene - synthesis controller provides bilkarepresora in an active state, which connects gene-blocking operatromi last. This is a violation moving RNA polimerazydo-structural genes and therefore suppressed their transcription. As a result, reduced synthesis of mRNA and protein, respectively.

If the environment where he lives E.soli make lactose, which is an inducer, it connects to the active protein represoromta inactivates it. The latter can now interact zhenom-operatoromi block it tomuRNK-polimerazalehko can go to the structural genes transcribe them to form appropriate m.RNK. The latter result provides broadcast vidpovidnohobilka synthesis enzyme (β-galactosidase) that will cleave the substrate - lactose.

II. By type of repression (consider onexample histidine or tryptophan operon).

In the absence among the amino acid histidine or tryptofanuhen-rehulyatorsyntezuyebilok-represorv inactive state. The latter does not interact with the operator and because no barriers to moving RNA polimerazydo-structural genes of transcription and mRNA synthesis protein enzymes that provide a synthesis of amino acid histidine or conditions tryptofanu.Za presence among the amino acid histidine or tryptophan, they bind to the protein -represor activate it. Active repressor protein is combined with the operator, which is a violation ruhuRNA polimerazydo-structural genes. Inhibited the transcription of the latter, and mRNA synthesis protein enzymes necessary for the synthesis of histidine or tryptophan.

Regulation of gene expression in eukaryotes

It is much more complex than in prokaryotes and multi-level (at the level of structural organization of the genome, transcription, translation).

I. At the level of structural organization of the genome gene expression regulation feature is provided by the structure of chromatin, the processes of recombination and gene amplification.

1. Features of the structure of chromatin.

There are hetero-taeuhromatyn. In heterochromatin are inactive genes in euchromatin and - active genes.

2.Recombination - this movement of genes within a chromosome or between chromosomes.

In eukaryotes recombination underlie these processes:

- crossinf - is identical exchange areas between homologous chromosomes in their konyuhatsiyi during meiosis.
- The emergence of a useful gene combinations in the evolutionary process.
- Formation variety of antibodies (immunoglobulins): IgG, IgA, IgM, IgD, IgE.
- differentiation of T lymphocytes.

3.Amplification - a process of increasing the number of copies of certain genes due
explosive (often repetitive) replication. Value
Amplification is the basis of:

- resistance to antitumor action of methotrexate
- compensatory reaction in response to intake of heavy metals (metallothionein gene amplification occurs, and therefore induced synthesis of the protein that binds heavy metals).
- polymerase chain reaction (PCR) - the process of obtaining the necessary large number of copies of DNA in vitro (in vitro) due to amplification. It is used for the diagnosis of genetic, infectious, viral and fungal diseases for identification, paternity in forensic medical expertise.

II. At the level of transcription. In acceptor (lider) zone transcrypton next DNA segments are:

- enhancers - when bound to their regulatory substances is enhanced transcription.
- Saylensery - the interaction with their regulatory matters is blocking the activity of transcription.

By regulatory substances that interact with the enhancer or saylenseramy include: steroid hormones, retinoic acid, calcitriol, thyroid hormones, insulin and others.

III. At the level of translation: Made by phosphorylation of translation initiation factor eIF-2 (this form is inactive) and defosforyluvannya (in the form of eIF-2 active). This process is carried cascade and activates cAMP-protein kinase.

Features protein synthesis and gene expression in humans.
1.Protses most active of protein synthesis in the liver.
2. processes of gene expression and protein synthesis respectively play an important role hormones.
3.Vklyuchennya and exclusion gene expression is very slow.
4.More genes are inhibited state.
Mutations - a quantitative or qualitative changes in the genotype of the organism.

Classification of mutations

1. For reasons of origin
- Spontaneous:
• depurynization (loss of DNA purine nuklotyd)
• due to replication errors
• deamination of nitrogenous bases
- induced, due to the impact of mutagens.
2. type of genetic change system:
• genomic mutation - a change in chromosome number. Views:
1.Poliploid - is to increase the number of chromosomes fold halide (ie 2, 3, 4 etc. times);
There are: tryplodiyi, tetraplodiyi etc.
2.Heteroploid - is to increase the number of chromosomes is not a multiple of haploid. For example trisomy on chromosome 21 (Down Syndrome) - chromosome 2n + 1.
• Chromosomal mutation - a chromosomal alteration without changing their number. Views:
1. loss specific chromosome areas;
2.Duplication: doubling the area of the chromosome;
3.Invertion, chromosomes break and rotation detached areas for 1800;
4.Translocation: Area chromosomes from one chromosome is transferred to another
• Gene (point mutations) - is a nucleotide changes in the chromosome. Views:
1.Po type inserts if inserted nucleotides number is not a multiple of "3", it will lead to a shift of reading frame if multiple "3" - is "no."
2.type of deletion: if the number falls nucleotides is not a multiple of "3", it will lead to a shift of reading frame if multiple "3" - is "no." Mutations of suvom reading frame is lethal without reading frame shift is more favorable.
3.type options:
- transitions:
• replacement of one pyrimidine to another pyrimidine nucleotides.
• replacement of one purine to another purine nucleotide.
- transversion: replacement of purine nucleotide to pyrimidine or vice versa.

Mutagens Classification:

1.Physical:
- ultraviolet radiation, causes the formation of covalent bonds between the nitrogenous bases tyminovymy located nearby. This leads to the breakdown of DNA - polymerase in these areas and replication errors.
- ionizing radiation causes:
• ionization of DNA is split off from one atomic electrons, which are joined to other atoms. The result may be DNA fragmentation.
• formation of free radicals (eg OH *), which are able to cleave nucleic acids oxidize their constituents.
2.Biological: viruses, bacteria, fungi, who mounted their nucleic acids in DNA host cells.
3.Chemical:
- analogs of nitrogenous bases, similar in structure to the nitrogenous bases of DNA, but not full compliance. For example: 2-aminopurine, which is able to replace the normal nucleotides in DNA.
- alkylating, able to modify the nitrogenous bases of DNA normal by acceding to the hydrocarbon radicals (methyl, ethyl, etc..). These include: mustard gas and others.
- dezamining (substances in the body's metabolism converts to nitrous acid) that causes the conversion of cytosine to uracil by deamination. These include nitrites and nitrosamines.

DNA repair - a process of resumption of normal primary structure of DNA involving enzyme systems.The biological significance: prevents the transmission of the defective genome from maternal cells subsidiaries.Conditions of reparations, should cover damage to only one chain.
Stages of repair:
1. endonuclease is the injury to the DNA and cleaves phosphodiester bonds. If the damage of UV starts act spetsyfichnaUF-endonucleoz that cleaves DNA chain near dymerT-T.

2.free of damage exonuclease removes the damaged area.
3. site removed the damaged section of DNA polimerazaβ completes DNA chain complementary type.
4.DNA-lihaza connects intact and re-synthesized area.
Pathology repair.
Xeroderma pigmentosum - a disease in which there are defects in DNA repair enzymes (UV-endonuclease). Result of hypersensitivity do UF-light, which leads to the appearance of red spots on the skin, then can develop scabies or cancer.

5.Material for self-control.

A. Tasks for self-control.

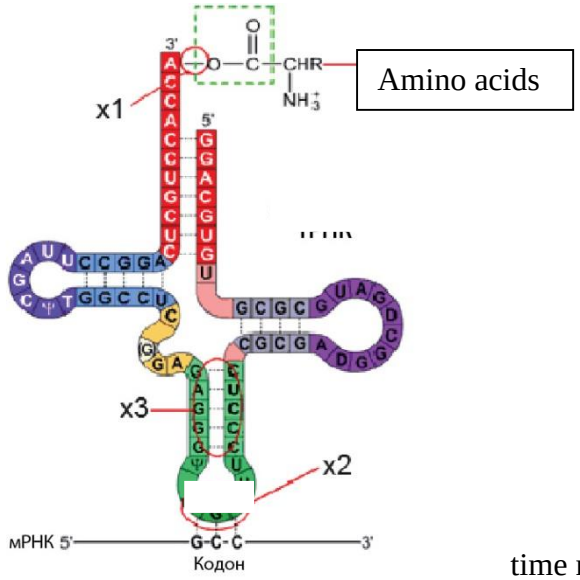
1**.** Fill the table "The composition of protein synthesis systems in pro- and eukaryotic translation for"

№	Stage broadcast	Prokaryotes Eukaryote	Prokaryotes Eukaryote
1	Activation of amino acids		
2	Initiation		
3	Elongation		
4	Termination		
5	The processing and formation of tertiary structure (post translational changes)		

2. Fill the table properties and mechanism of action of antibiotics - inhibitors of translation.

№	Stage broadcast	mechanism of action	antibiotics	Sensitivity (Prokaryotes, eukaryotes cytoplasm, mitochondria eukaryotic)
1	Initiation	…		
2	Elongation	…		
3	Termination	…		

3. Convert encrypted information in the mRNA codons in the sequence of amino acids in the protein molecule is implemented with the participation of tRNA. Using the figure below plots tRNA name and specify their role (x1, x2, x3).



4. The patient who takes a long time methotrexate, observed a gradual decrease in the efficiency of antitumor action of cytostatics. What is the process underlying the development of resistance to methotrexate? Expression of the gene is activated while taking methotrexate? The content of the products of expression of this gene in cells to grow under these conditions?

5. Alkylating agent is dymetylsulfat conversion guanine 6 metoksyhuanin who loses the ability to form complementary relationships with cytosine, and therefore falls outside the codon.
What type of mutation (genomic, chromosomal, genetic) causes dymetylsulfat? Will be marked shift reading frame in such conditions? What are the main stages of

B. Tests for self-control

1. For the treatment of urogenital infections using quinolones - inhibitors of the enzyme DNA hirazy.Hinolon break in bacterial cells:
A. reverse transcription

B. DNA repair
C gene amplification
D. recombination of genes
*IS. DNA replication
2. lagging polynucleotide chain "replicative fork" DNA polymerase forms Okazaki fragments. Name the enzyme that stitches these fragments into a single chain.
A DNA polymerase.
* B DNA ligase.
C RNA polymerase.
D primase.
E exonuclease.
3. Patients with xeroderma pigmentosum characterized by abnormally high sensitivity to ultraviolet light, resulting in skin cancer, due to the inability to restore enzyme systems damaged hereditary apparatus of cells. On the violation of any process related to this pathology?
A.hennoi komplementatsiyi
B.hennoi conversion
C.recombination DNA
* D.reparation DNA
E.reduplication DNA
4. In the second stage of elongation formed peptide bond in A-section, where the second aminoacyl tRNA. In the A-section of the U-N-tolerated tracts formilmetyonin. Add whereby the enzyme is formed first peptide bond?
* A Peptydyltransferaz.
B Translokaz.
C synthetase.
D RNA polymerase.
E DNA polymerase.
5. Streptomycin and other aminoglycosides by binding to the 30S ribosome subunit,, prevent accession formilmetionil-tRNA. What process is disturbed due to this effect?
A transcription initiation
B Termination broadcast
* C translation initiation
D transcription termination
E of replication
6. A man a course of radiation and chemotherapy. The complex drugs included 5-ftordezoksyurydyn - tymidylatsyntaz inhibitor. Synthesis of a substance blocked this drug?
* A. DNA
B. mRNA
C. rRNA
D. tRNA
E. Squirrel
7. Pulmonary tuberculosis patients for rifampicin, which inhibit the enzyme RNA polymerase in the process:
* A Transcriptions.
B broadcast.
C replication.
D reparations.
E amplification.
8.Steroyidni connects hormones with intracellular receptors and affect RNA synthesis. Specify a name for this process.
* A. Transcription
B. Reparation
C. Replication
D. Henetychnarecombination
E. Amplification
9. Given the prolonged intoxication determined a significant reduction in activity of aminoacyl-tRNA synthetase. What is the metabolic process is violated in this case?
* A. The biosynthesis of proteins

B. DNA replication
C. DNA repair
D. Genetic Recombination
E. RNA processing
10. Erythromycin binds to ribosomes sensitive to it prokaryotes and blocks broadcast. What process is hampered by the first of this antibiotic?
* A. protein synthesis
B. Biosynthesis mRNA
C. posttranslational modification
D. DNA repair
E. DNA replication repair are necessary to correct this error.

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"APPROVED"
Head of pharmaceutical, biological and toxicological chemistry Departmnet
PhD in Medicine, Professor _____ I.V.Nizhenkovska
protocol number 2 on August 31, 2017

GUIDELINES
FOR INDEPENDENT STUDENTS WORK
WHILE PREPARING FOR THE PRACTICAL LESSON

Academic discipline	Biological chemistry
Module number	module 2
Module	**Module 5: Exchange of simple and complex proteins.**
Subject lesson number 5	Biochemistry of intercellular communication. Molecular mechanisms of signal transduction hormone. *Qualitative reaction to insulin, adrenaline, folikulin.*
Course	3 year
Faculty	Pharmaceutical
Number of hours	2,5

Kyiv 2017

Prepared by PhD in medicine, Professor I.V.Nizhenkovska

1. Topic actuallity

Coordination of cell and tissue functions provided mechanisms of intercellular communication. In the evolution of living organisms were formed two systems that implement intercellular communication, namely the nervous system that operates through electrochemical conduction of nerve signals, and endocrine system, whose action is realized by chemical bioregulators - hormones. These systems and provide basically the coordination of physiological processes in multicellular organisms.

Hormones and other signaling molecules as ligands realize their biological effects in "target cells" through interaction with specific receptors - protein molecules. After the formation of ligand-receptor complex is transformed regulatory (hormone) signal corresponding genetically programmed for this type of cell biological effector response systems. Violation of the transfer of regulatory (hormone) signals is the basis of many diseases. Learning of molecular and cellular mechanisms of action of hormones needed to understand the role of the endocrine system in the regulation implementing the impact of hormones on the activity of intracellular systems helps to explain the reasons that underlie pathological conditions caused by disorders in the functioning of the endocrine glands and target cells, and shapes the students' approaches to correcting prescription hypo- or hyper- functionof glands.

2. Main goals:

- To interpret the function of hormones and other signaling bioregulation molecule system of intercellular integration and in the life of the human body.
- To analyze and explain the nature of compliance with chemical hormones and other signaling molecules (protein, peptide, amino acid derivatives and steroid) function and mechanism of the "target cells".
- To interpret the definition and structure of different types of receptors "target cells": inotropic, metabotropic, cytosolic
- to characterize the properties of the hormone-like substances or hormones local action, representatives and their biological role;
- Analyze changes in metabolic and biochemical parameters that characterize the metabolism of carbohydrates, proteins and lipids in the disruption of the endocrine glands
- To interpret the action of hormones as drugs and analyze the distribution and shape of calcium in the body, explain the mechanisms of hormonal regulation of calcium homeostasis
- Explain the principle method for determining the chemical structure of various hormones in biological fluids and interpret the data;

3. Basic knowledge, skills necessary for studying the subject (interdisciplinary integration)

Names of previous disciplines	Obtained skills
Physical methods of analysis and metrology	Master the techniques of laboratory research tools.

Biology with the basics of genetics	Classify the structure of biopolymers.
Organic chemistry	Write structural formulas of hormones - derivatives of amino acids.
Physiology	Explain the role of hormones in the regulation of body functions.
Pathological physiology	To explain the basic mechanisms of homeostasis infringement under the influence of hormones.

4.Tasks for independent work during preparation for the classes.

4.1. The list of key terms, parameters, characteristics which the student is to assimilate while preparing for classes

Term	Definition
Conductor proteins	Conductor proteins — G-proteins (or N-proteins) — intramembrane proteins that perceive the chemical signal from the receptor modified through interaction with a hormone or neurotransmitter and cause changes in the functional activity of effector cells.
Secondary mediators	Secondary intermediaries or messengers - biomolecules that transmit information from a hormone effector (primary messenger) in the system effector cells.
Inotropic receptors	Inotropic receptors - such that the interaction of physiologically active compounds cause the opening of ion channels in the plasma membrane and generate development extremely rapid (millisecond) ion currents (Ca^{2+}, Na^{+}, K^{+}, CI^{-})
Membrane receptors	Membrane receptor - a protein molecule (protein) or glycoproteins that are included on the cell surface and react specifically change their spatial configuration to join their molecule chemical compound, hormone or neurotransmitter, that the hormonal signal that passes to the middle of the cell via second messenger or transmembrane ion channels.
Metabotropic receptors	Metabotropic receptors - such that after the interaction of physiologically active compounds lead to the biochemical activation of effector cells through G-protein.
Receptors tyrosine kinase	Receptors tyrosine kinase - membrane receptors which simultaneously serve as the receptor and enzyme transducer.

Physiologically active compounds	Physiologically active compounds — normal, not abnormal compound involved in the natural functioning of the body, tissue or organ. This time, unlike the term biologically active substances, preferably taken with respect to the compounds (substances) that are found in living organisms, eg .: hormones, hormone-like compounds, biogenic amines (histamine, serotonin), vitamins and others. or come from the environment (vitamins, provitamins, plant hormones, etc.) and are directly involved in physiological (vital) processes of the body.
Cytosolic receptors	Cytosolic receptors - are specific receptors for steroid and thyroid hormones, which are localized in the cytosol of target cells, and the result of the activation of which is to change the conformation of the receptor that allows it to communicate with relevant sites and nuclear chromatin modify mRNA and protein synthesis.

4.2 Theoretical questions for the class.

1. Interstitial systems integration. Types of communication between cells.
2. Signal substances as regulators of metabolic processes in the body.
3. Classification of hormones:

- the place of synthesis;
- chemical nature;
- mechanism of action.

1. Molecular organization of metabotropic and inotropic receptors. Second messengers and their role in the mechanisms of hormonal effects on target cells (cAMP (structure, biological effect), cGMP (structure, biological effect) phosphoinositides, calcium ions).
2. The molecular mechanisms of steroid and thyroid hormones (hormone penetration into the cell, binding of cytosolic hormone receptor, the modification (activation) receptor as part of hormone-receptor complex, translocation modified hormone-receptor complex in the cell nucleus, the complex interaction of DNA with sensitive nuclear sites chromatin (impact directly on chromosomes), activation of specific genes, transcription stimulation (formation of mRNA) synthesis of enzymatic proteins that implement the biological effects of the hormone).
3. Cytokine system as the system controls the functional activity of cells (damage, regeneration and apoptosis).
4. The role of hormones in the regulation of calcium homeostasis in the body. Violation of calcium homeostasis (osteoporosis, hyperparathyroidism. Rickets, osteomalacia, marble bones).
5. Pharmaceutical correction functions in the endocrine glands.

4.3. Practical work that is done in class.

Experiment 1. A qualitative response to hormone pancreas (insulin) with nitric acid.

***The principle of the method*:** during the interaction of protein with nitric acid the precipitate is formed.

Process: To 1.0 ml of concentrated nitric acid cautiously along the wall of the tube, make the same amount of insulin solution. At the turn of two liquids formed white amorphous precipitate as a small ring.

Clinical and diagnostic value*.** Insulin regulates carbohydrate metabolism, increases penetration of glucose into cells and promotes its transformation into glycogen; lowers blood glucose, reduce its excretion in the urine, eliminates effects of diabetic coma. In addition hypoglycemic action, insulin causes a number of other effects: increases in muscle glycogen enhances the process of lipogenesis, glucose oxidation to CO2 pentose phosphate pathway, stimulates the synthesis of peptides, reduces consumption of protein, etc. ***Norm (blood serum, onanemptystomach): 29 – 181 pmol/l. A decrease is observed in diabetes, juvenile diabetes (diabetes type I insulin-deficient), as well as pancreatectomy and

others. In diabetes type II hyperglycemia is not dependent on insulin content and changes the structure of insulin-sensitive receptors (postreceptor defects), or decreasing their number, so insulin is no longer act on target cells, and they, in turn, no longer transport glucose inside the cell. Increase of insulin observed in type II diabetes, obesity, uremia, hypercorticoidism.

Experiment2.Qualitative response to epinephrine (reaction with iron chloride (III).

The principle of the method. Adrenaline (metylaminoetanolpirokatehin) - a hormone adrenal medulla - gives reaction characteristic of catechol. Ions of iron (III) it forms a compound phenolate type - emerald green. With further addition of alkali (NaOH), formed adrenochrome cherry - red color.

The process. In the test tube 5 drops of 0.1% solution of adrenaline and add 1 drop of 1-% solution of FeCl3. There emerald green color. By making the resulting solution 1 drop of lye (NaOH) - appears cherry-red color.

The results of the study concluded.

Clinical and diagnostic value. Catecholamine (Adrenaline and noradrenaline) have a wide range of biological effects, activate processes release of energy (stimulation of glycogenolysis, lipolysis), stimulating nerve cells show a tonic effect, as the myocardium (accelerated heartbeat) and the overall vascular (hypertensive effect), smooth muscle, including the gastrointestinal tract, kidney, bronchus. Study of urinary catecholamines allows to characterize the state of sympathoadrenal system. Catecholamines are two main classes of receptors: a-adrenergic and β-adrenergic. Norepinephrine in physiological concentrations is associated mainly with a-receptors. The sympathetic nervous system through the release of norepinephrine plays a central role in the mobilization of free fatty acids in adipose tissue (lipolysis increases the rate of triacylglycerols) that can activate thermogenesis (cold adaptation). The release of fatty acids during prolonged cold, leading to separation processes of tissue respiration and oxidative phosphorylation, resulting in not produced sufficient macroergic compounds, and the energy is dissipated as heat. Importantly, human adipose tissue is not sensitive to the majority of hormones that stimulate lipolysis than catecholamines.

