FACULTY OF MEDICINE
STUDY PROGRAM 0912.1 MEDICINE
CHAIR OF BIOCHEMISTRY AND CLINICAL BIOCHEMISTRY

APPROVED
at the meeting of the Commission for Quality Assurance and Evaluation of the Curriculum faculty Medicine
Minutes No. 6 of 27.02.2018

Chairman dr. hab., associated professor

Sergiu Suman _____

APPROVED
at the Council meeting of the Faculty Medicine nr. 2
Minutes No. 4 of 20.03.2018

Dean of Faculty dr., associated professor

Mircea Beţiu _____

APPROVED
approved at the meeting of the chair of Biochemistry and Clinical Biochemistry
Minutes No. 7 of 1.10.2017
Head of chair, dr. hab., associated professor

Olga Tagadiuc _____

SYLLABUS
DISCIPLINE BIOCHEMISTRY

Integrated studies

Type of course: Compulsory

Chisinau, 2017

I. INTRODUCTION

General presentation of the discipline: place and role of the discipline in the formation of the specific competences of the professional / specialty training program

The goal of biochemistry is to provide students with fundamental theoretical knowledge and general practical skills in medical biochemistry that are indispensable to the activities of all health professionals. Students will study biochemical bases of the existence and functioning of the human body, as well as biochemical features of organs under physiological conditions and in pathologies. The activities during the study of the discipline will create the students' individual and team working skills, the ability to set and solve a task, to use certain laboratory equipments, to analyze and interpret the results of laboratory investigations, to apply theoretical knowledge in medical practice, integration of information from different disciplines (fundamental and clinical), etc.

Mission of the curriculum (aim) in professional training consists of studying:

a) the structure of the main chemical compounds of the living matter and the fundamental metabolic processes that underlie the functionality of the living organisms;

b) the particularities of the chemical compounds and of the metabolic processes that ensure the functioning of the organs and mechanisms underlying the disturbances of their functions;

c) biochemical investigation methods of clinical utility and training of laboratory data analisis and interpretation abilities.

Language (s) of the course: Romanian, English and Russian

Beneficiaries: students of the 2nd year, Faculty of Medicine 2.

II. MANAGEMENT OF THE DISCIPLINE

Code of discipline		F.03.O.020/F.04.0.028	
Name of the discipline		Biochemistry	
Person(s) in charge of the discipline		Olga Tagadiuc	
Year	II	Semesters	III-IV
Total number of hours, including:			180
Lectures	68 (34 + 34)	Practical/laboratory hours	102 (51 + 51)
Seminars		Self-training	190 (95 + 95)
Form of assessment	C/E	Number of credits	12 (6 + 6)

III. TRAINING AIMS WITHIN THE DISCIPLINE

At the end of the discipline study the student will be able to:

a) at the level of knowledge and understanding:

- know the physico-chemical structure and properties of the main chemical compounds of medical interest;
- know the fundamental metabolic processes that ensure the viability and reproduction of the human body;
- be familiar with the structural and metabolic features of the organs;
- know the influence of various factors (vitamins, pharmaceuticals, toxins) and metabolic disorders on biochemical processes;
- know the normal values and physiological variations of the main biochemical markers.

b) at the application level:

- to determine by itself some biochemical markers of general clinical-diagnostic utility;
- to be able to work on the main devices used in the biochemical laboratory (simple and automatic pipettes, spectrophotometer, centrifuge, etc.);
- appreciate the usefulness of certain biochemical investigations in the diagnosis of specific pathologic conditions;
- to correctly interpret the results of biochemical investigations.

c) at the integration level:

- to appreciate the importance of Biochemistry in the context of Medicine;
- to know the correlations between Biochemistry and other fundamental and clinical disciplines;
- to objectify the connections and interdependence between structural, metabolic and clinical biochemistry;
- to appreciate the evolution of physiological metabolic processes and their disorders that condition various diseases.

IV. PROVISIONAL TERMS AND CONDITIONS

Biochemistry is a biomedical discipline, the study of which at the integrated studies stage will allow future medical professionals to know the molecular bases of physiological metabolic processes, biochemical mechanisms for regulating vital functions; to understand the causes and pathogenesis of hereditary and acquired diseases that cause damage to different organs; to justify the need for biochemical investigation; evaluate the results of the laboratory examination and correlate them with clinical and functional data for diagnosis purposes; to develop the lifecycle correction scheme; to determine the principles of treatment of the disease, depending on its mechanisms of development.

To study the discipline students need thorough knowledge in the field of Chemistry and Biology, obtained in the pre-university studies, as well as in the field of Human Anatomy, Histology and Physiology obtained in the undergraduate studies.

Internet skills are also needed to identify the materials needed for study and individual work, document processing, tables and presentations.