Catecholamine metabolism may play an important role in the development of nervous and mental diseases associated with the occurrence of skeletal disorder automatism and muscle tone (Parkinsonism), emotional sphere (affective pathology), higher forms of purposeful activity and thought (schizophrenia). The content of catecholamines in blood and urine depends on the passage of time per day and from different age children and adults.

Experiment 3. Qualitative reaction to folikulin (estrone).

The principle of the method. Folikulin with sulfuric acid painted in yellow color when heated turns into a yellow-hot.

The process. In a test tube 0.5 ml alcohol solution folikulin and put it in a water bath for 10 minutes. to remove the alcohol. By folikulin remaining in the test tube, adds 6.0 ml of concentrated sulfuric acid and again put the tube in a water bath for 10 minutes. The liquid in the tube painted in yellow color when heated turns into a yellow-green fluorescence with hot.

Clinical and diagnostic value. Estrone (folikulin) - belongs to the group of estrogen synthesized in ovarian follicles - is necessary for the normal development of the female body. Estrone with progesterone provided the menstrual cycle and performance of functions having children. Specific performance - proliferation of endometrial stimulation of the uterus and female secondary sexual characteristics, prevents disorders that occur in women on the background of insufficient function of the gonads. The content of the hormone in the blood serum of women depends on the phase of the menstrual cycle.

4.4. The content of the topic The nervous and endocrine systems provide communication and coordination functions of cells and organs in the whole organism, using electrical impulses or chemical mediators. Among the latter were the first to open hormones. The nerve impulse is perceived synapses, hormonal signal - receptor.

Types of communication between cells:

1.Direct contact cells (ions and signaling molecules are distributed intercellular channels).

2. Local chemical mediators, neurotransmitters, and paracrine factors autokryn.

3.Messenger distant action - endocrine signaling molecules that are transported in blood.

The speed of the signals following types of alarm:

1.For neurotransmitters - there and extinguished in milliseconds. Receptors - proteins ion channels of the postsynaptic membrane.

2. For protein- peptide nature hormone, catecholamines, prostaglandins (minutes). Receptors on the plasma membrane.

3. For the steroid and thyroid hormones (hours, days). Receptors in the cytosol and nucleus.

The organization of endocrine system

1.The central endocrine formation: the pituitary, hypothalamus, pineal gland.

2.Peripheral formation endocrine, thyroid and parathyroid, adrenal glands.

3. Organs with mixed functions, pancreas and gonads, thymus, placenta.

4. Diffuse endocrine system - hormone produced single cells scattered throughout the body (except for skeletal muscle) have a nervous origin and possess endocrine and non-endocrine functions (producing hormones and biogenic amines). Pierce identified these cells in a separate APUD-systeme. Ukrainian abbreviationADPA (Absorbing, Decarboxilation, Predecessors, Amines). There are about 50 types of APUD cells: neurosecretorial cell nuclei of the hypothalamus, pituitary, brain, C-cells of thyroid gland, pancreas, etc.insulocytes.

Classification of hormones according to their chemicalnature :

1.Hormones protein-peptide nature (growth hormone, insulin)

2.Hormones - derivatives of amino acids (thyroid hormones, adrenaline)

3.Hormones -lipids, steroids (hormones adrenal and sex), eicosanoids - derivatives of arachidonic acid (prostaglandins, thromboxanes, leukotrienes, isoprostanes).

Place of synthesis:

1.Hormones central endocrine structures

2.Hormones peripheral endocrine formations.

3.Hormones of mixed functions.

4.Hormones diffuse endocrine system.

The nature:

1. ***True ("real") -hipotalamus hormones,*** pituitary, pineal, thyroid and parathyroid glands, and brain cortical parts of the adrenal glands, pancreas islet staff, male and female gonads. Synthesized by specialized cells of the endocrine glands are secreted directly into the blood, lymph, cerebrospinal fluid, have distant effect, in violation of their synthesis occur characteristic pathology.

2***. Hormone-assosiated substances*** (tissue hormones) - intercellular communication signals have non - endocrine or neuroendocrine origin, synthesized by specialized cells of various organs and tissues are allocated in intercellular fluid, characterized by local (izocrine) action.

The diverse isoprene action

1. *Autocrine regulation* – the effect of free soluble forms of regulatory molecules on the membrane receptors of the same cell that produces them (platelet derived growth factor).

2. *Paracrine regulation* – effect of soluble forms of regulatory molecules that are synthesized effector cells to membrane receptors next few located cells targets (cytokines, acetylcholine).

3. *Juxtacrine* – interaction of membrane-bound forms of regulator on effector cells of membrane bound receptor target cells (hematopoiesis regulation).

4. *Retrocrine* – action free forms cytokine's receptors, that are detached from effector cells, to membrane bound form of cytokine located distant target cells.

The examples of hormone - associated compounds

1.Gastrointestinal hormones: gastrin - stimulate secretion of pepsin and hydrochloric acid secretin - bicarbonate pancreas.

2.Biogenic amines, epinephrine, norepinephrine, histamine, serotonin.

3.Eicosanoids, prostaglandins, leukotrienes, thromboxanes, prostacyclin, izoprostane.

4.Hormones and mediators of the immune system: thymosin, tymopoetyn - lymphopoiesis stimulants. 5.Opioid brain peptides, endorphins and enkephalins - proopiomelanokortyne degradation products (POMK) have the effect of morphine.

6.Natriuretic peptides stimulate diuresis increasing the urinary excretion of Na + and Cl- and water.

7.Peptides kinin-anhiotenzynovoyisystem blood: kalidyn, bradykinin, angiotensin.

8.Calcitriol - the active form of vitamin D3 - regulator of phosphorus - calcium exchange.

9.Cytomedine:

a) peptide growth factors that regulate cell proliferation and diferentiation; b) cytokines (interleukins) - a family of growth factors secreted mainly by leukocytes and shape the immune response (lymphokines, monokines).

Regulation of hormone secretion

1. *Nervous (neurohumoral)* -through sympathetic and parasympathetic nervous system. As example, adaptation syndrome Stress factors: hormones activate the hypothalamic - pituitary - adrenal.

2.*Metabolic* – due to the impact of metabolites in blood chemoreceptors. Increasing concentrations of glucose in the blood stimulates synthesis and inhibits insulin - adrenaline.

3.*Tropic (humoral)* – through tropic pituitary hormones influence the secretion of hormones of peripheral endocrine glands on a "straight-feedback" link or «plus - minus « interaction.

In the transition from one level to another is the increased hormonal signal (cascade system strengthening): 1 molecule release factor hypothalamus stimulates the synthesis of 10 molecules tropic hormone, the latter - 100 molecules executive hormone, which is perceived by receptors of cell - target often becomes stronger, causing the formation of millions metabolite molecules.

The mechanisms of hormonal signal transmission

1.Membrane mechanism – characteristic hormone protein and peptide nature and catecholamines, realized through receptors on the plasma membrane-cell target. The receptor - a protein (glycoprotein) that specifically recognizes a ligand. It consists ofseveral areas (domains): a) extracellular (identifying) in plasma membane; b) transmembrane, providing orientation in the membrane receptor; c) intracellular responsible for communication with the system of intracellular receptor signaling.

The types of receptors:

1.Inotropic type receptors – combine function and ion channel receptor - ligand binding causes the opening of ion channels and ion currents of appearance.

2.Metabotropic type receptors – ligand binding activates transducer G- protein through him membrane enzymes. This promotes the formation of secondary messengers that activating proteins kinase or braking-proteins phosphatase, phosphorylates executive proteins.

3.Tirosin kinase receptors, presented a protein that combines the functions receptor and enzyme transducers (insulin receptor).

Protein - transducers. Example of -G- protein of four types:

1.Stimulate adenilate cyclase and synthase of c-AMP(for adrenaline, glucagon).

2. And inhibit adenylate cyclase activating phosphodiesterase and lower level c-AMP (somatostatine, prostoglandin).

3. Activate phospholipase C (vasopresin).

4. Activate GTF-ase (related to oncoproteins).

Secondary messengers:

Cyclic adenosine monophosphate (c-AMP) ATP is formed by the action of adenylate cyclase, activates proteinkinase A family that transfer phosphate residues from ATP to serine and threonine oxy-groups proteins. A protein activates enzymes executive.

Cyclic guanosine monophosphate (c-GMP) synthesized from GTP guanylate cyclase, activates proteinkinase family G, phosphorylase proteins that transport chloride ions, water, relax smooth muscles of blood vessels and heart.

Calcium-kalmodulin messenger. Many enzymes are calcium-depends (phosphodiesterase, phosphorylase, proteinkinase etc.). Mechanism of many neurotransmitters and hormones include the release of calcium ions, which is due to the opening of calcium channels of the plasma membrane and extracellular calcium entry or exit of its domestic stores. Calcium binds to the protein calmodulin -

universal mediator effects of Ca2 +. This complex activates protein kinase and appropriate phosphorylates proteins with the executive functions of the change.

Phosphoinositideanddiacylglicerinemessenger. After they sell their effect vasopressin, oxytocin, kininogens. The receptor is composed of two domains (contact and catalytic) and depends on G-protein. The catalytic site activates phospholipase C, which hydrolyzes membrane phospholipids (phosphatidylinositol) to inositol-1,4,5-triphosphate (ITP) and dyacylglicerol (DAG). ITF opening calcium channels, stimulates the output of calcium in the cytosol and activation of protein kinases phospholipid - dependent. DAG is active through protein kinase C, which phosphorylates more than 10 enzymes.

Reactive oxygen species as messengers: superoxide radicals, hydrogen peroxide, hydroxyl radicals, hypochlorite. The presence of a protein cysteine and methionine does s sensitive to oxidants, especially regulatory proteins (protein, proteinphosphatase, transcription factors). Nitrogen oxide (NO) is synthesized from arginine, nitrogen forms complexes with metals. Some proteins (guanylate cyclase) activates other (catalase, cytochrome oxidase) brakes. Forms methemoglobin to hemoglobin. There is a relaxation factor vessels. Nitroglycerin, viagra exert their effect by NO, which using c-GMP, relaxes smooth muscles of blood vessels. The powerful mediator of inflammation.

Peroxynitrite activates proteins through their nitration..

Carbon monoxide is formed from heme when exposed to it hemoxydase, relaxes blood vessels, bile ducts, inhibits intestinal motility, activate platelets.

2. Cytozolic mechanisms hormonal signal transmission hormone lipid nature (sex, steroids, eicosanoids, hormone form of vitamin A and D3, thyroid hormones.

Mechanisms of action:

1. Penetration into the cell hormone.
2. Cytosolic receptor binding that has an affinity for the hormone to specific DNA segments.
3. Penetration hormoneretseptor complex in the nucleus.
4.Interaction with specific DNA segments.
5. Activating transcription of specific genes.
6. Protein synthesis, realizing the biological effect of hormones.

Eicosanoids – derivatives of arachidonic acid, prostaglandins, prostacyclin, thromboxanes, leukotrienes, izoprostany.

Bioeffects of prostaglandins, regulate the tone of smooth muscles of blood vessels (lower or raise blood pressure), bronchi (relaxation or spasm), stimulate the muscles of the uterus, inhibit secretion of hydrochloric acid and so on. Prostacyclin has vasodilatations and antiagregative action. Thromboxane stimulate platelet aggregation. Prostaglandins, thromboxanes and leukotrienes - inflammation mediators.

Hormones as drugs:

1.Hormone replacement therapy, insulin diabetes.
2. Stimulating hormone - HGH.
3. Blocking or braking hormone - inhibitors of the synthesis of sex hormones in some oncologic diseases.

Table 1. List of major human hormones:

Structure	Name	Short name	Place of synthesis	Mechanism of action
Tryptamine	melatonin (N-acetyl-5-*Methoxytryptamine*)		pineal gland	
Tryptamine	serotonin	5-ht	*Enterochromaffin*-like *cells*	
Tyrosine derivative	thyroxine	T4	thyroid	thyroid hormone receptor
Tyrosine derivative	Triiodothyronine	T3	thyroid	
Tyrosine derivative (Catecholamine)	epinephrine		adrenal glands	

Structure	Name	Short name	Place of synthesis	Mechanism of action
Tyrosine derivative (Catecholamine)	norepinephrine		adrenal glands	
Tyrosine derivative (Catecholamine)	dopamine		hypothalamus	
Peptide	Anti-Müllerian hormone (Müller substance, inhibitor)	AMH	Sertoli cells	
Peptide	adiponectin		adipose tissue	
Peptide	Adrenocorticotropic hormone (corticotropin)	ACTH	prehypophysis	cAMP
Peptide	angiotensin, Angiotensinogen		liver	
Peptide	antidiuretic hormone (Vasopressin)	ADH	posterior pituitary	
Peptide	Atrial natriuretic peptide	ANP	heart	cGMP
Peptide	Gastric inhibitory polypeptide	GIP	K-cells of duodenum and small intestines	
Peptide	calcitonin		thyroid	cAMP
Peptide	corticotropin-releasing hormone	CRH	hypothalamus	cAMP
Peptide	Cholecystokinin (pancreozymin)	CCK	i-cells of duodenum and small intestines	
Peptide	erythropoietin		kidneys	
Peptide	follicle-stimulating hormone	FSH	prehypophysis	cAMP
Peptide	gastrin		G-cells of the stomach	
Peptide	Ghrelin (hunger hormone)			
Peptide	glucagon		pancreas (alpha-cells)	cAMP
Peptide	Gonadotropin-releasing hormone (gonadoliberin)	GNRH	hypothalamus	Inositol-3-phosphate

Structure	Name	Short name	Place of synthesis	Mechanism of action
Peptide	somatotropin-releasing hormone	GHRH	hypothalamus	IP3
Peptide	human chorionic gonadotropin	hcg, HCG	placenta	cAMP
Peptide	placental lactogen	PL, HPL	placenta	
Peptide	somatotropin hormone (GH)	GH or hgh	prehypophysis	
Peptide	inhibin			
Peptide	insulin		pancreas (beta cells)	tyrosine kinase Inositol-3-phosphate
Peptide	insulin-like growth factor (somatomedin)	IGF		tyrosine kinase
Peptide	Leptin			
Peptide	luteinizing hormone	LH	prehypophysis	cAMP
Peptide	Melanocyte-stimulating hormone	MSH	prehypophysis	cAMP
Peptide	neuropeptide Y			
Peptide	oxytocin		posterior pituitary	Inositol-3-phosphate
Peptide	Parathyroid hormone	PTH	parathyroid gland	cAMP
Peptide	prolactin		prehypophysis	
Peptide	relaxin			
Peptide	secretin	SCT	upper small intestine	
Peptide	somatostatin	SRIF	pancreas (delta cells of the islets of Langerhans), hypothalamus	

Structure	Name	Short name	Place of synthesis	Mechanism of action
Peptide	thrombopoietin		liver, kidneys	
Peptide	Thyrotropin		prehypophysis	cAMP
Peptide	Thyrotropin-releasing hormone	TRH	hypothalamus	Inositol-3-phosphate
Glucocorticoid	cortisol		adrenal cortex	
Mineralocorticoid	aldosterone		adrenal cortex	
Sex steroid(androgen)	testosterone		testicular	nuclear receptor
Sex steroid(androgen)	*Dehydroepiandrosterone*	DHEA	adrenal cortex	nuclear receptor
Sex steroid(androgen)	androstenediol		ovaries, testes	
Sex steroid(androgen)	dihydrotestosterone		multiple	
Sex steroid(androgen) (estrogen)	estradiol		follicular apparatus of the ovaries, testicles	
Sex steroid (progestin)	progesterone		ovarian corpus of luteum	nuclear receptor
sterol	calcitriol		kidneys	
eicosanoid	prostaglandins		Semen	
eicosanoid	leukotrienes		leukocytes	
eicosanoid	prostacyclin		endothelium	
eicosanoid	thromboxane		platelets	

Table 2. Humoral mechanism of regulation of the intensity of metabolism

Hormone	Carbohydrates	Lipids	Protein
Adrenalin	↑ glycogenolysis (liver and muscles)	↑ lipolysis	-
Glucocorticoids	↑ gluconeogenesis	↑ lipolysis	↓ synthesis ↑ decay

Glucagon	↑ glycogenolysis (liver not in muscles) ↑ gluconeogenesis ↓ glycogenesis	-	-
Insulin	↑ transport in cells, especially muscle and liver ↑ glycogenesis ↓ *Glycogenolysis* ↓ gluconeogenesis	↑ lipogenesis from carbohydrates ↓ lipolysis	↑ synthesis ↓ decay
Thyroid hormones	Strengthening of many metabolic processes especially ↑ protein synthesis and ↑ decay of lipids and carbohydrates		
growth hormone	↓ transport in cells, especially muscle and liver ↑ gluconeogenesis	↑ lipolysis	↑ synthesis
Testosterone	-	-	↑ synthesis, mainly in the muscles
Estrogen	-	↑ lipogenesis in specific places	↑ synthesis

5. Materials for self - control.

A. Tasks for self-control.

1. Fill in the table and set the overall effect of insulin on carbohydrate, lipid and protein metabolism.

Metabolic way	**Effect**	**Enzyme - target**
(Example) Glycolise	Increase	Glicogenes↑ Phosphofructokinase↑ Piruvatkinase↑
Gluconeogenes		
Glicogenes		
Glicogenolis		
ПФШ		
Lipogenes		
Lipolis		
Ketogenes		
Synthase of proteins		
Protein breakdown		

2. The lifetime of most hormones in the blood is relatively small. For example, if you enter an animal radiolabeled insulin, the hormone half entered inactivated in the blood within 30 minutes. Why is relatively fast inactivation of circulating hormones? As can be maintained a constant level of hormone

in the blood under normal conditions, given its rapid inactivation? What are the ways the body makes rapid changes in the concentration of circulating hormones in the body?

3. When the disease of women with breast cancer, one of the treatments is to remove the ovaries. Besides introduce additional male sex hormones. Explain the biochemical basis of this treatment.

4. The patient with angina for nitroglycerin. Add a messenger that comes of it. Which it is formed amino What is the mechanism of this messenger?

5. A patient 20 years entered the endocrinological clinic, diagnosed with Type I diabetes. With the lack of which hormone synthesis related to this pathology? Is it appropriate to determine the blood content of insulin in the patient? Research content of a substance in the blood indicates the activity of insulin synthesis?

B. Test for self - control

1. The child has been delayed physical development. What hormone is designed to stimulate growth?

A. Insulin
B. Glucagon
***C.** Somatotropin
D. Adrenalin
E. Paratirin

2. Injection of adrenaline leads to increased blood glucose levels. What process is activated mainly with?

A Synthesis of glicogen.
***B** The collapse of glycogen.
C Synthesis of fatty acids.
D Pentose phosphate cycle.
E Alcoholic fermentation.

3. As a result there is a violation of the tumor adenohypophysis synthesis of trophic hormones and there acromegaly. Specify the level of which increases hormone?

***A** Somatotropin.
B Vasopresin.
C Lutein.
D Oxytocin.
E Follicle.

4. Glucocorticoids have anti-inflammatory activity. This is due to the increase in their participation of the synthesis of specific proteins that inhibit the activity of phospholipase A2. Which compound is released as a result of this phospholipase and is a precursor of pro-inflammatory substances?

A. phosphatidic acid
B. diglyceride
C. Phosphoinositide
***D.** Arachidonic acid
E. Phosphoholin

5.During the operation on a thyroid gland disease on diffuse toxic goiter was mistakenly removed parathyroid glands. Having cramps, tetany. The exchange is initiated bioelements?

A. Magnium.
*B. Calcium.
C. Kalium.
D. Iron.
E. Natrium.

6. Patients with insulin-dependent diabetes treatment using daily injections of insulin. After binding to its receptors of this hormone activates ...

A. The formation of uric acid
B. Synthesis of ammonia

***C.** Transport of glucose to the cells

D. Cell division

E. The synthesis of phospholipids

7. The patient complains of constant thirst. Daily urine output of 3 - 4 l, the concentration of glucose in the blood is situated in the normal range. The lack of which hormone can lead to these changes in the body?

A. Adrenaline

B. Glucagone

C. Insulin

D. Tiroxin

***E.** Vasopresin

8. The patient after injection to high doses of thyroxine increased body temperature. Hyperthermia in this case caused by the separation of biological oxidation and:

A Oxidative decarboxylation of pyruvate

B Oxidative deamination of amino acids.

C Lipid peroxidation.

* D Oxidative phosphorylation.

E Beta-oxidation of fatty acids.

9**.** The patient was administered the drug during the week theophylline - cAMP phosphodiesterase inhibitor. Action is the hormone may increase against the background of such treatment and lead to hyperglycemia?

* A. Glucagon

B. Testosterone

C.Aldosterone

D. Insulin

E. Estradiol

10**.** The 4-month-old baby pronounced occurrence of rickets. Disorders of digestion is not selected. A child is much in the sun. For two months she received vitamin D_3, but signs of rickets is not decreased. What can explain the development of rickets in children?

A. Violation synthesis of calcitriol.

B. Violation synthesis of calcitonin.

* C. Violation of PTH synthesis.

D. Violation of the synthesis of thyroxine.

E. Violation of the synthesis of insulin.

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GUIDELINES
FOR INDEPENDENT STUDENTS WORK
WHILE PREPARING FOR THE PRACTICAL LESSON

Academic discipline	Biological chemistry
Module number	module 2
module	**Module 6: Molecular mechanisms of action of hormones and vitamins**
Study subject number 6	Biochemical basis vitaminology. Vitamins as pharmaceuticals. *Qualitative reaction to vitamins B2, B6 and E.*
Course	3 year
Faculty	Pharmaceutical
Number of hours	2,5

Kyiv 2017
Prepared by Assistent V.P.Narokha

1. Topic actuallity

Vitamins - a low molecular weight organic substances are essential components of food that are essential for normal metabolism, so knowledge of their structure and mechanisms of diseases that occur when vitamin deficiency, are important components of higher medical education.

Water-soluble and fat-soluble vitamins are involved in metabolism as coenzymes and activators of many enzymatic and non enzymatic processes. All B vitamins after intake of metabolized to physiologically active compounds - coenzyme constituting the active centers of many enzymes that catalyze key metabolic processes and energy.

Fat-soluble vitamins in the body perform coenzyme, antioxidant, regulatory, visual and other important functions, so knowledge of their structure, mechanisms of action and ways to prevent diseases that occur in their failure, are useful for practical medicine.

Violation of assimilation and intake of vitamins in the body or pathology of metabolism, reduces the intensity of energy and plastic metabolism, accompanied by dysfunction of several organs, reduced immunity to viral and infectious diseases, the loss of the body's ability to adapt to various adverse factors.

Lack of adequate supply of vitamins leads to hypovitaminosis with typical clinical manifestations.

2. Concrete objectives:

- characterize biological properties, sources, daily need and role in the metabolism of water- and fat-soluble vitamins and vitamin-like substance.
- explain the role of water-soluble vitamins as pharmaceuticals.
- Explain antivitamins use as enzyme inhibitors as drugs.
- Explain the use of dietary supplements as a means of prevention of hypo- and beriberi.
- Know the principle method for determining various water-soluble and fat-soluble vitamins in biological fluids and interpret the data;

3. Basic knowledge, skills necessary for studying the subject (interdisciplinary integration)

Names of previous disciplines	Obtained skills
Physical methods of analysis and metrology	Master the techniques of laboratory research tools
Biology with the basics of genetics	To classify the structure of biopolymers.
Organic chemistry	Write structural formulas water- and fat-soluble vitamins and vitamin-like substance.
Pathological physiology	To explain the basic mechanisms of metabolism of vitamins

4. Tasks for independent work during preparation for the classes.

4.1. The list of key terms, parameters, characteristics which the student is to assimilate while preparing for classes

Term	Definition
Vitamins	low molecular weight organic compounds of different chemical nature that are necessary for the life of a living organism in small doses, and do not form in the same body in sufficient quantities, because that should come from food.
Provitamin	precursors of vitamins in the body.
Antivitamins	substances that cause suppression or complete loss of the biological activity of vitamins and lead to hypo- or avitaminosis even under conditions sufficient security body with vitamins.

Vitamin-like substance	a group of organic compounds of different chemical structure, in which a lack of food or insufficient flow at which the body is not sharply marked changes in the metabolic processes of the body.
Biologically active additives (BAA)	a special food product intended for consumption or administration within the physiological norms to diets or food in order to provide them with diet, health, health care properties to ensure normal and restore disturbed functions of the human body.

4.2 Theoretical questions for the class.

1. Vitamins as essential biologically active food components, their classification and nomenclature, the role and importance in metabolism.

2. Water-soluble coenzyme vitamins (B1, B2, PP, B6, B12, H, folic acid, pantothenic acid, vitamin C, P):

• structure of biologically active forms;

• biochemical function and role in metabolism;

• sources and daily need.

3. Fat-soluble coenzyme vitamins (A, D, E, C, F):

• structure of biologically active forms;

• biochemical function and role in metabolism;

• sources and daily need.

4. The vitamin-like substance and their biological functions.

5. Antivitamins most important representatives, their mechanism of action.

6. The use of vitamins and antivitamins medicine.

4.3. Practical work

Experiment 1. Determining the vitamin B_2 (ribophlavin)

The principle of the method: response based on the ability of vitamin B2 to oxidation and reduction. In the transition from the reduced form of riboflavin in oxidized observed the color change from yellow (riboflavin) to red (rodoflavin) and in the future - colorless (leykoflavin). The transformation of the reduced form of vitamin B2 is oxidized in the reaction with concentrated hydrochloric acid in the presence of zinc. ***The process***: 1 ml of riboflavin added 0.5 mL of concentrated HCl, and a small piece of metallic zinc. Observe the color change. Conclude.

The clinical – diagnostic meaning: Riboflavin is part of the flavin cofactors, including FMN and FAD, which is the prosthetic group of enzymes flavoproteyidiv participating in numerous oxidation substances in cells, carrying electrons and protons in the respiratory chain; oxidation of pyruvate, succinate, α-ketoglutarate, α-hlitserolfosfatu fatty acids in the mitochondria; oxidation of biogenic amines, aldehydes, and so on. d. In clinical practice using riboflavin and coenzyme preparations: flavinmononukleotyd (FMN) and flavinat (FAD) in various dosage forms. They are used in hiporyboflavinozi, skin diseases, eye; dermatitis and ulcers that are not healing, inflammation of the cornea (keratitis), conjunctivitis (inflammation of the conjunctiva).

Experiment 2. Determining the vitamin B_6 (pirudoxin)

The principle of the method: Vitamin B6 in the interaction with a solution of ferric chloride forms a complex salt type iron phenolate red.

The process: 5 drops of vitamin B6 (1% solution) was added the same amount of 1% solution of ferric chloride and stirred. The liquid is colored red. Conclude.

The clinical – diagnostic meaning: Primary coenzyme pyridoxal-5-phosphate

part of almost all classes of enzymes: oxidoreductases, transferases, hydrolases, and LiAZ isomerase. Now we know more than 20 pirydoksalevyh enzymes that catalyze key metabolic reactions nitrohenovoho. Pyridoxal-5-phosphate is a coenzyme aminotransferase that carry the amino group of the amino acids in α-keto acids, decarboxylase amino acids involved in the formation of biogenic amines, enzymes MAO and DAO that neutralize biogenic amines, enzymatic reactions neokysnyuvalnoho deamination of serine and threonine, lipid tryptophan to nicotinamide in the synthesis of δ-aminolevulenovoyi acid forerunner of heme in the process of glycogenolysis and others.

Experiment 3. Determining the vitamin E.

***The principle of the method*:** alcoholic solution of α-tocopherol oxidized ferric chloride (Fe + 3) tocopherol quinone red.

The process: in dry tube pour 4-5 drops of 0.1% alcoholic solution of α-tocopherol, add 0.5 ml of 1% ferric chloride, intensely mixed. The contents of the tube becomes red. Conclude.

The clinical – diagnostic meaning. Vitamin E (tocopherol) is a powerful antioxidant and a major. Its action is aimed at strengthening tissue respiration and maintaining constant free radical peroxidation. Indirectly as a cofactor vitamin E is involved in the transport of electrons and protons in the respiratory chain, stimulates the synthesis of ubiquinone.

Tocopherol is a "trap" for free radicals - forms with them inactive forms that break off free-radical chain. This vitamin E protects against lipid peroxidation polyunsaturated fatty acid composition of cell membranes. Hypovitaminosis accompanied membrane pathology as peroxide hemolysis of red blood cells, fetal resorption during pregnancy, muscular dystrophy, liver necrosis, softening of brain atrophy sim'yannykiv, leading to infertility.

4.4. The context of the topic

Currently, there are more than 30 vitamins, deciphered their chemical structure that gave opportunities to synthesize most of them.

For vitamins from a number of features:

1. Unlike other essential substances (amino acids, fatty acids, etc.). Vitamins are not plastic material or energy source.

2. Vitamins active in minimal amounts. Daily demand for them is calculated in thousandths and even millionths of a gram.

3. Vitamins are not synthesized human body, except for some of them. Thus, vitamins B6, B12, K, folic acid formed in the body microflora of the large intestine, Vitamin D - synthesized under the action of ultraviolet rays on human skin, but in insufficient quantities.

4. Vitamins are usually not deposited "in reserve". Therefore, these substances should ingested at every meal.

5. The most efficient synthetic vitamins are not, and those contained in food. This is because of the food consists of several different vitamins that enhance physiological effect each other as well as stimulants, stabilizers or their actions.

Vitamin's functions. Vitamins provide normal biochemical and physiological processes in the body. They participate in catalysis of metabolism, as contained in the active groups of enzymes. For example, vitamin PP is a coenzyme dehydrogenase carrying out the first stage of oxidation of proteins, fats, carbohydrates; Vitamin B1 is part of an active enzyme that catalyzes the splitting of one of the main metabolic intermediates - pyruvic acid; Vitamin B12 plays a role in the synthesis of proteins. That is why the lack of vitamins in the diet or the violation of their assimilation negative impact on many fundamental metabolic processes.

Vitamins have a protective effect, neutralizing the impact of various negative factors. In healthy people, they increase resistance to cold, infectious diseases, physical overload. Patients vitamins help to normalize metabolism, improves the effect of remedies, neutralize the side effects of drugs, reduce the effects of radiation.

With no food in one or more vitamins vitamin deficiency develops. It comes in two levels: vitamin deficiency and vitamin deficiencies.

Beriberi - a state of profound deficiency of a vitamin in the body of expanded clinical deficiency (scurvy, beriberi, pellagra, etc.).

Hypovitaminosis - the state body in low content of one or more vitamins in food. Vitamin deficiencies are more common in late winter, spring, when the intake of vitamins from food is very limited because they are destroyed in the process of food storage. There are primary and secondary hypovitaminosis.

Primary hypovitaminosis linked with low vitamin in foods that may occur due to the following reasons:

1. unilateral unbalanced diet mainly refined products, insufficient use of products of plant origin.
2. Wrong culinary processing of food, leading to the destruction of vitamins.
3. The use of preservatives which destroy vitamins.
4. Improper storage conditions of products containing vitamins.

Secondary hypovitaminosis develop in cases where the reduced ability to absorb vitamins or increased demand for them. This may be associated with dysfunction of the gastrointestinal tract. In infectious diseases increased need for vitamins because of their cost in the formation of antibodies. Treatment of some drugs may increase the need for vitamin as a result of their increased allocation from the body or disturbance of synthesis in the colon. In this way, affect the body, such as antibiotics and other antibacterial agents.

When excessive intake of vitamins are usually excreted through the kidneys in urine. In some cases, their content increases and developing hypervitaminosis, which leads to metabolic disorders. Especially dangerous in this respect overdose of vitamins A and D, which is prescribed to children to prevent rickets and growth disorders.

Widely systematization of vitamins based on their solubility in water or fats. One group consisted of water-soluble vitamins, the other - soluble. However, some fat-soluble vitamins was synthesized water soluble analog. For example, vikasol is a water soluble analog of vitamin C, soluble in fats.

Several vitamins is presented not one but several compounds that show biological activity. An example is the group of vitamin D. To indicate these compounds are numbers - D2, D3.

Under distinguish vitamins vitamin-like substance, the degree of indispensability are not yet defined. However, they do a beneficial effect on metabolism, especially in extreme conditions.

A number of products containing provitamins, ie compounds of which are formed in the body vitamins. These include carotenes, which are split in several tissues with the formation of retinol (vitamin A), some sterols (ergosterol, 7 and dehidroholesterol al.), Which are converted into vitamin D when exposed to ultraviolet rays.

Water-soluble vitamins

This group includes a large number of vitamins, including vitamin B complex, vitamin C and others.

Table 1. Water-soluble vitamins

Name	Daily norm	Co-enzyme form	Biological functions	Avitominoses
B_1 tiamin	2-3	tiaminpyrophosphate	decarboxylation α-keto acids, the transfer of active aldehyde (transketolase)	polinevrit
B_2 ryboflavin	1,8-2,6	flavinmononucleotide	In the respiratory enzymes that transfer hydrogen	The defeat of the eye (keratitis, cataracts)
B_5 pantotanic acid	10-12	(KoA-SH)	Transportation acyl groups	Degenerative changes in the adrenal glands and nervous tissue
B_6 pirydoxin	2-3	pyridoksalphosphate	The exchange of amino acids (transamination, decarboxylation)	Increased excitability of the nervous system, dermatitis
PP niacin	15-25	nicotinamid	Hydrogen acceptors and carriers	Symmetrical dermatitis on exposed areas of the body dementia and diarrhea
H biotin	0,01-0,02	biotin	Fixing CO2 reaction karboksyluvannya (Naprykladr, pyruvate and acetyl-CoA)	Dermatitis, accompanied by enhanced activity of the sebaceous glands
B_c folic acid	0,05-0,4	Tetrahydrofolic acid	Transportation one carbonic groups	Violation of hematopoiesis (anemia, leukopenia)

B_{12} cobalamin	0,001-0,002	Dezoksyadenozyn- and metylkobalamin	Transportation methyl group	Macrocytic anemia
C Ascorbinic acid	50-75		Hidroksyluvannya proline, lysine (collagen synthesis), antioxidant	Bleeding gums, loosening teeth, subcutaneous hemorrhage, edema
P rutin	Is not determined		However, vitamin C is involved in redox processes, inhibits the action of hyaluronidase	Bleeding gums and pinpoint hemorrhages

Fat-soluble vitamins

All fat-soluble vitamins are derived isoprene diene hydrocarbons. They are hydrophobic, are part of the membrane, and with the exception of vitamin D, are antioxidants. The main functions of these vitamins are coenzyme and hormone. They are absorbed in the intestine involving bile, bile duct obstruction so can lead to vitamin deficiency. Unlike water-soluble these vitamins can accumulate in the tissues and cause hypervitaminosis status (vitamins A and D).

Vitamin A (antykseroftalmichnyy, retinol). The original β-iononu.Ye two main forms of vitamin, retinol and dehidroretynol. Biological effects of retinol needs to convert it into active metabolites. Ethyl alcohol retinol is oxidized to aldehyde (retinal) and further involving retinal aldehyde is oxidized to retinoic acid, which is a hormonal form of vitamin A and operates at the level of the genome. Another way exchange of vitamin A - related to participation in the act of perception of light and requires trans isomerization retynoluv11-cis-retinol. There are three main functions of vitamin A:

1. Visual - carried aldehyde form of vitamin A.

2. Control the differentiation and proliferation of epithelial cells. This function of vitamin A is implemented at the level of the genome and requires penetration of retinoic acid into the nucleus, where it binds to receptors. Last acquires the ability to bind other regulators (hormones). This ternary complex is joined to DNA and regulates the transcription of genes that express the factors of differentiation and cell growth.

3. Participation in the reproduction gametes realized retinoic acid. Vitamin A deficiency is accompanied by decreasing production of sperm, ova violation implantation of a fertilized egg, miscarriage.

Coenzyme function. Retinol is involved in the synthesis of glycoproteins as a cofactor hlikozyltransferaz that carries oligosaccharide residues through the membrane. Glycoproteins - the basis of mucin - mucus that covers harboring epithelial digestive tract and respiratory tract, urinary and genital tract, eyeball, sloznyh channels because of vitamin A deficiency also causes dryness of mucous membranes.

The importance of vitamin A and, especially, its precursor β-carotene, has both antioxidant that protects membranes from oxygen radicals.Vitamin A is only found in animal products, egg yolks, liver, butter, fish oil, in plant foods (carrots, tomatoes) contain carotenes. For the absorption of vitamin A and carotene needs fat.

Daily requirement: 1,5-2,5mh (3-5mh carotene).

The main manifestation of vitamin A deficiency is a day-blindness (night blindness) - a violation of the dark, dark adaptation period podovzhyennya pathology of epithelial tissues - keratomalyatsiya, keratinization. Deficiency leads to increased risk of malignancies.

Hypervitaminosis: eye inflammation, hyperkeratosis, hair loss, hiperdozy can lead to death.

Vitamin K. This naphthoquinone derivatives. Vitamin K1 - filohinon. Vitamin K2 - farnohinon less active. It has vitamin activity and water-soluble synthetic analog K3 - without side chain - vikasol (Ukrainian scientist Palladin, 1942). Vitamin K - Antihemorrhagic vitamin, its deficiency is accompanied by bleeding. Deficiency is rare, due to large amount of vitamin K in foods and the completion of synthesis by intestinal microflora. Hypovitaminosis can develop liver disease and biliary tract due to violations of the flow of bile into the intestine; when taking large doses of antibiotics and sulphonamides and antagonists of vitamin (pelentan, dykumaryn which is used to prevent blood clots, salicylic acid, aspirin). The biological role and mechanism of action: Vitamin K is a cofactor γ-hlutamilkarboksylazy that introduces vγ-polozhennyahlutaminovoyi acid protein - clotting factors (prothrombin, factor UII, IX, X, protein C and protein S), 5 protein of bone (including osteocalcin and matrix protein) additional carboxyl group. Having two carboxyl groups enables the proteins to bind dvohvalentnyy calcium ion, which is an activator of the vitamin K.

Daily demand 200-300mkh.

Vitamin E (tocopherol). *These vitamins are derived tocol. Tokos -potomstvo, phero - bear such name reflects its biological effect. In avitaminoznyh animal embryogenesis is broken and there are degenerative changes in the reproductive organs, leading to sterility. There has muscular dystrophy, nekrozno-dystrofichniprotsesy in the liver. Typical manifestations of failure tocopherol is the activation of lipid peroxidation and damage of lipid bilayer membranes, with the development of membrane pathology - atherosclerosis, cancer, anemia, etc. Man profound deficiency is rare because of the fat body gets enough vitamin E. But vitamin deficiencies widespread phenomenon.*

The biological role and mechanism of action of vitamin E.

1. Vitamin E - the main fat-soluble antioxidant, can neutralize free radicals of oxygen radicals fatty acids.
2. Stabilizes lipid bilayer membranes.
3. tocopherol metabolite - tokoferolhinon is a coenzyme desaturazy fatty acids in the mitochondria. Myazevu dystrophy that occurs when vitamin E deficiency is associated with violations of this enzyme.
4. Hormonal function of vitamin E is its ability to inhibit protein kinase C, and because of her influence on cell growth, influence gene expression of collagenase, alpha-tropomyosin.

Sources: vegetable oils. Most of all grains in prorosshyh pshenytsi.Dobova need 10 mg.

Vitamin D (calciferol, antyrahitychnyy). Vitamin activity have two ingredients: Vitamin D3 (cholecalciferol) and D2 (ergocalciferol).

Metabolism and functions of vitamin D. Vitamin D3 is converted to hormonal forms hydroxylation influenced tsytohromivR-450.Spochatku formed in the liver kaltsidiol - 25 (OH) D3 then in the kidney - calcitriol 1,25 (OH) 2D3 or 24,25 (OH) 2 D3.Holovnymyorhanamy mishenyamytsyh-hormonal forms is the small intestine, kidneys and bones. Hormones regulate the level of genome-syntezSa zv'yazuyuchohobilka which is necessary for calcium absorption in the intestine, its reabsorption in the kidneys and mobilization of calcium and phosphorus from the bones. Also important function of vitamin D is the regulation of cell proliferation and differentiation. Zokrema1,25- (OH) 2D3 stimulates osteoblastic differentiation of bone and hematopoietic cells.

Deficiency of vitamin D - rickets occurs in children due to insufficient income holekaltseferolu with food, or as a result of reduced sun exposure skin. There is osteomalacia - rozmyahchennya bone, muscle hypotonia; adults - there is osteoporosis (leaching salts from the bones). Biochemical signs of rickets is a reduction of calcium and phosphorus in the blood, increased alkaline phosphatase activity. Rickets is usually easily cured with vitamin D. However, there are forms of rickets, which can not be treated. This led to the idea that the activity has not had vitamin D, and its transformation products. "Oksydevit" - hydroxylated form of vitamin for the treatment of genetically caused rickets associated with defective cytochrome P450 in the kidneys of children.

Hypervitaminosis D leads to increased delay hydroxyapatite in bone calcification and internal organs. If overdose death. Sources of Vitamin: animal products - butter, egg yolk, liver, fish oil, vegetable oil, yeast, UV exposure.

Daily demand for ditey10-25mkh (500-1000)

Antivitamins - a antagonists vitamins that can cause hypo- or beriberi (usually a competitive inhhibitory dependent on vitamins enzymes).

Table 2. Antivitamins and properties

Antivitamins	Appropriate vitamin	Mechanism of action	Using
Hidroksytiamin, piry thiamine, neopirytiamin	Vitamin B1 (thiamine)	Compete with tiaminovymy coenzymes for interaction with enzymes.	Experimental failure.
Dyhlorryboflavin, iso riboflavin, lactochrome	Vitamin B2 (riboflavin)	Antimetabolites. Compete in the synthesis of riboflavin coenzymes FMN Fadi.	Experimental failure.
Isoniazid (isonicotinic acid hydrazide)	Vitamin B3 (niacin)	May be included in the composition of coenzymes NAD and NADP nicotinamide instead of forming inactive compounds. Also isoniazid causes a deficiency of vitamin B6.	Treatment of tuberculosis
Homopantotenova acid, ω-acid metylpantotenova	Vitamin B5 (pantothenic acid)	Compete with pantothenic acid derivatives for interaction with enzymes.	Experimental failure.
Dezoksypirydoksyn	Vitamin B6 (pyridoxine)	Antimetabolites. Compete with pirydoksalevymy coenzymes for interaction with enzymes.	Experimental failure.
Pterydyny	Vitamin B9 (folic acid)	Compete with folic acid for interaction with folate-dependent enzymes, resulting nucleotide synthesis stops. The strongest influence on the cells divided.	Cancer treatment.
Coumarins (dykumarol, warfarin, tromeksyn)	Vitamin K (naphthoquinones)	Compete with vitamin K for interaction with enzymes, blocking the formation of blood clotting factors in the liver.	Anticoagulants are used for the treatment of thrombosis.
Sulfonamide	P-aminobenzoic acid	Included in the composition instead of PABA Folic acid is synthesized in bacterial cells.	Treatment of bacterial infections.