V. THEMES AND ESTIMATE ALLOCATION OF HOURS

Lectures, practical hours/ laboratory hours/seminars and self-training

No. d/o	THEME	Number of hours		
		Lectures	Practical hours	Self-training
1	Biological role of enzymes. Chemical nature and enzyme´s structure. Coenzymes. Vitamins as coenzymes. Microelements as cofactors.	2	3	4
2	Mechanism of action of enzymes. Nomenclature and classification of enzymes. Enzyme specificity. Kinetics of chemical reactions.	2	3	6
3	Regulation of enzyme activity. Activation and inhibition of enzymes. The role of biomedical enzymes.	2	3	6
	Concluding test on chapter „Enzymes”		3	
4	Bioenergetics. Metabolism, role, phases, stages. Energy regulation of metabolism.	2		6
5	Oxidative decarboxylation of pyruvic acid. The Krebs cycle.	2	3	6
6	Biological oxidation. Respiratory chain and oxidative phosphorylation. Microsomal oxidation. Oxidation with free radicals.	2	3	6
7	Carbohydrates. The role of biomedical. Digestion and absorption of carbohydrates. Metabolism of glycogen. Glicogenoses.	2	3	6
8	Metabolism of glucose. Aerobic and anaerobic oxidation of glucose.	2	3	6
9	Gluconeogenesis. Cori and glucose-alanine cycle. Mutual regulation of glycolysis and gluconeogenesis.	2	3	6
10	Pentosophosphates pathway of glucose oxidation . Metabolism of fructose and galactose. Synthesis of lactose.	2	3	6
11	Regulation of carbohydrate metabolism. Disruptions of carbohydrate metabolism.	2		6
	Concluding test on chapters „Energy metabolism” „Carbohydrates metabolism”		3	
12	Biological role of lipids. Lipid digestion and absorption. Disorders of digestion and absorption of lipids. Resist lipids in the intestinal epithelium. Residual lipid metabolism.	2	3	5
13	Biosynthesis and beta-oxidation of fatty acids. Biosynthesis and use of ketone bodies.	2	3	6

No. d/o	THEME	Number of hours		
		Lectures	Practical hours	Self-training
14	Metabolism of structural lipids: biosynthesis and catabolism of cholesterol, phospholipids	2	3	6
15	Structural lipid metabolism: biosynthesis and catabolism of sphingolipids. Lipidase tissues	2	3	6
16	Plasma lipoproteins.	2	3	4
17	Hereditary and acquired pathology of lipid metabolism	2		4
	Concluding test on chapter "Metabolism of lipids"		3	
	Total hours for the I semester	34	51	95
18	Metabolism of simple proteins. The dynamic state of proteins. The nitrate balance. Digestion and absorption of proteins.	2	3	5
19	General ways of amino acid metabolism: deamination, transamination.	2	3	6
20	The final products of nitrate metabolism. Ammonia detoxification. Ureogeneză	2	3	6
21	Particularities of the metabolism of some amino acids. Biosynthesis of nonessential amino acids.	2	3	6
22	Metabolism of chromoproteins.	2		6
	Concluding test on chapter "Metabolism of simple proteins and chromoproteins"		3	
23	Metabolism of purine nucleotides. Metabolism of pyrimidine nucleotides.	2	3	6
24	DNA biosynthesis - mechanism, regulation.	2	1.5	5
25	RNA biosynthesis, regulation	2	1.5	5
26	Biochemical bases of translation. Posttranslational changes of proteins. Folding.	2	3	6
	Concluding test on chapter „Metabolism of nucleotides. Biosynthesis of nucleic acids and proteins”		3	
27	Hormones, biological role, classification, mechanism of action. Neuro-hormonal regulation of metabolism. Hypothalamic-pituitary hormones.	2	3	6
28	Hormones of the thyroid gland. Hypo- and hyperfunction of the thyroid gland.	2	1.5	5

No. d/o	THEME	Number of hours		
		Lectures	Practical hours	Self-training
29	Hormones of the pancreas. Diabetes mellitus: Medulloadrenal hormones.	2	1.5	5
30	Hormones of the adrenal cortex. Sex hormones. Hormones that regulate calcium and phosphate homeostasis (parathyroid hormone, calcitonin and calcitriol).	2	3	6
31	Biochemistry of blood. The chemical composition of blood plasma. Plasma proteins, blood enzymes, residual nitrogen, mineral substances	2	3	6
32	The biochemical bases of maintaining the fluid state of the blood. Clotting. Fibrlinolysis.	2	3	6
33	Biochemical bases of gas transport. Acid-base balance.	2	3	5
34	Integration of metabolism. Complete regulation of metabolism.	2	3	5
	Concluding test on chapters „Hormones” and „Biochemistry of the blood”		3	
	Total hours for the II semester	34	51	95
	Total fours for the year	68	102	190