Vitamin-like substance

Inositol - a component of membrane phospholipids. Inozytfosfaty involved in the transmission of nerve impulses in intracellular signaling, causing calcium mobilization. Inositol has lipotropic effect - prevents fatty liver.

Choline -vhodytdo of phosphatidylcholine, prevents fatty liver. Is part of acetylcholine - a neurotransmitter involved in transmetylyuvannya reactions in the biosynthesis of methionine, purine and pyrimidine nucleotides. Sources - liver, kidney, meat, fish, cabbage

PABA (P-aminobenzoic acid) is a part of folic acid. Factor reproduction of microorganisms. Enables tyrosinase - the enzyme of melanin synthesis.

B15 (pangamic acid) - gluconic acid ester and dimethyl glycine - a source of methyl groups in the synthesis of choline, methionine, creatine.

KoQ, ubiquinone (ubiquitous quinone). The component of the respiratory chain. The lack of children causes anemia. It is used in the treatment of muscular dystrophy

Vitamin U - antiulcer factor. Takes part in the synthesis of choline, creatine as a donor of methyl groups. Many raw vegetables, especially cabbage.

Lipoic acid. Included in the multyfermentnyh complexes involved in oxidative dekarboksylyuvannyuα-ketokyslotTauryn. Function - bile acid conjugation, detoxification of xenobiotics, neurotransmitter

function in the brain, retina, heart.

Taurine deficiency causes degeneration of the retina, growth retardation, cardiomyopathy.

Carnitine - perenoschyk fatty acids in the mitochondria.

5.Materialy for self-control.

A Tasks for self-control.

2. Pilots and transport drivers, working in conditions of switching attention from the illuminated devices to the darkness, you must increase the daily requirement of vitamin A. Explain the biochemical mechanism of this phenomenon.

3. As a result of overdose dykumarolu the treatment of thrombosis emerged bleeding. What is the basis of its development? Which vitamin can prevent this bleeding?

4. The patient appealed to the doctor with complaints of increased bleeding (especially gum), the emergence of "petechiae" on the skin and mucous membranes, loosening and tooth loss, fatigue, decreased performance. The survey revealed that the patient had long consumed plant foods. A patient diagnosed with scurvy. Deficiency of vitamins which two are the cause of beriberi? What can explain the origin of the symptoms listed above? What are the sources of these vitamins and medication that is used to treat scurvy.

5. The patient in '37 against the backdrop of prolonged use of antibiotics increased bleeding observed with small damages, reduced activity of clotting factors II, VII, X, prolonged clotting time. Lack of vitamin which caused these changes? What is the cause of lack of this vitamin in this case? Explain the mechanism of action of this vitamin in blood clotting

B. Test for self - control

1. Patients with coronary heart disease for riboksin (inosine), which is an intermediate metabolite synthesis:

A. Glycoprotein
B. Iron - protein
C. Lipoprotein
* D. Purine nucleotides
E. Ketone bodies

2. In patients with alcoholism often observed disorders of the central nervous system - memory loss, psychosis. It is these symptoms in the body of vitamin B1 deficiency. Violation of coenzyme formation which can cause these symptoms?

A NADP
B Coenzyme A
C FAD
* D Tiaminpirofosfate
E Piridoksalfosfate

3. Injection of the drug dykumarol causing a sharp decline in blood coagulation factors. Antivitamins vitamin which is dykumarol?

A Vitamin C.
B Vitamin A.
C Vitamin E.
* D Vitamin K.
E Vitamin B2.

4. Co - carboxylase is used in medicine as a pharmaceutical for the treatment of myocardial dystrophy, muscle lesions and peripheral and central nervous system. Which vitamin is a component of the drug?

A. B12
B. B2
C. B6
D. C
* E. B1

5. Askorutin used for bleeding gums and bleeding point. Which vitamin is part of this drug?

A Vitamin K.
B Vitamin E.
* C Vitamin C.
D Vitamin A.
E Vitamin B1.

6. Antitumor pharmaceuticals methotrexate is a structural analog of folic acid. The mechanism of action of this drug is inhibiting the enzyme:

* A Dihydrofolate reductase

B Xanthine oxidase
C Hexokinase
D Kreatin kinase
E lactate dehydrogenase
7. For the formation of bone during fetal development intra womb
receipt of necessary vitamin D derivative chemical compound which is this vitamin?
A Sphingosine;
B Glycerol;
* C Cholesterol;
D Inositol;
E Ethanol.
8. For the treatment of dermatitis, wounds and ulcers that heal poorly, use
coenzyme drugs and flavinmononukleotide flavinate. Active forms of which
Vitamin is it?
A. Vitamin B9
B. Vitamin B1
C. Vitamin B6
D. Vitamin B12
* E. Vitamin B2
9. In clinical practice, pharmaceuticals isoniazid that included a coenzyme competitive structure that can not participate in redox processes and this leads to growth arrest Koch's bacillus. Specify that inhibited enzyme systems:
A Cytochrome c.
B FAD-dependent enzymes.
C KoQ.
* D NAD-dependent enzymes.
E Cytochrome aa3.
10. One way sulfonamides metabolism in humans is their acetylation involving acetyl-CoA. Which vitamin is part of coenzyme A?
A. Ascorbic acid
* B. Pantothenic acid
C. Linoleic acid
D. Glucuronic acid
E. Arachidonic acid

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protocol number 2 on August 31, 2017

GUIDELINES
FOR INDEPENDENT STUDENTS WORK
WHILE PREPARING FOR THE PRACTICAL LESSON

Academic discipline	Biological chemistry
Module number	module 2
module	**Module 7: Fundamentals of Pharmaceutical Biochemistry and Biochemistry of tissues**
Study subject number 8	Biochemistry of blood. Exchange of hemoglobin and its violation. Regulation hemostasis. *body Qualitative reaction to gemin group of hemoglobin.*
Course	3 year
Faculty	Pharmaceutical
Number of hours	2,5

Kyiv 2017
Prepared by PhD in medicine, Professor I.V.Nizhenkovska

1. Topic actuallity

Blood is a specialized liquid fabric body, its internal environment, which provides communication and integration of metabolism of various organs and tissues in the whole system, supports the constancy of its composition. Pathological conditions involving disorders of systemic hemodynamics and microcirculation disorders leading to profound physiological and biochemical functions.

Blood plasma contains more than 300 different proteins, different physical, chemical and functional properties, transport proteins, enzymes, proenzyme inhibitors, enzymes, hormones, antibodies, coagulation factors, anticoagulants like. Plasma Proteins serve as a reserve of amino acids in the body,

maintaining the plasma cations, provide necessary for normal blood viscosity hemodynamics, create oncotic pressure involved in maintaining acid-alkaline balance. Nonprotein beznitrohenni nitrogen and blood components are final and intermediate products of nitrogen, carbohydrate and lipid metabolism. Evaluation of quantitative and qualitative composition of blood plasma, including determining the activity of certain enzymes that are widely used to diagnose various pathological conditions.
Blood clotting is a complex physiological and biochemical process, a protective reaction to loss. Knowledge of the biochemical characteristics of coagulation, and fibrinolytic systems antyzhortalnoyi blood is necessary for understanding the mechanisms of maintaining aggregation of blood under conditions of normal and many diseases, and for their timely correction prescription.

2.Specific goals:

- characterize the chemical composition of the blood in health and its changes in pathology
- Explain the basic functions of blood proteins based on their physical and chemical properties.
- characterize enzymes of blood plasma, know their main representatives and clinical significance assessment of their activity in plasma
- Explain biochemical mechanisms support the acid-base status, causes and types of violations
- To interpret biochemical mechanisms of coagulation, and fibrinolytic systems antyzhortalnoyi blood.
- Explain the role of vitamin K in clotting reactions and the effect of drugs - agonists and antagonists of vitamin K.
- Master the method of determination of hemoglobin geminovyh benzydynovoyu breakdown.

3. Basic knowledge, skills necessary for studying the subject (interdisciplinary integration)

Names of previous disciplines	Obtained skills
Physical methods of analysis and metrology	Master the techniques of laboratory research tools
Biology with the basics of genetics	To classify the structure of biopolymers.
Inorganic chemistry	To explain the mechanism of action of buffer
Organic chemistry	Write glutamic acid formula
Physiology	1. Describe the composition and properties of blood. 2. To interpret the mechanisms of hemostasis.
Pathological physiology	To explain the basic mechanisms of blood clotting.

4. Tasks for independent work during preparation for the classes.

4.1. The list of key terms, parameters, characteristics which the student is to assimilate while preparing for classes

Term	Definition
Azotemia azotemia	a rise in residual nitrogen levels.
Acute phase proteins	These include C-reactive protein (CRP), serum amyloid A protein, alpha-1-acid glycoprotein, alpha-1-antitrypsin, alpha 1 macroglobulin, fibrinogen, ceruloplasmin, C9 component of the complement system.
Hemoglobinopathies	Hemoglobin - a molecular defect in the primary structure of polypeptide chains of globin.
The residual nitrogen blood	The residual nitrogen of blood - a non-protein nitrogen, ie nitrogen organic and inorganic compounds, which remains after the deposition of proteins in the blood.
Immunoglobulins	Immunoglobulins - a plasma protein produced by B-lymphocytes and implement specific humoral protection by recognizing and binding to antigens and haptenes have an important effect opsonizuyuchyy and is the main activator of the complement system.
Complement system	Complement system - a multicomponent system self serum proteins, which itself does not recognize antigens and activated at a meeting with the relevant receptors on other cells or immune factors. Complement system is the primary humoral effector system of inflammation, which, along with natural antibodies and phagocytes a first line of host defense during pathogen ingress.
Thalassemia	Thalassemia - a hereditary disease characterized by the violation of the synthesis of α- or β-chain of hemoglobin.

4.2 Theoretical questions for the class.

1. Chemical composition and physico-chemical properties of the blood of a healthy person. Residual nitrogen levels. Types of azotemia.

2. Hemoglobin: structure, types, biosynthesis, pathology synthesis.

3. The main group of plasma proteins; their composition and content in normal and pathological conditions.

4. Plasma Enzymes: own (secretory) and excretory Indicator (tissue) enzymes.

5. Buffer systems of blood, their types, functions hydrocarbonate, phosphate, hemoglobin and protein buffer systems in the body.

6. blood coagulation system:

• clotting factors;

• mechanism of activation of blood coagulation;

• operation of the cascade of blood coagulation in the coagulation system and its features;

• internal way of coagulation;

• appearance by coagulation;

• The role of vitamin K in reactions of the coagulation cascade (carboxylation of glutamic acid in □-karboksyhlutaminovu acid role in the binding of calcium).

7. Antyzhortalna blood system:

• anticoagulants: antithrombin, □1-proteinase inhibitor, □2-macroglobulin, heparin, coumarin, prostacyclin citrate;

• mechanism of action of anticoagulants.

8. Fibrinolytic system of blood. Stages fibrinolysis:

• Stage 1 - convert plasminogen to plasmin;

• Stage 2 - splitting fibrin.

9. The components of blood as pharmaceuticals.

4.3. Practical work

Experiment 1. Determination of hemoglobin geminovyh benzydynovoyu breakdown.

The principle of the method. To determine geminovyh groups use benzydynovu test based on the catalytic properties of derivatives of hemoglobin (oxyhemoglobin, carboxyhemoglobin). Benzidine oxidation product is blue, which may gradually move into the red. The sample is very sensitive.

The process. In the test tube 5 drops of diluted blood, add 5 drops of benzidine and 2-3 drops of hydrogen peroxide. Look for changes in color.

Clinical and diagnostic meaning. The concentration of hemoglobin in the blood of women is 120-140 g / l, cholovikiv- 130-140h / l. Reducing the concentration of hemoglobin is the main laboratory symptoms of anemia. Reducing the level of hemoglobin in the blood depends on the form of anemia.

4.4. The context of the topic

Blood - liquid tissue (connective kind). The volume of blood is around 7% of body weight (5.2 liters) in men, 6% (3,9l) - women, more than 10% - in infants.

Blood consists of a liquid part - plasma and formed elements (erythrocytes, leukocytes, platelets). Normally plasma is 55-60% of the blood forming elements -40-45% (from yakyh39-44% - red cells, 1% - other cells). Percentage formennyh elements to the plasma is called hematocrit. Serum blood - the liquid part of blood plasma, which remained after coagulation (without fibrinogen).

The functions of blood:

1. Breathing function - to transport oxygen from the lungs to the tissues and carbon dioxide from the tissues to the lungs.

2.Trofic function - to transport nutrients to the cells where they are used in anabolic and catabolic processes.

3.Ekskretorn function - end transport of metabolites metabolism (urea, uric acid, bilirubin, etc.). Products and biotransformation of xenobiotics (drugs, toxic substances) in the selection of (kidney, lung, intestine, skin, etc.).

4.Zahysna function - the body's defense against violations of internal homeostasis foreign proteins and other macromolecules, which is provided by the various types of leukocytes, specific proteins and complex enzyme systems of blood plasma.

5.Participating in haemostasis. The ability to provide a rare blood condition, and in case of damage to the vessel wall - stop the bleeding by clotting and interoperability protyzhortannya blood. 6.Termorehulyatorna function - to transfer heat from more to less energy bodies.

Provides high heat capacity and thermal conductivity levels.

7.Humor - transport of hormones and other bioregulators of endocrine organs to target organs.

8.Hold acid-base balance, osmotic pressure and water and salt balance.

Hemoglobin - a protein complex class Chromoprotein Division hemoprotein containing globin and heme as a prosthetic group .. MM 66 - 68 000. hemoglobin has 4 subunits - two α- and two β-, each wrapped around one molecule heme. α - chain contains 141, and β -lantsyuh- 146 amino acid residues. The structure of heme porphyrin ring is substituted pyrrole of 4 interconnected metynovymy (CH =) bridges. Substituted porphyrin called porfin. In heme molecule porfin presented protoporphyrin 1X containing methyl 4, 2 and 2 vinyl groups propanoic acid residues. After joining the iron protoporphyrin converted to heme. The coordination number of iron in the hemi - 6. It is connected to two pyrrole nitrogen and 2 covalent coordination bonds. For rahunok5-ohozv'yazku combined with heme protein, A6-ympryyednuye oxygen, CO, cyanides, etc.

There are physiological and pathological (abnormal) form of hemoglobin.

Basic adult hemoglobin - is HbA, containing 2α- and 2δlantsyuhy (from the Latin adultus - adult). In the early stages of embryo appears HbP (3-hmisyatsiv). Primitive hemoglobins replaced by HbF (fetal, Latin - fetus - fruit) instead of ε--lantsyuhivsyntezuyutsyaγ lantsyuhy.Do fetus at birth is about 70% HbF. In the later stages of fetal Hb A. Protyahom3-4misyatsiv appears after birth is a sharp decrease in HbF do1-2% and replace it on HbA. HbP HbF and have a greater affinity for oxygen.

As a result of mutations in the genes that control the synthesis of circuits may cause abnormal hemoglobin variants that differ in amino acid composition, physico-chemical properties and the ability to transport oxygen. Pathological conditions arising from the presence of blood in pathological forms of hemoglobin, called hemohlobinozamy share on thalassemia and hemoglobinopathies. Clinically manifest anemia that are incompatible with life.

HbS - mutant hemoglobin β-chain in which the provisions of the sixth glutamic acid is substituted navalin. Decreases negatively charged hemoglobin reduced its affinity for oxygen, certain molecules stick together forming filamentous aggregates that give form erythrocytes serpa- "sickle klitynnaanemiya." These easy hemolizuyut red blood cells in the blood vessels.

HbC - glutamic amino acid, B6 mupolozhenni β-lantsyuhazamischena for lysine. Red blood cells containing hemoglobin that are capable of hemolysis.

Hemohlobin compounds: Physiological

1.Oksyhemohlobin - hemoglobin that carries oxygen

2.Karbhemohlobin - the connection of hemoglobin with carbon dioxide.

Pathological

1.Karboksyhemohlobin - the composition of hemoglobin with carbon monoxide (CO). The affinity of hemoglobin for CO is 300 times higher than oxygen

2.Methemohlobin formed by the action of hemoglobin oxidants. This form of iron trehvalenten. He can not bind oxygen, but easily binds cyanide.

The biosynthesis of hemoglobin The human body contains about 5 g of iron, of which the share of hemoglobin falls to 60-70%, the share of myoglobin -3-5%, ferritin - 20%. Iron is absorbed in the gut as dvohvalentnoho ion after his release from complexes with proteins. In the cells of intestinal mucosa have iron in the form of trivalent ion apoferytynom combined with protein to form a stable complex ferritin. More iron is transported in combination with β-1 hlobulinovoyufraktsiyeyu serum (transferrin) or iron combines with apoferytynom tissues, where deposited in the form of ferritin. The source of iron for synthetic purposes are foods and iron that is released by the decay of red blood cells. Protein part - globin is synthesized all the proteins. In the synthesis of heme involved glycine and succinyl-CoA. First-succinyl KoAvzayemodiye of glycine with utvorennyamδ-aminolevulinovoyi acid (δ-ALA). The reaction occurs in the endoplasmic retykulyumi liver cells under the influence pirydoksalfosfatzalezhnoho enzyme key, allosteric enzyme in the synthesis pirroliv. The enzyme steroid induced, inhibited heme. In the second stage, the condensation of 2 molecules of δ form the first -ALKz monopirolnoyi compounds - porfobilinohenu influenced porfobilinohensyntetazy, which is a regulatory enzyme which is inhibited the synthesis of the end products. Then 4 monopiroliv porfobilinohenu

synthesized complex tetrapyrrole protoporphyrin 1X - precursor of heme, which is the final stage of iron molecule attaches involving hemsyntetazy to form heme.

Digestion of hemoglobin in the digestive canal Food in the stomach hemoglobin under the influence of hydrochloric acid breaks down into heme and globin. Globin hydrolyzed to amino acids under the influence of digestive proteases. Heme is oxidized to muriatic hematin, which is excreted in the faeces, giving it a dark color. Hematin gives positive for occult blood similar to heme. Therefore, the diagnosis of bleeding from the esophagus and stomach sick before analysis is recommended not to eat meat during 2-3dib.

Catabolism of hemoglobin in the tissues. The bulk of erythrocytes (90-95%) is hemoglobin. Red blood cells live an average of 100-120 days. The destruction of red blood cells occurs in the cells of the reticuloendothelial system mainly spleen, liver, bone marrow histiocytes of connective tissue. Hemoglobin that is released, binds haptoglobin (plasma protein). This set does not pass through the kidneys.

The chemical composition of blood Whole blood consists of water at 75-85% solids - up to 21% low molecular weight substances -1,5-2% .Vmist hemoglobin -130-160h / l. Plasma contains 90% water and 10% solids (inorganic and organic substances). Inorganic substances Plasma sodium - 130-157mmol / l potassium -3,4-5,3mmol / L calcium - 2,3-2,7mmol / L phosphate -1-2mmol / l and others. Organic substances are divided into plasma and high-low. Macromolecular organic materials are mostly simple and complex proteins (total protein - 65-85h / l fibrinogen -2-4h / l). In the plasma by protein fibrinogen found at 2-4h / l more than in serum. Newborn plasma protein slightly smaller (50-60h / l) and reaches adult levels at 3 years old.

Organic substances are divided into low beznitrohenni (glucose, cholesterol, ketone bodies, glycerol, AML, fatty acids, etc.) And of nitrogen (non-protein nitrogen blood or residual nitrogen is - 14-28mmol

Residual nitrogen (rest-nitrogen) consists of urea (50%), free amino acids (25%), creatinine (2,5-7,5%), creatine (5%), uric acid (4%), ammonia and indican (0.5%), the rest - bilirubin, choline, glutathione and other products of protein metabolism.

Azotemia - an increase of residual nitrogen content in the blood more than 35 mmol / L. There retention and productive azotemia.

Retention azotemia violation occurs when the output of nitrogen compounds in the urine, especially by urea.

Reasons: nedostnist renal (glomerulonephritis, acute tubular necrosis, etc.) Pozanyrkovi - obstruction of the urinary tract, heart sudynnanedostatnist, blood loss, prolonged diarrhea and vomiting.

Productive azotemia - excessive intake of nitrogenous compounds in the blood when the strong protein breakdown (urea increased moderately to 10 mmol / l). Causes: burns, trauma, infectious diseases, tuberculosis, diabetes.

Physico-chemical constants blood:

1.Schilnist blood - normally stanovyt1,050-1,064h / ml plasma -1,024-1,030h / ml -1,080-1,097h cells / ml.

2. Viscosity of blood. Due to the fact that blood vessels in constant motion. Blood

has a high viscosity - in 4-5raziv higher than that of water, due to the high content of red blood cells.

3.Osmotic pressure - defined osmotic concentration, ie the sum of all particles contained in unit volume. Osmotic pressure plasma stanovyt7,6-8,1 atm (762,788 kPa). It is caused mainly sodium chloride and other low molecular weight substances contained in plasma. It regulates the exchange of water between plasma and formennyh elements. Some osmotic pressure (about 0.03 bar), created by blood proteins, primarily albumin, called oncotic pressure. He regulates water exchange between the plasma and tissues. As the protein content decreased oncotic pressure, causing a shift of water in the tissue and the development of edema.

4. The blood pH ranges from 7.36 (in venous blood) to 7,44 (arterial blood). Critical limits fluctuations 6,8-7,8nesumisni with life. Acid-base arivnovaha (KLR) is supported by buffer systems plasma and blood cells of lung function - the selection or retention of CO2 Kidney - excretion of acid or alkaline products, digestive tract and skin.

Buffer systems - is solutions that resist change in pH when adding acid, alkali, dilution or concentration. Buffer systems of blood:

1.Hemohlobin-okyhemohlobinova. The most powerful buffer system (75% buffer capacity of blood). Hemoglobin consists of NNb weak acid that will neutralize increased

the concentration of H +, and its salts KNb which neutralizes -ON- .Oksyhemohlobinova - with NNbO2 acid and its salts KNbO2. By increasing the concentration of H + neutralization provides KNbO2. Given the increasing number of OH, joined them NNbO2.

2.Bikarbonatna 10% buffer capacity of the blood. It consists of a weak coal

acid and its sodium (plasma) or potassium (erythrocytes) salt. By increasing the concentration of H + neutralization zabezpechuyeNSO3-.pri zrostanniON- with them connected H2CO3.

3.Bilkova. 7% buffer capacity of the blood. More important in cells. Proteins are able to demonstrate buffering properties due to its amphoteric. H + is neutralized amino groups of proteins; OH - hydrogen ions carboxyl group.

4.Fosfatna. 1% buffer capacity of the blood. It consists of sodium or potassium dihydrogen phosphate,

which exhibits acidic properties and so neutralizes excess OH, hydrogen and sodium or potassium, which shows basic properties, and therefore neutralizes excess H +.

Blood alkaline reserves - the difference between all the carbon dioxide and carbon dioxide-free (ie CO2) in the blood. This is mainly bicarbonates blood in their normal content 20 times higher than CO2. Blood alkaline reserves show that the number of bases you can add or take away from blood samples to its pH was 7.4. In normal plasma bicarbonate content - 25 mg / dL.

Violation of the acid-base balance acidosis and alkalosis There, each of which can be compensated (without changing the pH) and decompensated (with change in pH)

I. Acidosis - increased concentration of H + in the blood

Types acidosis:

1.Respiratornyy: there is an attack of asthma, pneumonia, atelectasis, emphysema. Diagnosis: increase in blood rCO2.

2.Metabolichnyy: the accumulation of organic acids in the blood, loss NSO3-, violation H + excretion. Reasons: starvation, diabetes, fever, burns, injuries, loss of bicarbonate (diarrhea).

Diagnosis: NSO3- reduction, reducing blood alkaline reserves.

II. Alkalosis - reducing the concentration of H + in the blood

Types alkalosis:

1.Respiratornyy, marked with mechanical or hysterical hyperventilation, increased intracranial pressure. Diagnosis: reduction rCO2 levels.

2.Metabolichnyy: loss of H +, alkali equivalents accumulation observed vomiting, hypoparathyreosis, the introduction of large amounts of sodium bicarbonate. Diagnosis: NSO3- growth, increased blood alkaline reserves.

Biochemistry erythrocytes

Of red men 4,5-5,5 • 1012 / L in women-3,9-4,5 • 1012 / l.Tse dvoyakovihnuti drives easily change their shape under the influence of external forces. This form of erythrocyte increases the total area of its surface, and gas exchange. Not containing nucleus and mitochondria. Life 90-120dniv. Functions - transport of oxygen and carbon dioxide, involved in regulation of pH.

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Metabolism: in the absence of mitochondrial respiratory chain and ATP is the only source of anaerobic glycolysis. Glucose comes from blood plasma, and the plasma goes back to lactate. The important role of glycolysis in red blood cells - the presence dyfosfohlitseratmutazy enzyme that catalyzes utvorennya2,3-dyfosfohlitseratu.ATF provides the Na + -K + -ATPase, which maintains a high level of K + in erythrocytes taSa2 + -ATPase (removes Ca2 +). Active pentose phosphate cycle, which supplies NADPH, which prevents hemolysis of erythrocytes.

Respiratory function of erythrocytes

1. ***The processes occurring in the capillaries of the lungs.*** Oxygen diffuses through the air in the erythrocyte plasma due to the difference of partial pressures. In red blood cells the oxygen reacts with:

-Karbhemohlobinom of oxyhemoglobin formation and release of CO2 into the air;

-Hemohlobinom to form oxyhemoglobin. Oxyhemoglobin takes potassium from the potassium bicarbonate to form KNbO2 and H2CO3. Last influenced carbonic anhydrase decomposes to water and CO2, which diffuses into the air.

2. The processes occurring in capillaries tissues.

Carbon dioxide diffuses from the tissues due to erythrocyte plasma due to the difference of partial pressures. In erythrocyte CO2 interacts with:

-Oksyhemohlobinom - formed karbhemohlobin NbSO2 and oxygen, which diffuses into the tissue. Up to 15% CO2 transferred as part of erythrocytes karbhemohlobinu

-vodoyu to form carbonic acid. The latter reacts with KNbO2 formed K + NSO3-, NNb and released in tissue oxygen. It is in the form of NSO3- transferred most of the carbon dioxide erythrocytes.

Plasma proteins (serum) blood.

Functions of plasma proteins.

1. Transport: proteins carry fat and bile acids, bilirubin, hormones, inorganic ions, vitamins and others.
2. Enzymatic: function: the blood contains large amounts of enzymes from a variety of agencies.
3. Backup function: the hydrolysis of proteins break down into amino acids.
4. Regulatory function: proteins regulating blood viscosity, acid-base balance oncotic pressure.
5. Protective function provided immunoglobulins, proteins of blood coagulation and complement system.
6. Synthesis of plasma proteins occurs mainly in the liver, only a few proteins synthesized in other tissues. For example, γ-globulins are synthesized by B-lymphocytes.

Proteins consist of plasma fractions albumin, globulin and fibrinogen. Value albumin and globulin 1,5-2,3 (albumin-globulin ratio). Its reduction is observed at lower albumin content or increase the content of globulins.

Hypoproteinemia - reducing the total protein in the conditions involving:

· inhibition of protein synthesis (liver disease - hepatitis, cirrhosis);

· activation decay of tissue proteins (starvation, trauma, burns, tumors);

· large protein loss (nephrotic syndrome);

· violation of digestion and absorption of food proteins (gastroenteritis).

Clinical manifestations hypoproteinemia - edema (by reducing the oncotic pressure).

Hyperproteinemia - increasing the total protein in the plasma. There are:

1. The relative hyperproteinemia - due to the loss of blood thickening fluid, hemodynamic disorders (diarrhea, vomiting, diabetes insipidus, cholera).

2. Absolute hyperproteinemia s - if toxic, infectious and parasitic diseases (malaria, toxoplasmosis), multiple myeloma. Usually it hyperhamahlobulinemiya.

Characteristics of certain plasma proteins.

Albumin - simple proteins, blood levels 40-60h / l. Synthesized in the liver. Provide 80% of oncotic plasma pressure. Albumins perform the transport function - transporting fatty and bile acids, bilirubin, steroid hormones, inorganic ions.

Globulin participate in the transport of lipids, hormones, vitamins, metal ions; blood clotting; immune processes. Some are acute phase proteins (glycoproteins). By globulin fractions include: α1-, α2-, β- iγ globulin.

Acute phase proteins. When inflammation in the liver synthesized acute phase proteins. For their levels in the blood are judged on the severity of the inflammatory response, control of dynamics during treatment. Their concentration increases in the first 24-48 hours and stored 7-10dniv.

Abnormal proteins Kriohlobulin - a protein that is deposited on the bottom of the tube cooling. There is blood in leukemia, multiple myeloma, nephrosis, cirrhosis of the liver.

Alpha-fetoprotein - fetal protein in adults appears only in malignant tumors, most often with liver cancer (diagnostic value - 90%).

Enzymes plasma (serum) blood

1.Own enzymes plasma (plazmospetsyfichni) - mainly synthesized in the liver, normally allocated in plasma. These include enzymes of blood coagulation and fibrinolysis, complement protease kinin and renin-angiotensin system and others.

2.Indykater (organ) enzymes - into the blood from the tissues where they perform intracellular function. Normally in plasma, most of them defined in trace amounts. By indicator enzymes include myocardial CK-MB (creatine phosphokinase), AST (aspartataminotransferase) LDH1,2 (lactate

dehydrogenase), liver - ALT (alaninaminotransferase), AST, LDH4,5, ALP (alkaline phosphatase) HHTP (γ- hlutamiltranspetydaza).

3. Excretory enzymes - mainly synthesized in the liver (alkaline phosphatase, leytsynaminopeptydaza) and normally isolated from bile. In violation selection excretory enzymes in the bile is increasing their activity in plasma.

Blood drugs:

1.blood and canned (acd, oxalic, heparynizovana etc.);
2.drugs of complex action (native plasma, albumin, etc.);
3.imunolohic drugs (hamahlobuliny, interferons, etc.);
4.hemostatic medication (thrombin, hemostatic sponge, platelet mass, fibrinogen, etc.);
5.antyanemichni (eritrotsitarnaja mass etc.).

5.Materialy for self-control.

A Tasks for self-control.

1. To characterize the function of blood follows:
- respiratory
- trophic
- excretory
- protective
- regulatory

2. To characterize buffer systems blood, bicarbonate, phosphate, protein, hemoglobin.

3.Describe hemoglobin derivatives - oxyhemoglobin, dezoksyhemohlobin, karbhemohlobin, carboxyhemoglobin, methemoglobin, tsianmethemohlobin:

iron	hemoglobin valence	Place accession derivatives	Place and origin	Properties

4.Fill the table "Diagnostic value of research activity of enzymes and isoenzymes plasma"

Enzymes of blood plasma	Examples	Place of synthesis	The direction of change (increase or decrease on normal)	Pathology, in which the observed changes
own (secretory)				
excretory				
Indicator (tissue)				

5.To fill the table

Type of azotemia	Reasons of azotemia	What are the components of the blood are increased
Relative		
Absolute productive		
Absolute retention		
renal retention		
retention pozanyrkova		

B.Tests for self - control

1.In patients with acute myocardial infarction conducted anticoagulation inhibitor antithrombin III, which prevents intravascular coagulation. Which compound has anticoagulant action?
A Hondroitynsulfat.
B Hyaluronic acid.
* C Heparin
D Tetracycline.
E Histamine.

2. The patient was hospitalized with intestinal bleeding. What preparation should include regimen?
* A Vikasol
B Sulfanilamide
C Co-carboxylaze
D Aspirin
E Riboflavin

3. If a blood test revealed structural changes of red blood cells and hemoglobin. Replacement by amino acids in the β-chain of hemoglobin can lead to this?
* A glutamic acid to valine
B arginine to serine
C aspartic acid to valine
D aspartic acid leucine
E phenylalanine to alanine
4. The patient with varicose veins is recommended to prevent blood clots gel containing natural anticoagulant heparin. What is the chemical nature of the compound?
* A. Glycosaminoglycans
B. Lipoprotein
C. Nucleoprotein
D. Hemoprotein
E. Phosphoprotein
5. Heparin is a typical representative of proteoglycans, in which some polysaccharide chains linked to the protein core. Specify where he synthesized:
A. Cartilage
B. Heart
* C. Liver
D. Bone
E. Muscles
6. In electrophoretic study found patient serum interferon. In the area where this protein fraction is?
A. Beta-globulins
B. Alpha-1-globulin
C. Alpha-2 globulin
* D. Gamma globulin
E. Albumin
7. Apart from protein factors in the coagulation participating cations. Indicate which of the cations plays a leading role in this process.
* A. Ca2 +
B. K +
C. Na +
D. Mn2 +
E. Mg2 +
8. Fibrinolytic drugs are able to dissolve clots already formed in the body. Which pharmaceutical drug has fibrinolytic activity?
A. Phenobarbital.
* B. Streptokinase.
C. Vikasol.
D. Riboflavin.
E. Isoniazid.
9.The patient, who was diagnosed thrombosis of the lower limbs, a doctor appointed to take sinkumar that is Antivitamins K. What process is inhibited under the influence of this drug?
A Proline hydroxylation
B Phosphorylation of serine residues
C Methylation amino radicals
* D Carboxylation of glutamate residues
E Hydroxylation of lysine
10. Patient with atherosclerosis and blood clots prophylactically prescribe aspirin (acetylsalicylic acid). Biochemical basis of the therapeutic effect of the drug is inhibiting synthesis:
A. Leukotrienes
* B. Arachidonic acid
C. Thromboxane
D. Phospholipids
E. Cholesterol

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MINISTRY OF HEALTH OF UKRAINE
BOHOMOLETSNATIONAL MEDICAL UNIVERSITY

Department of Pharmaceutical, Biological and toxicological chemistry

"APPROVED"
Head of pharmaceutical, biological and toxicological chemistry department
PhD in medicine, Professor _____ I.V.Nizhenkovska
protocol number 2 on August 31, 2017

GUIDELINES
FOR INDEPENDENT STUDENTS WORK
WHILE PREPARING FOR THE PRACTICAL LESSON

Academic discipline	Biological chemistry
Module number	module 2
module	**Content module 7: Essentials of pharmaceutical biochemistry and biochemistry of tissues**
Study subject number 9	Biochemical functions of the liver. The role of the liver in biotransformation of xenobiotics and endogenic toxins. *Quantitative determination of total bilirubin in the blood.*
Course	3 year
Faculty	Pharmaceutical
Number of hours	2,5

Kyiv 2017

Prepared by PhD in medicine, Professor I.V.Nizhenkovska

1. Topic actuallity

The liver is Central to metabolism, maintaining homeostasis of the internal environment of the body. It functions as the primary regulator of blood levels of substances entering the body with food. After absorption in the digestive tract through the liver are not only nutritional compounds but also a large number of foreign chemicals (xenobiotics). Xenobiotics – foreign substances which are not used by the body as sources of energy, plastic materials or catalysts and are subject to removal (elimination) from the body. To xenobiotics include chemicals domestic and industrial use, most drugs, and the like. Also, the body constantly produces toxic endogenous metabolites, which are subject to clearance. The enzymatic system of the liver maintain chemical homeostasis of the internal environment of the human body by biotransformation of toxic compounds into less toxic molecular form that can be excreted from the body by the various excretory systems. Violation of the functional state of the liver adversely affects the homeostasis of the organism as a whole.

2.Specific objectives:

- To explain biochemical functions of hepatocytes.
- To explain biochemical mechanisms of detoxification systems in the liver: reactions of microsomal oxidation and conjugation in biotransformation of xenobiotics and endogenous toxins;
- To explain the molecular basis of genetic polymorphism and inducible nature of cytochrome P-450;
- To analyze the causes of the development of tolerance to medicines for their long-term use;
- To explain the stages of heme catabolism and metabolism of bile pigments;
- To be able to determine the total, direct and indirect bilirubin in blood serum and interpret the research results.

3. Basic knowledge, abilities, skills necessary for studying the topic (interdisciplinary integration)

Names of previous disciplines	Obtained skills
Physical methods of analysis and Metrology	To own methods of conducting laboratory research tools
Organic chemistry	1. To determine the types of chemical reactions 2. To describe conducting chemical reactions 3.To write the formula of blood, glucuronic acid, glycine, glutathione, acetic acid.

Biology with fundamentals of genetics	To classify the structure of biopolymers.
Physiology	Describe the composition and properties of bile.
Pathological physiology	To interpret the definition, types, reasons and mechanisms of development of jaundice.

4.Tasks for independent work during preparation to the lesson.

4.1. A list of the main terms, parameters, characteristics that need to learn by the student during the preparation to the lesson

Term	Definition
Xenobiotics	Xenobiotics are substances foreign to the body. They are divided into three groups: 1) the products of human activities (industry, agriculture, transport), 2) substances of household chemicals (detergents, agents for combating parasites, perfumery), 3) most medicine.
Endogenous toxins	There are 5 classes of substances-endotoxins: products of normal metabolism in abnormally high concentrations (lactate, pyruvate, creatinine), the products of disturbed metabolism (aldehyde, ketone, carboxylic acid), immunological alien cleavage products of plastic material (degradation products of proteins, GLA and lopotev, phospholipids), the components of the effectors of the regulatory systems of the body (enzymes coagulate blood system, inflammatory mediators, biogenic amines, antibodies and circulating immune complexes, products of lipid peroxidation), disseminated organic- and citrocasa substances (trypsin, amylase, transaminases, myoglobin, proteins and lysosomal enzymes).
Biotransformation	Biotransformation is the enzymatic conversion of lipid-soluble exogenous or endogenous compounds to polar, water soluble metabolites that are easily excreted from the body.
Screenline oxidation	Screenline oxidation is a set of reactions of the first phase of the biotransformation of xenobiotics and endogenous compounds that are catalyzed by enzyme systems in the membranes of the endoplasmic reticulum of hepatocytes by the cytochrome P-450. In differential centrifugation endoplasmic reticulum is in chrosomal fraction, therefore these reactions were called microsomal, and the enzyme microsomal oxygenase
Cytochrome P-450	Cytochrome P450 (CYP) (COL. F. 1.14.14.1) is a family of heme-monooxygenases local, carrying out the metabolism of xenobiotics, including drugs. Localized in the smooth ER of the cell
Reactions of conjugation	Reactions of conjugation (complex formation) is biosynthetic processes in which drugs or their metabolites interact with metabolites of the organism (endogenous substrates), such as glucuronic acid, glycine, sulfate, glutathione and others, and form conjugates (complexes). The resulting compounds are excreted from the body by excretion

4.2 Theoretical questions to the lesson.

1. The role of the liver in carbohydrate metabolism (synthesis and breakdown of glycogen, gluconeogenesis, etc.).
2. Role of liver in lipid metabolism (synthesis and breakdown of fatty acids, metabolism of acetone bodies and cholesterol.)
3. The role of the liver in the metabolism of proteins and amino acids, detoxification of ammonia.
4. Showcartservlet liver function. Biochemical composition of bile.
5. Pigment function of the liver. Patoka of jaundice: hemolytic (perepechenova), parenchymal (liver), obstructive (plapack). Enzymatic jaundice.
6. Detoxification function of the liver:

• reactions of microsomal oxidation (catalytic cycle of cytochrome P-450 genetic polymorphism and inducibility of the biosynthesis of cytochrome P-450).

• reactions of conjugation in hepatocytes (reaction glukuronirovania with the participation of D. O.-glucuronic acid; reaction sulfateand 3□-phosphoadenosine-5□-phosphosulfate; methylation reactions involving S-adenosylmethionine; acetylation reaction involving acetyl-S-COA; the reaction of the conjugation with glycine.).

7. The origin and nature of the development of tolerance to drugs

4.3. Practical work performed in class.

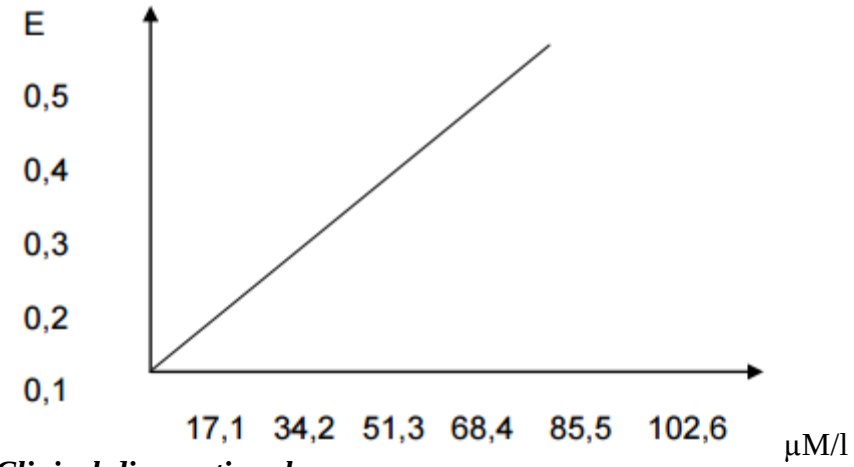
Experiment 1. Quantitative determination of total, direct and indirect bilirubin in blood serum (by the method Harasaki)

The principle of the method: diazoreactive gives a direct (connected) bilirubin pink color. The color intensity of the solution (azobilirubin) is proportional to the concentration of direct bilirubin and can be determined fotometrica. Indirect (free) bilirubin can be translated in a soluble state by the addition of serum caffeine reagent that increases solubility of this pigment, and to define datarect. The total content of both forms of bilirubin is the total bilirubin. The difference between the number of total and direct bilirubin indirect bilirubin.

Progress: the serum is diluted 1:1 with 0.9% NaCl. The tubes are filled in accordance with the table.

№ tubes	1	2	3
Reagent	Total bilirubinl	Direct bilirubin	Control
Serum, ml	0,5	0,5	-
Caffeine reagent, ml	1,75	-	1,75
NaCl 0,9%, ml	-	1,75	0,5
Datsuns, ml	0,25	0,25	0,25

Mix and leave the tube No. 2 for 10 min and the vial No. 1 for 20 min. Fotometrii with green filter (530 nm) in a cuvette of 5 mm against the control. Find the content of direct and total bilirubin according to the calibration schedule.. According to the difference of total and direct bilirubin calculate the content of indirect.



Clinical-diagnostic value

Normal content of total bilirubin in serum is 8.5-20.5 μM/l, indirect - 1,7-17,1 μM/l, direct - 0,86 - 5,1 μM /l. blood of the newborns have a higher bilirubin (23.1l μM/l).

The accumulation in the blood of bilirubin above 27,36-34,20 μM/l leads to its deposition in the tissues, the appearance of jaundice. In hemolytic jaundice the liver does not have time to associate a large number of indirect (free) bilirubin formed as a result of enhanced hemolysis. As a result, in the blood plasma observed high content of indirect bilirubin. Hepatocellular jaundice occurs in hepatitis (viral, toxic), cirrhosis of the liver. As a result of damage of membrane of hepatocytes direct bilirubin partially falls back into the blood. It also reduces the liver's ability to neutralize indirect bilirubin. As a result, when hepatocellular jaundice see different degrees bilirubinemia as due to the fraction of direct and indirect bilirubin. When obstructive jaundice due to blockage (stones, tumor) bile duct bile overwhelms them and gets in the bloodstream. So it will be pronounced hyperbilirubinemia (up to 170-700 μM/l) mainly due to direct faction of bilirubin

4.4. The content of the topic

The liver is the largest unpaired organ. She has a mass of 1.5 kg In liver cells occurs over the thousands of interrelated and interdependent biochemical reactions. Cellular composition of the liver: 80% parenchymal cells - hepatocytes, 16% cells of the reticuloendothelial system (RES), 4% in the endothelial cells of blood vessels and bile ducts. Is a kind of circulatory system to liver: portal vein to the liver from the intestine the products of breakdown of proteins, carbohydrates, lipids, vitamins, and

partly of mineral substances as well as toxic substances to the body of exogenous and endogenous origin; system of the hepatic artery to the liver supplied with oxygen.

The liver produces about 1/3 of the internal energy of the body. This is synthesized on half of the total number of proteins formed per day in General. Features of the anatomical and morphological structure, enzyme system and the relationship with other bodies responsible participation of the liver in the regulation of almost all types of metabolism.

The most important and most unique liver function is "a function of chemical protection" - detoxification function, the mechanisms of which are quite diverse, ranging from urogenese - formation of urea from ammonia before formation of paired non-toxic compounds from the products of putrefaction of amino acids in the large intestine, products of the conversion chromoproteins (hemoglobin etc.) as well as of xenobiotics, including the metabolism products of certain drugs.

A unique feature of the liver is also the ability to form such excrete as bile, which ensures the digestion and absorption of lipids in the intestine.

Structure of the hepatocyte is ideally suited to the implementation of the aforementioned functions. This hexagonal cell has two poles - one that is addressed to the capillary and contact with the blood, it is called a sine wave, the second - the reverse of the bile duct is called biliary. The membrane of the hepatocyte, which forms these poles, covered with microvillus, thereby increasing the area of contact of the hepatocytes with blood and bile. In addition, the membrane of hepatocytes permeates a large number of pores. All of the structural organization of hepatocytes and their enzyme apparatus ideally suited for the realization of their biochemical functions

Thus, the liver performs the following main biochemical functions:

1) regulatory-homeostatic;
2) zhelcheobrazovanie and excretory;
3) chemical protection or zashkalivalo.

Regulatory-homeostatic function. The liver is involved in metabolism of proteins, carbohydrates, lipids, vitamins, pigments, non-protein nitrogenous substances, and partly in maintaining water-mineral homeostasis.

The metabolism of proteins and amino acids (Fig.1.) is realized thanks to intensive biosynthesis of proteins of the liver, most of the blood proteins, protein-protein complexes (gluco - and lipoproteins) as well as metabolism of amino acids. A day in the adult human body produces about 80-100 g of protein, half of which is in the liver. A day in the liver is synthesized about 12 g of albumins of blood plasma, a large part of the α - and β-globulins, proteins that participate in hemostasis (fibrinogen, prothrombin, and other protein coagulation factors and anticoagulation systems of blood), enzyme proteins, transport proteins such as ceruloplasmin, transferrin, transcortin.

The liver is particularly active flows synthesis of amino acids, the synthesis of such non-protein nitrogenous compounds, such as creatine, glutathione, Niacin, purine and pyrimidine bases, porphyrin, dipeptide, co-enzymes of Pantothenate the like, as well as the reaction of deamination of amino acids to form ammonia. During fasting, the liver is primarily spends its reserve proteins to provide amino acids to other tissues. As a result of the loss of protein in the liver is about 20%, while in other organs do not exceed 4%.

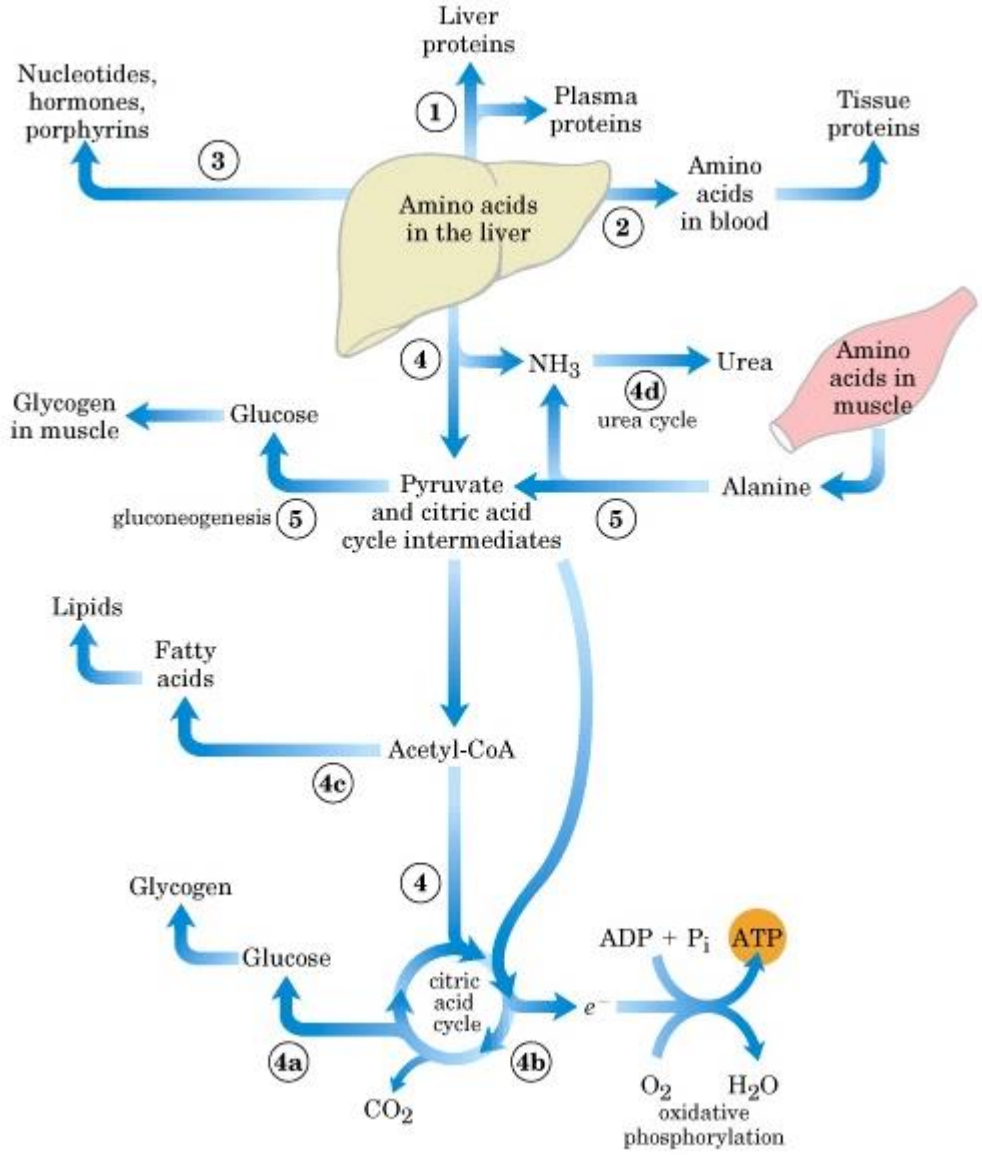


Fig.1.The scheme of the metabolism of proteins and amino acids in the liver

The metabolism of carbohydrates (Fig.2.) is due to the fact that the liver is the only organ that maintains a constant level of blood glucose even under starvation conditions. Being absorbed in the intestine, glucose enters the blood of the portal vein to the liver where a large portion of its phosphorylated with the formation of glucose-6-phosphate. Glucose-6-phosphate is a key intermediate product of carbohydrate metabolism – can turn into the liver in various ways, and the choice of any one of them depends on the needs of both the liver and the whole organism With glucose-6-phosphate is synthesized glycogen, the spare form of glucose in the body. Excess glucose-6-phosphate, which not used for the formation of blood glucose and the glycogen of the liver, is cleaved by glycolysis to pyruvic acid and then to acetyl-CoA and CO_2, which are used for the synthesis of fatty acids. From the intermediate product of glycolysis – doxazosin by recovery of the formed glycerol-3-phosphate. Fatty acids and glycerol-3-phosphate are used for the synthesis of fats (triacylglycerols), phosphoglyceride, which partially remain in the liver and partly are carried to other tissues in the composition of lipoproteins. A certain portion of acetyl-CoA in the liver is used for cholesterol synthesis. Part of the glucose-6-phosphate in the liver is oxidized in pentose phosphate cycle.

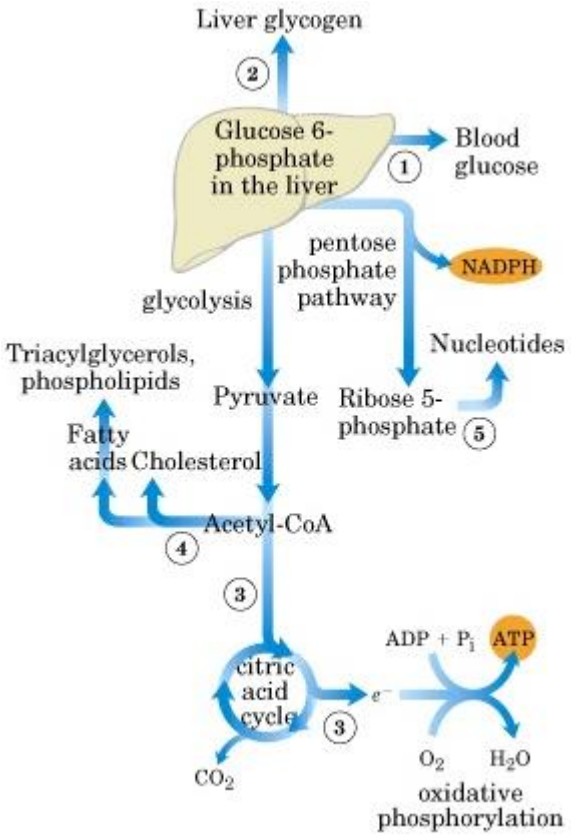


Fig.2.The scheme of the metabolism of carbohydrates in the liver

A few hours after a meal glycogen the liver gradually breaks down to free glucose to provide the body's need for carbohydrates (but the same is synthesized from glucose meal). Glucose produced in the liver in the processes of glycogenolysis and gluconeogenesis, enters the bloodstream and is used by other tissues, especially nervous.

Lipid metabolism (Fig.3.) is provided by the reactions of biosynthesis of various lipids (cholesterol, triacylglycerols, phosphoglycerides, sphingomyelin the like), which enter the bloodstream and distributed to other tissues. In the liver from acetyl-COA is synthesized by cholesterol more than comes from food. So, with the food a person consumes per day, about 0.3-0.5 g of cholesterol and in the liver it is formed of 2-4 g. Synthesizing α-and β-lipoproteins, the liver is involved in the distribution of lipids between the other organs and tissues, because these fractions are the transport forms of different classes of lipids. In addition, fasting dramatically increases the oxidation of fatty acids formation of ketone bodies. Ketone bodies are formed in the liver, where transported by blood to peripheral tissues, where it is used as a source of energy.

Important biosynthetic by the liver is formation of fatty acids and fats (lipogenesis). Fatty acids are synthesized rapidly and in large quantities with acetyl-COA, which can be glucose and amino acids, not used for other functions.

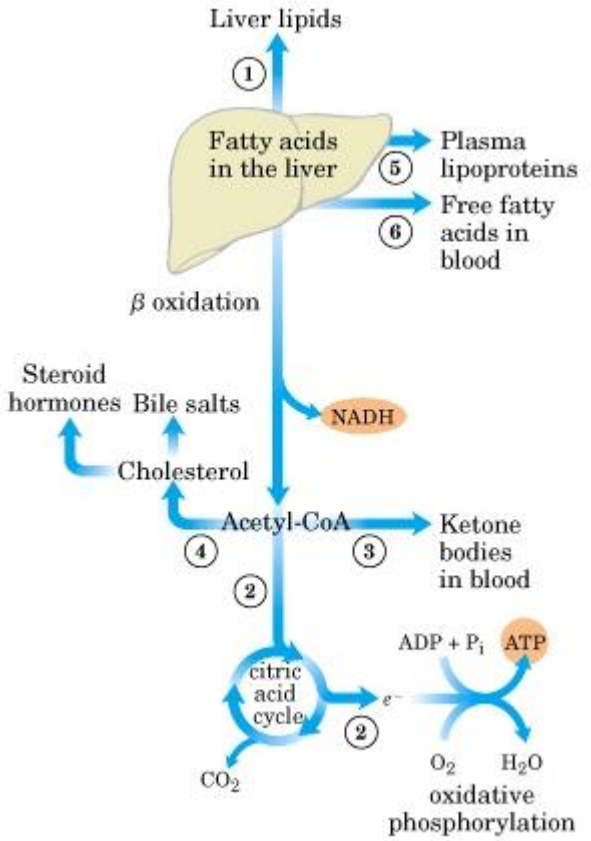


Fig.3.Scheme of lipid metabolism in the liver

Participation of the liver in metabolism of vitamins is ensured by the Deposit in it, mainly the fat soluble vitamins, synthesis of nicotinic acid and coenzymes, transformation, calciferols to 25-hydroxy calciferol.

Involvement of the liver in water-mineral metabolism. The liver complements the function of the kidneys in maintaining electrolyte homeostasis and is an internal filter of the body (Kupffer cells). There is evidence that the liver holds the ions n+, K+, CI-, Ca2+ and water and releases them into the blood. The liver deposits some minerals and participates in their distribution among other tissues with the help of transport proteins.

Participation of the liver in metabolism of nitrogenous bases of nucleic acids is manifested in their synthesis from simple compounds and oxidation of purine bases to uric acid. Nitrogenous bases are used in other organs for the synthesis of nucleotides, nucleosides and nucleic acids, and uric acid stands out as the end product exchange.

Synthesis of bile and excretory functions. In hepatocytes formed a special liquid excreta - the bile that is stored in the gallbladder and then the bile duct enters the 12-duodenum, participating in digestion and absorption of lipids. Bile performs the following functions: a) emulsifies the lipids, resulting in optimal conditions for the action of pancreatic lipase; b) activates lipase promotes the hydrolysis and absorption of products of digestion of fats; C) participates in the neutralization of acids that come from the stomach into the duodenum; g) activate intestinal and pancreatic proteolytic enzymes, stimulates the secretion of pancreatic juice; d) improves the absorption of fat-soluble vitamins (A, D, E, K) cholesterol; e) activates peristalsis of intestine;f) are allocated with bile bilirubin, cholesterol, drugs, poisons, therefore, the bile is not only a secret, but excreta.

In the composition of bile includes bile acids, proteins, cholesterol and its esters, various ions (Ca2+, K+ etc), water, metabolic products of heme is bilirubin in the form of pair compounds with glucuronic acid (bilirubinometer), the products of metabolism of hormones, vitamins, and xenobiotics entering the body, including drugs. The pathological States associated with disorders of excretory function of the liver, adversely affect the digestion and absorption of lipids and enhance the accumulation of toxic products of metabolism of pigments, and xenobiotics.

Cleavage of heme. Bile pigments. In the composition of hemoglobin occurs oxidative fission bridge between the first and second rings protoporphyrinogen cycle with the participation of NADPH-dependent hemoxygenase. Red hemoglobin is converted into green verdoglobin (hologlobe). Erdogan globin spontaneously decomposes into iron and biliverdin (tetrapropylene molecule) (Fig.4.).

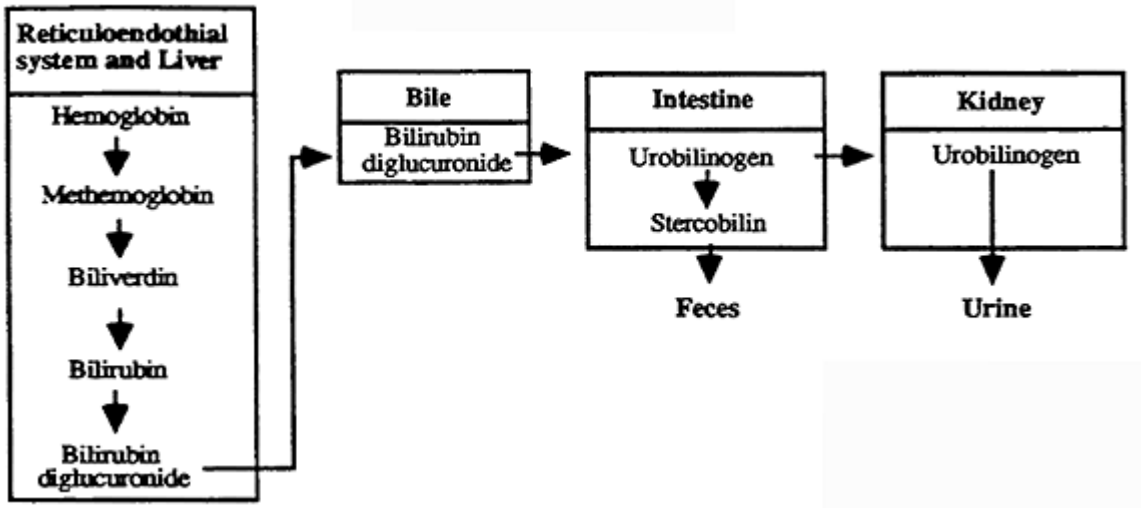


Fig.4. The decay scheme of the heme in body tissues.

The biliverdin is converted into bilirubin (recovery connection between 3 and 4 pyrrols) enzyme of the NADPH-dependent biliverdinreductase. Bilirubin enters the blood, adsorbed albumin. Its characteristics are: insoluble, toxic, free, indirect (not defined directly by the Ehrlich's reagent without prior protein precipitation). The range of bilirubin to albumin is transported to the liver, where it is absorbed by hepatocytes.

In the membranes of the endoplasmic reticulum, bilirubin interacts with UDP-glucuronic acid under the influence UDP-glucuronyltransferase, the formation of mono - and diglucuronide bilirubin. Now he's getting straight, soluble, have low toxicity, but is associated. The majority of bilirubin is excreted in bile.

In the blood serum of a healthy person the concentration of bilirubin low. This bilirubin (total bilirubin" serum of the blood consists of two fractions:

1) free bilirubin (approximately 75% of total bilirubin)

2) bound bilirubin (respectively up to 25% of total bilirubin) that underwent conjugation with glucuronic acid (conjugated bilirubin); this form is secreted by normal hepatocytes into bile, and only partially, in a minor amount enters the blood.

The glucuronide of bilirubin in the composition of bile enter the intestine, where they split off the glucuronic acid and sequentially forming such compounds as tetrapropyl mezoben and mesobilinogen (in small intestine) and stercobilinogen (colon). A number mesobilinogen is formed in the liver and enters the gall bladder along with glucuronide bilirubin. Stercobilinogen and urobilinogen are colourless compounds, but in the air (faeces and urine) are oxidized to the yellow pigment urobilin and stercobilin.

Tetrapyrrols absorption in the gut.

Most of the products of the transformation of bilirubin in the intestine (95%) is excreted in feces. However, the part stercobilinogen absorbed in the lower parts of the colon through the hemorrhoidal vein up to the overall flow. From the blood enters the urine in the form of urobilin in very small amounts, so is that in the urine of a healthy person, urobilin is absent.

Mesobilinogen (urobilinogen) is absorbed by the mucous membrane of the small intestines via the portal vein enters the liver where it is broken down to diprol, which are excreted in the bile. For violation of the barrier function of the liver mesobilinogen not split, enters the bloodstream and excreted by the kidneys, also called urobilin urine, which is attached to urobilin product suction stercobilinogen.

Pathology of pigment metabolism – ***jaundice***. The increase in the concentration of total bilirubin 2 times or more in the serum appears avtovesti of the skin and mucous membranes (especially eyes) and is called jaundice. Distinguish perepechenova (hemolytic), hepatic (hepatocellular), cholestatic (obstructive) and enzymatic (familial) jaundice.

1.Hemolytic – develops as a result of enhanced destruction of erythrocytes (hemolysis). Causes of hemolysis: Rh-conflict of the newborn, transfusion of incompatible blood groups, radiation, malaria parasites, snake venom, etc. The increase in the concentration of total bilirubin due to indirect, of sterkobilin in feces and urobilin in the urine.

2.Hepatic due to violations of the structure and properties of hepatocytes (viral, toxic, infectious hepatitis). Hyperbilirubinemia due to the increase in indirect bilirubin due to violation of conjugation with UDP-glucuronic acid (damage to membranes of the endoplasmic reticulum and a decrease in

activity UDP-glucuronic acid transferase),as well as a direct violation of the secretory function of hepatocytes, necrosis of liver cells. In urine appears bilirubin-glucuronide and "urobilin" in violation of the ability of hepatocytes to destroy tetrapyrroles. Increases the activity of transaminases, especially ALT.

3.Obstructive – the impossibility of the transfer of bile to duodenum due to blockage biliary tract (tumors, stones, postoperative scars, worms and the like). There is a discoloration of feces ("Acholi" feces) because they the lack stercobilin and the absolute lack of urobilin. In the blood an increase in direct bilirubin, its excess is excreted in the urine (urine color of beer). Transaminase activity in normal.

Hereditary jaundice:

1.Syndrome Kryhlera-Najjar – jaundice caused by insufficient synthesis UDP-glucuronic acid ltransferase.

2.Gilbert's syndrome – a violation of cinesouth-glucuronyltransferase ability of hepatocytes to uptake of bilirubin from the blood

3.Syndrome Dana-Johnson – violation transportable-glucuronides hepatocytes into the bile.

4.Neonatal jaundice is a temporary condition caused by the late the inclusion of the genes encoding UDP-glucuronic acid transferase. Treatment with phenobarbital is an inducer of hepatic enzymes as microsomal oxidation, and glucuronidation substrates..

The function of detoxification. This feature involves several main ways of neutralization of toxic products of endogenous and exogenous origin. One of them is a function of urea synthesis (urogenese), in which the ammonia formed during deamination of amino acids and other nitrogen compounds, is transformed into an indifferent product is urea, which is secreted into the blood and then excreted by the kidneys in urine composition. The liver is the only organ that has the enzymes of the urea cycle from ammonia.

The second way of disposal of toxic products of endogenous and exogenous origin is the biosynthesis of pairwise non-toxic compounds using sulfuric acid to its active form, PAPS (3'-phosphoadenosine-5'-phosphosulfate), glucuronic acid, active form of which is UDP-glucuronic acid (uridinediphosphate glucuronic acid), and amino acids glycine. In this way, that is by synthesizing the pair of compounds is the clearance of bilirubin. phenol, cresol, skatole and indole, which are absorbed from the gut, benzoic acid, which enters the body with food and drugs.

The processes leading to a decrease in the concentration of a certain substance in the blood, organs and tissues are called elimination, which can be done in ways:

-excretion – removal of xenobiotics from the body. Urine derived mainly water soluble substances of low molecular weight; bile substance with a weight that is greater than 500 Da, and are poorly soluble in water.

-biotransformation (metabolism) and chemical reactions of the xenobiotic to water-soluble compounds due to the modification (oxidation or reduction) and (or) conjugation of the xenobiotic with polar compounds. Therefore, at all stages of the runs the main principle is the elimination of water-soluble xenobiotics and the conversion of lipophilic xenobiotics into water-soluble compounds that are able to leave the body.

Biotransformation of chemical compounds can take place in 3 phases (Fig.5). Detoxification reactions carried out by enzymes EPR and mitochondria. In addition, a significant role in these processes plays cytosolic enzyme – glutation reductasa.

In the liver occur both phases of biotransformation, namely, modification and conjugation.

Phase 1 biotransformation or phase modification, is provided, primarily, of the numerous family of enzymes - cytochromes P450 and microsomal epoxys and some other enzymes of the detoxification system. All these enzymes are localized in the membranes of the endoplasmic reticulum and belong to the so-called microsomal monooxygenase system or metabolism. They catalyze the oxidation reaction, garageland, decarboxylation, dehalogenase, recovery, hydrolysis of esters and so on. As a result of reactions And phase composition of xenobiotics appear functional group-OH,-COOH,-NH_2,-SH,which increases the polarity of their molecules and facilitates further detoxification and elimination.

The system of cytochrome P-450 that includes multiple functional proteins are grouped into two electrontransport circuit in which the family of cytochrome P-450 is the main active element. The total equation of the reaction of microsomal oxidation with participation of cytochrome P-450 is:

$RH + O_2 + NADPH + H+ \ P_{450} > ROH + H_2O + NADP+$

In the process of phase 1 is often the activation of hydrophobic xenobiotics by formation of the active intermediate metabolites, which are the main substrate system detoxification phase 2 enzymes.

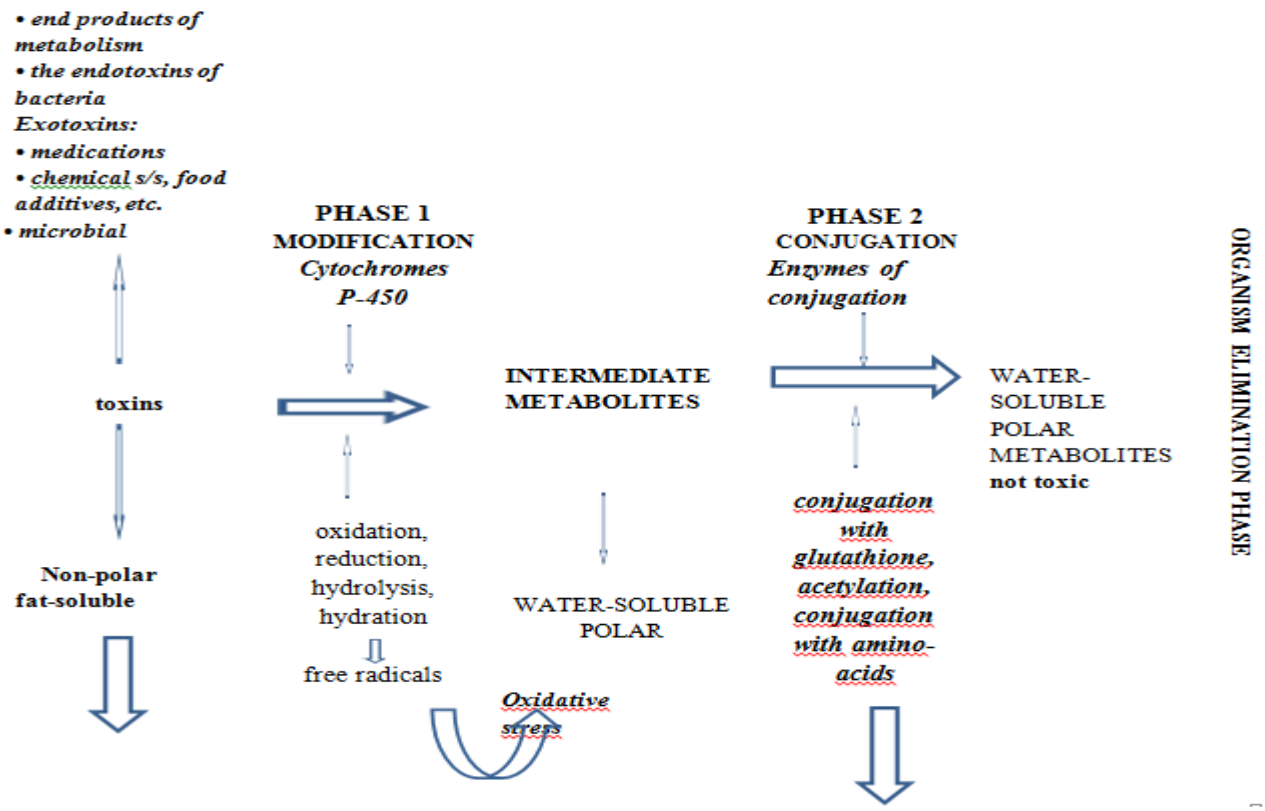


Fig.5. Diagram of the pathways of biotransformation of xenobiotics and endotoxins

All the enzymes of phase 2 or phase conjugation belong to the class of transferases, are mainly located in the cytoplasm of cells, with the exception of enzymes glucuronyltransferase and acyltransferase that also can be accommodated in the EPR. At this stage there is a bond of endogenous or exogenous substrates with the agents, conjugation and the formation of soluble, non-toxic derivatives, which are readily are excreted in the urine.

Features stages:

1. Agents of conjugation produced by the body. So, for example, glucuronic acid is formed from glucose; glycine and cysteine can be synthesized or formed by hydrolysis of food proteins and self.

2. The reaction of conjugation occurs primarily in the liver, only some of them in the kidneys.

3. As a result of conjugation are formed are less toxic and more soluble compounds that are excreted in the urine.

4. Conjugation can be second stage modifications of the substrate (after oxidation, reduction and hydrolysis) or occur independently as a single mechanism for modifying connection (without 1st stage).

The main reactions of conjugation:

1.Conjugation with the active form of glucuronic acid is UDP-glucuronate.

2. Conjugation with sulfuric acid phosphoadenosine-5-phosphosulfate (PAPS).

By binding with glucuronic or sulfuric acids are neutralized xenobiotics phenol and amino nature.

3. Conjugation with glutathione. The system of neutralization of xenobiotics with the participation of glutathione is the most important defense mechanism of the cell.

4. Conjugation with amino acids (glycine, glutamine, ornithine, taurine). For example, with glycine conjugium benzoic and salicylic acid, aspirin.

5. Acetylation with the acetyl-CoA. By conjugation with acetic acid is the neutralization of aromatic amines - sulfonamides, anti-tuberculosis drugs (isoniazid, and the like). Accordingly, the activity of the process of acetylation of people are divided into fast and slow ацетилятори4-aminoantipyrine. This should be considered in determining the dose of drugs that are metabolized by the data (e.g., isoniazid anti- tuberculosis means).

In phase 3 burusports is the excretion products from the body detoxification via lungs, kidneys, intestines. An important role in these processes belongs to the squirrel of plasma albumin, which binds

to and transportorul metabolites of exogenous and endogenous substrates, including the products of phase 1 and phase 2 detoxification.

Enzyme inducers of the metabolism of xenobiotics. Induction of enzymes is the phenomenon of strengthening of synthesis of molecules of the enzyme by its substrates. The body takes action for fast removal of debris. The effects of this induction is the following:

1) increases the efficiency of detoxification in the hepatocytes;

2) decrease the pharmacologic effects of certain drugs in case of their long-term use for example. sleeping pills quickly lose the ability to induce sleep, and to lull the alcoholic needs to increase several times the dosing of drugs for anesthesia.

Inducers: barbiturates, steroid hormones, polycyclic hydrocarbons (benzpyrene, methylcholanthrene), ethyl alcohol, acetone, tobacco smoke.

Enzyme inhibitors the metabolism of xenobiotics. Competitive. For example, ethanol is an inhibitor of the metabolism of methanol or ethylene glycol.

Non-competitive (inhibit the activity of the enzyme, changing the past, but not similar to the substrate). For example, disulfiram (antabus) - an inhibitor of aldehyde dehydrogenase, causes the growth of the content of acetaldehyde and a toxic reaction in humans who consume ethanol. This effect is used for the treatment of alcoholism.

Metabolic activation of xenobiotics. Biotransformation may be accompanied by increased biological activity of the xenobiotic: forming a reactive metabolite. The common feature of reactive metabolites is their high elektriliste. They react with the electron rich nucleophilic molecules – proteins and nucleic acids. Thus, chloroform, a well-known tool for the anesthesia, turns into a chemical warfare agent (phosgene), and paracetamol (analgesic) – N-acetylphenanthrene which causes centrolobular necrosis of the liver. To substances capable of forming toxic metabolites are carcinogens (benzpyrene, nitrosamines), mutagens, hepatotoxin. For example, in the process of oxidation and demethylation nterstitial formed carbocation able alculate DNA, transforming guanine to methylguanine. The change of the structure of DNA is a mutation, and if DNA repair does not occur, it may be cancer.

Thus, biotransformatia of xenobiotics plays a key role in the mechanisms of adaptation of the organism to environmental factors. The most effective detox system is functioning under the United, harmonious action of enzymes-phase 1 and phase 2; desynchronization of these processes leads to the rapid poisoning of the body from the accumulation of products of peroxidation of different carcinogens, mutagens and teratogens. It is particularly unfavorable combination of high activity of enzymes of phase 1 and low activity of phase 2 enzymes.

Each individual is inherent in the unique configuration of genes responsible for synthesis of enzymes of the biotransformation system, and, accordingly, the unique reaction of each person to the damaging effect of environmental factors and endogenous factors. The reason for phenotypic differences is polymorphism of the relevant genes of great interest for the study.

5.Materials for self-control.

A. Tasks for self-control.

1. Write reactions of conjugation in hepatocytes:
- glucuronidase with the participation of UDP-glucuronic acid.
- sulfateand 3-phosphoadenosine-5-phosphosulfate
methylation involving an S-adenosylmethionine
- acetylation with the acetyl-S-CoA.
- conjugation with glycine.
2. Write the reaction of neutralization of bilirubin in the liver.
3. Write the reaction of neutralization of the skatole and indole in the liver.
4. Write the reaction of neutralization of ammonia in liver

B. Tests for self-control

1. Owing to biotransformation of drugs involving microsomal oxidation system can be all these transformations, EXCEPT...(select one):

A. The decrease in pharmacological activity of drugs

*B. Formation of an intermediate. metabolites common metabolic pathways.

C.. Increased activity of drugs.

D . The formation of toxic metabolites.

E . The appearance of soluble products.

2.Which of the following enzymes increases the solubility of substances by joining UDP.-glucuronic acid?

A. P-glycoprotein.

*B. UDP.-glucuronyltransferase.

C.. Cytochrome P-450.

D . Glutathionetransferase.

E Sulfotransferase.

3.In the liver of the patient violated detoxicate natural metabolites of xenobiotics. Name the cytochrome, the activity of which can be reduced:

A. Cytochrome c_1

B. Cytochrome Oxidase.

C. Hemoglobin.

D .Cytochrome b.

*E. The Cytochrome P-450.

4. In a patient with cirrhosis of the liver. Study any of the following substances, excretiruthan urine can characterize the state of antitoxic liver function?

*A. Hurova acid.

B. Ammonium salts.

C. Creatinine

D. Uric acid

E. Amino Acids.

5. In the reactions of conjugation can participate all of the following connections in addition to...(select one answer)

A. Glutathione.

B . S-adenosylmethionine.

*C. ATP.

D . UDP.-glucuronate.

E . PAPS.

6. Reactions of biotransformation of xenobiotics and endogenic toxins in hepatocytes occur or by redox and hydrolytic transformations, or by conjugation. During conjugation to the compounds, neutralized, could not join the rest:

*A. Gluconic acid.

B. Glucuronic acid.

C. Sulfuric acid.

D. Glycine.

E. Glutamine.

7 Have full-term newborn is observed yellow staining of the skin and mucous membranes. The probable cause of such condition may be a temporary deficiency of the enzyme:

*A. UDP.-glucuronyltransferase.

B. Uridyltransferase

C. Geminates

D. Genocides

E Blondinettes

8, decomposition of xenobiotics (pharmaceutical drugs, epoxides, arenose, aldehydes, nitro-derivatives, and the like) and endogenous metabolites (estradiol, prostaglandins, leukotrienes), which results in the liver by conjugation with:

A. 3-phosphoadenosine-5-phosphosulfate.

B. Asparaginovuyu acid.

C. Glycine.

D. S-adenosylmethionine.

*E. Glutathione.

9. The young man, 20 years old, diagnosed with hereditary deficiency UDP.-glucuronyltransferase. Increasing the level of index blood confirms the diagnosis?

A. Stercobilinogen.

B. Direct (conjugated) bilirubin.

S. Urobilin.

*D. Indirect (conjugating) bilirubin.

E. Animal indican

10. A newborn that suffers on physiological jaundice, he was prescribed Phenobarbital. For what purpose this prepare used for the treatment of neonatal jaundice?

A. To lock gem-oxygenase system.

*B. For inducing reactions of conjugation of bilirubin.

C. For inhibiting decomposition of bilirubin in the intestine

D To activate the binding of bilirubin by albumin.

E To increase the number of haptoglobin in the blood

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MINISTRY OF HEALTH OF UKRAINE
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Department of Pharmaceutical, Biological and toxicological chemistry

"APPROVED"
Head of pharmaceutical, biological and toxicological chemistry department
PhD in medicine, Professor _____ I.V.Nizhenkovska
protocol number 2 on August 31, 2017

GUIDELINES
FOR INDEPENDENT STUDENTS WORK
WHILE PREPARING FOR THE PRACTICAL LESSON

Academic discipline	Biological chemistry
Module number	module 2
module	**Content module 7: Essentials of pharmaceutical biochemistry and biochemistry of tissues**
Study subject number 10	Biochemistry of the kidneys. Normal and pathological components of urine. The regulation of water-mineral metabolism. *Physicochemical properties of urine.*
Course	3 year
Faculty	Pharmaceutical
Number of hours	2,5

Kyiv 2017
Prepared by PhD in medicine, Professor I.V.Nizhenkovska

1. Topic actuallity

The kidneys perform several homeostatic functions in humans and higher animals. The functions of the kidneys include the following: 1) participate in the regulation of blood volume and extracellular fluid (polymolecular); 2) the regulation of the concentration of osmotically active substances in blood and other body fluids (osmoregulation); 3) regulation of the ionic composition of blood serum and ion balance (ion regulation); 4) participates in the regulation of acid-base status (pH stabilization of the blood); 5) participate in the regulation of blood pressure, erythropoiesis, blood clotting, modulation of hormone action due to the formation and release into the blood of biologically active substances (incretory function); 6) participation in the metabolism of proteins, lipids and carbohydrates (metabolic function); 7) the body's excretion of end products of nitrogen metabolism and foreign substances, excess of organic substances (glucose, amino acids, etc.) received with food or formed during the process of metabolism (excretory function). Thus, the kidney is a homeostatic organ involved in maintaining the constancy of the fundamental physico-chemical constants of the internal medium fluids in circulatory homeostasis, stabilization of the exchange indices of various organic substances.

From blood plasma the kidneys form a liquid called urine. The volume and composition of urine in contrast to other secrets can vary within very wide limits; it is due to its ability to change the composition of urine depends on state of metabolism and changes in environmental conditions, effectively the kidneys are involved in the regulation of volume and composition of extracellular fluid.

Biochemical analysis of urine is required in the outpatient and clinical setting in the diagnosis of several diseases. In biochemical find both normal and pathological components of urine, which gives the possibility to judge about the functional state of the kidney, metabolism in different organs and the organism as a whole, helps to find out the causes, nature and prognosis of the pathological process, to evaluate the effectiveness of treatment.

2.Specific objectives:

• To characterize the biochemical mechanisms mocheobrazovanie of kidney function.
• To analyze biochemical composition of urine in norm and at pathological processes, to estimate functional role of end products of nitrogen metabolism.
• Analyze the impact of pharmaceuticals on renal function and physico-chemical properties of urine.
• Be able to determine the physico-chemical properties of urine and interpret the results.

3. Basic knowledge, abilities, skills necessary for studying the topic (interdisciplinary integration)

Names of previous disciplines	Obtained skills
Physical methods of analysis and Metrology	To own methods of conducting laboratory research tools
Biology with fundamentals of genetics	To classify the structure of biopolymers.
Physiology	1. To characterize the role of the kidneys in maintaining homeostasis 2. To explain the mechanisms of urine formation.
Pathological physiology	To analyze the causes and mechanisms of development of violations of the basic functions of the kidneys.

4.Tasks for independent work during preparation to the lesson.

4.1. A list of the main terms, parameters, characteristics that need to learn by the student during the preparation to the lesson

Term	Definition
Not protein nitrogentetroxide components of urine	Not protein nitrogentetroxide components of urine is urea, uric acid, creatinine, creatine, hurova acid, indica n, pigments, amino acids.
Beznen components of urine	Beznen components of urine is glucose, ketone bodies, pyruvate, lactate, mineral salts.
Pathological components of urine	Pathological components of urine is glucose, protein, ketone bodies, bilirubin, creatine, hemoglobin.
Bilirubinuria	Bilirubinuria - the allocation of bilirubin in the urine
Glucosuria	Glucosuria - the presence in urine of glucose in high concentrations
Hematuria	Hematuria - presence of blood in the urine or red blood cells
Creatinuria	Creatinuria - availability of creatine in the urine.
Ketonuria	Ketonuria - increased secretion of ketone bodies in the urine.
Proteinuria	Proteinuria - increased protein in the urine.
The active form of vitamin D3	The active form of vitamin D3 is a steroid hormone that is produced in the cells of the proximal tubule and stimulates the absorption of calcium in the intestines, which significantly increases the resorption of bone and stimulates reabsorption of calcium in renal tubule.
Kinins	Kinins - low-molecular peptides in the blood that are involved in the regulation of vascular tone (dilates them), lower blood pressure, regulate the microcirculation, involved in inflammatory and allergic reactions. The most important is cnname bradykinin and caldin. Inactive their predecessors – cinnoline – proteins that are synthesized in the liver and bind to α2 – globulins. Kinins have a short-long-action – half-life of these molecules is 20 – 30 sec. This fact is due to the high activity cnns – enzymes that split them apart.
Kallikrein	Kallikrein - specific enzymes transformation cenogen in kinins. Kalchini are also in an inactive form, precarn and are activated with the participation of factor XII of blood coagulation . Due to the fact that kinins play a significant role in the pathogenesis of inflammation, the clinic is the wide use of purchased drugs – inhibitors of kinins (contrical, gordox and others). From the lungs and salivary

	glands of the bull is highlighted inhibitor kalekin – trasilol. He is also a trypsin inhibitor, so it is used in the treatment of acute pancreatitis.
The renin-angiotensin-aldosterone system	Renin is proteolytic enzyme produced by juxtaglomerular apparatus of the kidneys. Renin, entering the blood turns angoringen (α2-globulin) synthesized in the liver, to angiotensin I. Angiotensin And, under the influence of angiotensin converting enzyme in the blood vessels of the lungs turns to angiotensin II. Angiotensin-II, or into angiotensin III stimulates the release of aldosterone.
Erythropoietin	Erythropoietin is a peptide hormone which participates in regulating the production of erythrocytes from the bone marrow. The impetus for its secretion is to reduce the content of oxygen in the kidneys.

4.2 Theoretical questions to the lesson.

1. Features of metabolism in kidneys.
2. Biochemical mechanisms mocheobrazovanie of kidney function.
3. Physico-chemical properties of urine: urine volume, pH, transparency, odor, relative density.
4. Normal organic components of urine: urea, uric acid, creatinine, amino acids, pigments, lactate, and pyruvate.
5. Pathological components of urine: glucose, protein, ketone bodies, bilirubin, creatine, hemoglobin.
6. The influence of pharmaceutical agents on renal function and physico-chemical properties of urine
7. The renin-angiotensin-aldosterone system in the regulation of blood pressure and water-salt metabolism in the human body.

4.3. Practical work performed in class.

Experiment 1.. Analysis of the physico-chemical properties of urine.

A. Determination of daily volume of urine (diuresis).

The progress of the work. The daily amount of urine is measured using measuring cylinder to 1 or 2 L.

Clinical, diagnostic and practical value. In norm, the daily urine volume is about 1500 ml to 1200 ml Colovic in women. Urine volume more than 2200 ml and less than 500 ml per day, suggests the pathology. The amount of urine may be reduced (oliguria), increased (polyuria); and the complete cessation of urine output (anuria).

B. Determination of relative density of urine.

The progress of the work. In a small cylinder with the same diameter to prometr freely swam in it, poured over the wall (to prevent the formation of foam, but, if it is formed, it snma
out using filter paper) research urine and carefully immerse in it orometer with divisions from 1.00 to 1,030 g/l. carry out counting, given the line on the scale of prometra, which corresponds to the lower meniscus of the liquid. In the case of a large relative density of urine study take the second type of prometra (from 1,030 to 1,060). All the definitions usually carried out at a temperature of 15 °C because the scale of prometra calibrated in accordance with this temperature. If the urine has a different temperature and bring it to 15 °C, then for every 3 °C above the specified temperature must be added, and for every 3 °C below—subtract 0.001 from the reading on the scale of prometra.

Clinical, diagnostic and practical value. The relative density depends on the amount of soluble substances in the urine and is closely linked with the amount of urine. It normally (measured at 15 °C) is in the range of 1,010—1,025, but is usually 1,017—1,020. The discrepancy between relative density and amount of urine occurs in case of diabetes, when the relative density remains high, despite large amounts of urine. Relative density changes in various pathological conditions. Abrupt decrease observed in diabetes insipidus. Determination of relative density of urine is performed using a special areometers small size, are called aromatami.

C. Characteristics of urine color.

The progress of the work. The color of urine evaluated visually.

Clinical, diagnostic and practical value. Normally it is straw-yellow and is due to the presence of pigments: urochrome (dark yellow), urobilin (pale pink), uroerythrin (red). Consumption of some products (in particular, beet) and taking drugs (amidopyrine, antipyrine) give the urine a pink red color. If the urine are blood pigments, it is colored pink or brown color in the presence of bile pigments in green or yellow-brown color in the presence of pus in the urine opalesce, black color observed in alkaptonuria and depends on the presence of dark pigments (melanin) in alkaline urine, which are the

products of the conversion homogentisic acid. Green-blue color is observed in bacterial contamination of urine; with excessive content of indican, which is transformed into Indigo blue.

D. Assessment of the transparency of urine.

The progress of the work. The transparency of the urine is determined in a beaker of colourless glass after shaking.

Clinical, diagnostic and practical value. Normal urine is transparent. Upon standing deposited a loose mucous mass, composed of sloenogo epithelium of the urinary tract and mucous membranes Taurus. Blood, pus, protein cause the appearance of turbidity, which indicates the pathological processes that occur in the kidneys and urinary tract.

E. Determination of urine.

Clinical, diagnostic and practical value. Normal fresh urine has an odor of volatile substances it contains. When the decay of the urine has an unpleasant pungent smell of ammonia, by the decay of cells in the urinary tract, the urine becomes putrid smell, in the presence of a large number of acetone bodies—fruit smell (diabetes mellitus). Odorous foods or medications can make urine smell peculiar to them.

F. Determination of acidity (pH) of urine.

The progress of the work. Strip of universal indicator paper is immersed in the test urine, take it out, and determine the pH value on the color scale. For change of color one of the painted stripes that matches the color of test strips, determine the pH of urine.

Clinical, diagnostic and practical value. Normal urine pH ranges from 5.0 to 7.0. Offset acidic side is observed in the secretion of acetone bodies (diabetes, starvation) or in severe renal failure. A shift of urine pH towards the alkaline environment, marked by the consumption of dietary bicarbonates, alkaline mineral water, dairy and plant products, inflammation of the bladder mucosa after prolonged vomiting.

4.4. The content of the topic

Functional and structural unit of renal tissue is the nephron. Each kidney contains 1 million nephrons. Part of the nephron includes renal pyramid (of Malpighi) contains Shumlyansky vascular glomerulus surrounded by a Bowman's capsule. Components of the nephron: the proximal and distal winding tubules; collecting duct; descending and ascending knee of a loop of Henle; distal segment consisting of a thick ascending knee of a loop; the distal convoluted and connecting tubules. Connecting tubule connected to team tube. Renal tubules, along with ducts penetrate cortex and medulla of the kidneys.

The main function of the kidneys is reduced to regulate the volume, osmolarity, mineral composition and acid-base status of the organism by excretion of water and mineral electrolytes in the quantities necessary to maintain their balance and normal concentrations of these substances in the extracellular fluid. Ions, which are regulated in this manner include sodium, potassium, chlorine, calcium, magnesium, sulfate, phosphate and hydrogen ions.

The kidneys guarantee the removal of end products of metabolism. Such substances include urea is formed from protein), uric acid (from nucleic acids), creatinine (formed from muscle creatine), the end products of the breakdown of hemoglobin, metabolites of hormones, etc.

Many foreign substances that enter from outside the body, are excreted in the urine. It's drugs, food additives, pesticides, etc.

In the kidneys produces the active substance, can be considered as an important endocrine organ that produces renin, erythropoietin, active form of vitamin D_3.

Renin, entering the blood, triggers the renin-angiotensin-aldosterone system. Renin secretion in juxtaglomerular apparatus is regulated by the following main influences. First, the value of the arterial pressure in afferent arteriole. The pressure reduction leads to increased renin secretion and Vice versa. Second, renin secretion depends on the concentration of sodium in the urine distal tubule. The increase in the concentration of sodium in the urine tubule, leading to increased secretion of renin. Thirdly, the secretion of renin is regulated by cute nerves via beta-adrenergic receptors. Fourthly, regulation is by a feedback mechanism due to the blood content of angiotensin II and aldosterone. Angiotensin II has a strong vasoconstrictor action. This is due to the presence of sensitive to angiotensin II receptors (AT1 and AT2) precapillary arterioles, really located in the body unevenly. Therefore, the vascular effects in different areas vary. System sadanosuke effect is accompanied by a decrease of blood flow to the kidneys, intestines and skin, and increase it in the brain, heart and adrenal glands. However, very large doses of angiotensin II can cause constriction of blood vessels of heart and brain. It is established that the increase in the content of renin and angiotensin in the blood increases the feeling of thirst and Vice

versa. Aldosterone, secreted in the cortical layer of the adrenal glands, has an unusually high ability to enhance reverse absorption of sodium in kidneys, salivary glands, the digestive system, thus altering the sensitivity of blood vessels to the effects of adrenaline and noradrenaline. Given the close relationship between renin, angiotensin and aldosterone physiological effects combined with a the name of the renin-angiotensin-aldosterone system (Fig.1.).

The hypertensive effect of angiotensin II is regulated by kinins plasma, which increases capillary permeability and dilates blood vessels, causing a decrease in blood pressure. An example of such mediators can be calden and bradykinin (Fig.2).

Medicines that affect kidney function. Diuretics — drugs of different chemical structures, which contribute to increasing urine output and reducing the amount of fluid in the body. For a better understanding of the mechanism of action of modern diuretics recommended classification, which takes into account not only the movement but the localization of their action:

1. Tools that operate at the level of the cells of the renal tubules.

1.1. Tools that operate at the level of the apical membrane:

a) competitors in a carrier of sodium(triamterene, amiloride);

b) aldosterone antagonists (spirono-lactone).

1.2. Tools that operate at the level of the basement membrane:

a) carbonic anhydrase inhibitors (diakarb);

b) derivatives benzothiazepine - thiazides (gidrokhlorisiazit, tsiklometiazid, oksodolin);

C) derivatives of acids dichlorophenoxyacetate (ethacrynic acid);

d) derivatives of Anthranilic acid (furosemide, bufenoks, klopamida, torasemid).

2. Osmotic diuretics (mannitol,urea).

3. Agents that increase blood flow to the kidneys (theobromine, theophylline, aminophylline, etc.).

4. Medicinal plants (horsetail,bearberry leaves, birch buds, leaves of orthosiphon, strawberries, etc.).

Inhibitors of angiotensin converting enzyme (ACE) – captopril, enalapril, lisinopril, and ramipril are widely used in the treatment of cardiovascular diseases due to its role in blocking the pathological effects of hyperactivation of the renin-angiotensin system. The mechanism of action is inhibition of the activation of angiotensin converting enzyme, a key enzyme of this system. The latter, on the one hand, promotes the formation of angiotensin II (vasoconstrictor, inducer of the release of aldosterone, norepinephrine, endothelin, myocardial hypertrophy), on the other – stimulates the breakdown of bradykinin (an inductor of synthesis of natural adenotonsillar substances prostacyclin and nitric oxide). The result of the application of ACE inhibitors dilate peripheral blood vessels, prignutsya the activity of the sympatho-adrenal system, reduced the energy consumption of the myocardium, increases natriuresis. Observed kalisberegate and system vasoprotective action. Long-term use of ACE inhibitors, these effects do not decrease, but even increase.

Antagonists of angiotensin receptors II (ARA II) group of drugs used for the treatment of patients with chronic heart failure recently. Drugs, including losartan (cozaar), block angotensin receptors And the type that prevents the interaction of angiotensin II and reduces its vasoconstrictor action. Proved the feasibility of combined use of ACE inhibitors and ARA II.

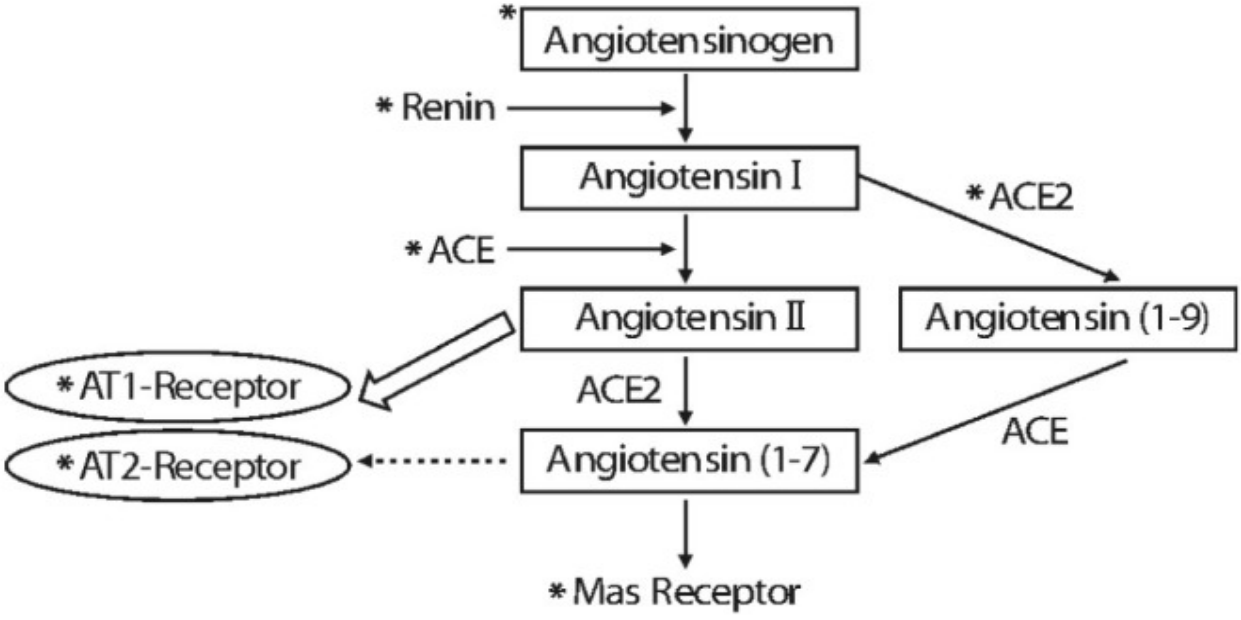

Fig.1.The main effects of the renin-angiotensin-aldosterone system (ACE - angiotensin converting enzyme)

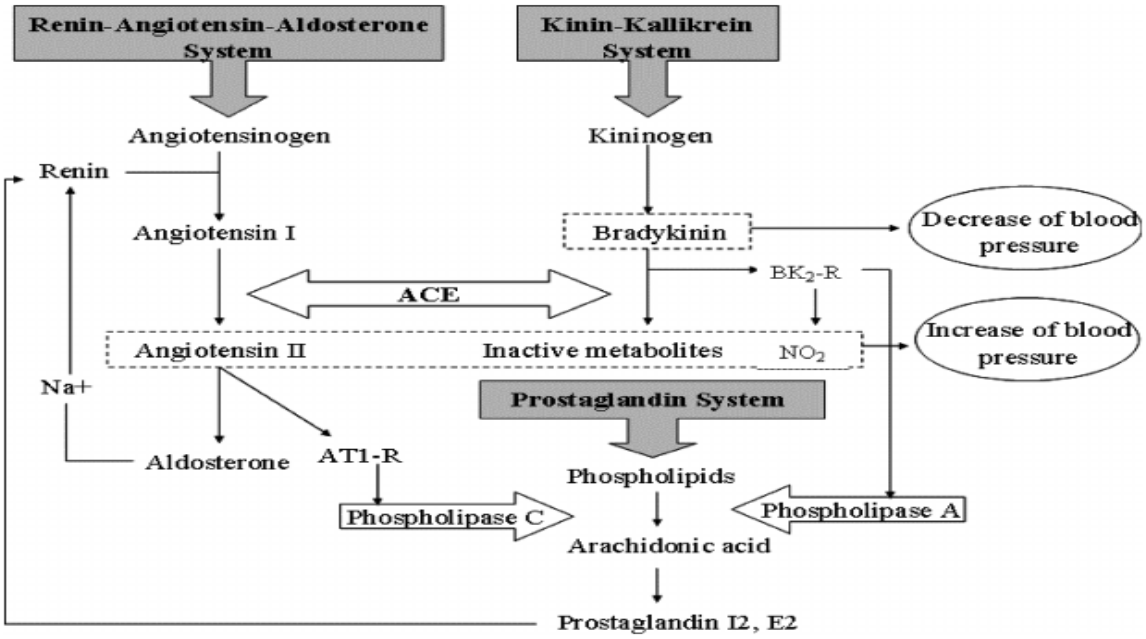

Fig.2. The relationship of the renin-angiotensin and kalikrein-kinin system regulation of blood pressure

Table 1. Physico-chemical characteristics of normal urine

	Urine volume	**Density of urine**	**Urine color**	**Transparency urine**	**pH urine**
NORMAL	from 1000 ml to 2000 ml/day	1,015-1,022 kg/l	shades of yellow color	transparent	pH=5,3-6,5

Table 2.The inorganic constituent parts of normal urine

	Cl^-	**Na^+**	**K^+**	**Mg^{++}**	**SO_4^{2-}**	**NH_4^+**	**HPO_4^-**	**Ca^{++}**
NORMAL	120-240 mmol/l	100-150 mmol/l	60-80 mmol/l	60-80 mmol/l	30-60 mmol/l	30-50 mmol/l	10-40 mmol/l	4-11 mmol/l

Table 3. Organic components of normal urine

	Urea	**Uric acid**	**Creatinine**	**Creatine**	**Hipyric acid**	**Amino acids**	**Without nitrogen tetroxide components**
NORMAL	330-580 mM/day	1,6-3,54 mM/day	7,1-17,7 mM/day (man), 5,3-15,9 mM/day (woman)	-	0,6-1,5 g/day	1 g /day	Not more than 1 g /day

Table 4. Pathological components of urine

	Protein	Glucose	Ketone bodies	Bilirubin
NORMAL	no	no	no	no

CLINICAL-DIAGNOSTIC VALUE	nephrotic syndrome; diabetic nephropathy; glomerulonephritis; nephrosclerosis; impaired absorption in the renal tubules (Fanconi syndrome, heavy metal poisoning, sarcoidosis, sickle cell disease); multiple myeloma (protein Bence-Jones in urine) and other paraprotein; impairment of renal hemodynamics in heart failure, fever; malignant tumors of the urinary tract; cystitis, urethritis and other urinary tract infections.	diabetes mellitus; acute pancreatitis; gpartition; renal diabetes; steroid diabetes (receiving anabolic steroids in diabetics); poisoning by morphine, strychnine, phosphorus; dumping syndrome; Cushing's syndrome; myocardial infarction; pheochromocytoma; big injury; burns; tubulointerstitial-each of the kidney damage; pregnancy; taking a large amount of carbohydrates.	diabetes mellitus (decompensated diabetic ketoacidosis); prekomatosnoe condition, cerebral (berglen) coma; prolonged fasting ; heavy fever; alcoholic intoxication; gparsons; hypercatecholaminemia; poisoning isopropranolol; eclampsia; Glycogenosis I, II, IV types; the lack of carbohydrates in the diet.	jaundice; viral hepatitis; cirrhosis of the liver; metastases of tumors to the liver

5.Materials for self-control.

A. Tasks for self-control.

1. What is regulatory-homeostatic function of the kidneys?
2. Explain the mechanism of urine formation in different parts of the nephron. Call the number and composition of the primary urine. Why are the substances of primary urine are divided into threshold and non-threshold?
3. What determines the amount of urine? What term is noted in the urine abnormalities?
4. Compare the color, odor, relative density and acidity of the urine in healthy and sick people.
5. What quantity of proteins is manifested in normal urine, and their origins? What are the types of proteinuria, their causes.
6. List neblo nitrogentetroxide substances in the urine, call their number. Under what conditions these figures change?
7. Name benazolin components of urine, contents and abnormalities in pathology.
8. Explain the involvement of the kidneys in the regulation of vascular tone and blood pressure due to the functioning of the renin-angotensin and kallikrein-klinovo system.

B. Tests for self-control

1. In the urine of the patient increased the content of indole and a low content of indican. This indicates a violation of:

A. protein synthetical function of the liver.
*B. Detoxification of the liver
C. the Secret of the pancreas.
D. renal Filtration function.
E. Reabsortion of kidney function.

2.The patient with progressive muscular dystrophy were conducted biochemical research of urine. The emergence of any substance in a large amount of urine may confirm muscle disease in this patient?

A. Burova acid.
B. Creatinine.
* C. Creatine.
D. The Porphyrins.
E. Urea.

3.The examination of the patient is determined by the presence of hyperglycemia, ketonuria, polyuria and glycosuria. What form of acid-base balance occurs in this case?

A. Metabolic alkalosis.
B. Gas alkalosis.
*C. Metabolic acidosis.
D. Gas acidosis.

E. Negativi alkalosis.
4.In the composition of urine of a patient identified creatin, creatine, urea, amino acids, uric acid, sterkobilina, ketone bodies, 17-ketosteroids, lactose, macro-and micronutrients. Which of these components is not contained in the urine of a healthy person
A. Urea and 17 ketosteroids.
B. Creatine and sterkobilina.
*C. Ketone body and minerals.
D. Creatine and lactose.
E. Amino acids and macronutrients.
5.After the birth of the child revealed a positive reaction of urine with a 10% ferric chloride. What hereditary disease is characterized by?
A. Alkaptonuria.
B. diabetes mellitus (hereditary form).
C. Histidinemia.
* D. Phenylketonuria.
E. Galactosemia.
6.What buffer system plays an important role in maintaining a constant pH of urine:
*A. the Phosphate buffer system
B. Hemoglobina buffer system
C. the Bicarbonate buffer system
D. Protein buffer system
E. Urinary buffer system
7.What pathological compound appear in urine at diabetes mellitus:
*A. Sugar, acetone, acetone acid; β-garageman
acid.
B. Phenyl ICR, acetone, glucose.
C. Sugar, blood, bilirubin.
D. Protein, blood, bile pigments.
E. Bile pigments, indica n, homogentisate acid.
8.The workers working in hot shops, diuresis is reduced to 0.5 L. Specify a reason for this phenomenon.
A.* Increases the allocation of water skin.
B. Disturbed hormonal regulation.
C. the Water is retained in the gastrointestinal tract.
D. Increased allocation of water light.
E. Increasing the allocation of water in the gastrointestinal tract.
9.The ammonia coefficient of the urine in the examined patient's increased 8%. About the condition of the body may indicate such an increase in ammonium konu urine?
A. Acidosis.
V. Alkalosis.
C. increasing the amount of protein in the diet.
D. violation of the detoxification functions of the liver.
* E. Violation of ecoventura liver function.
10.The patient with urolithiasis in the blood and urine was found an increased content of uric acid. The reaction of the urine was strongly acidic. The presence of what type of stones can be expected in this patient?
* A. Urate.
B. Oxalate.
C. Fostert.
D. Calcium.
E. Holesterinove.

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