VI. REFERENCE OBJECTIVES OF CONTENT UNITS

Objectives	Content units
Chapter 1. Enzymes	
1. Know the structure of enzymes and their mechanism of action. 2. Specify the properties of the enzymes resulting from their protein nature. 3. Identify the importance of vitamins as coenzymes. 4. Apply methods for the separation and purification of proteins and the evaluation of enzyme activity.	1. Notion of enzymes and their biological role. Similarities and differences between enzymes and non-biological catalysts. 2. The chemical nature of enzymes. Evidence of the protein nature of enzymes. Structure of enzymes. Active and allosteric centers of enzymes. 3. Simple and conjugated enzymes. The notion of holoenzyme, apoenzyme, cofactor, coenzyme, co-substrate and prosthetic group. Coenzyme functions of vitamins and microelements. 4. Structure of vitamins B_1, B_2, B_6, PP, pantothenic acid, biotin, folic acid, B_{12} and their role as coenzymes. 5. Mechanism of action of enzymes. The enzyme's active center and its role in the formation and transformation of intermediate complexes between enzyme and substrate. The role of reciprocal

Objectives	Content units
5. Identify the type of enzyme specificity and its biomedical role. 6. Be able to represent the graphs of enzyme´s activity dependence on various environmental factors. 7. Identify types of inhibition and represent them graphically. 8. Be able to explain the mechanisms of regulation of enzyme activity. 9. Define the notion of isoenzymes and their biomedical role. 10. Be able to identify the enzymatic profile in the blood in various organ disorders. 11. Explain the clinical-diagnostic value of enzymes in general and of individual enzymes used in medical practice.	conformational changes of the enzyme and substrate molecules in the catalysis process. 6. Nomenclature and enzyme classification. The general characteristic of the main classes and subclasses of enzymes. Enzyme code number. 7. Specificity of enzymes (types, examples). 8. Enzyme kinetics. Influence of enzyme and substrate concentration, pH and temperature on enzyme activity and reaction velocity. 9. Principle of enzyme activity assay. Units of enzymes activity (international unit, katal, specific activity). 10. Activation and inhibition of enzymes: – activation of enzymes by partial proteolysis. Zymogens (proenzymes). – Inhibition of enzyme activity (specific and non-specific, reversible and irreversible, competitive and non-competitive). 11. Regulation of enzyme activity (allosteric regulation, covalent regulation). The importance of the retro inhibition principle. 12. Isoenzymes - the structural and functional particularities, their biomedical value. 13. Organization of enzymes in the cell (enzymatic assemblies, compartmentalization). 14. The differences in the enzymatic composition of organs and tissues. Organ specific enzymes. 15. Use of enzymes in medical practice: – Enzyme diagnostic. – Enzyme therapy. – The use of enzymes in the laboratory. 16. Methods of enzymes separation and purification. Affinity chromatography.
Chapter 2. Energy metabolism	
1. Define the notions of metabolism, anabolism, catabolism and amphi-bolic phase of metabolism. Identify the connections	1. Notion of metabolism. Anabolism and catabolism. Metabolic pathways. The amphibolic stage of metabolism, its role. 2. Methods of metabolism study. 3. The laws of thermodynamics. Enthalpy, entropy and free energy. Standard free energy, its significance. Endergonic and exergonic

Objectives	Content units
between them. 2. Apply the laws and main principles of thermodynamics to living organisms. 3. Know the biological importance of the main energy processes in the human body. 4. To know the main bioenergetic processes in human cells - pyruvate oxidative decarboxylation, Krebs cycle, electron transport chain and oxidative phosphorylation 5. Know the regulatory enzymes of each metabolic pathway, levels and types of their regulation. 6. Explain the mechanism of oxidation and phosphorylation coupling. 7. Be able to calculate the energy yield of pyruvate oxidative decarboxylation and Krebs cycle. 8. Explain the mechanism of electron transport chain inhibition and uncoupling of oxidative phosphorylation. 9. Define microsomal oxidation and free radicals oxidation. 10. To be able to assess the impact of microsomal oxidation disturbances and excessive formation	reactions. 4. High energy compounds: role, main representatives, structural particularities. Super high energy compounds. Chemical structure and role of ATP. The ATP cycle. Variants of ATP hydrolysis. ATP synthesis mechanisms. 5. Energy regulation of cellular metabolism. Energy state of the cell indices. 6. Oxidative decarboxylation of pyruvate: polyenzyme complex, coenzymes, overall reaction, steps, process regulation, Krebs cycle and respiratory chain. The role of biomedical. 7. Tricarboxylic acid cycle (Krebs): functions, reactions, enzymes, overall reaction, connection with the electron transport chain, energy output, regulation. 8. Anaplerotic reactions. Their significance. 9. Biological oxidation. Dehydrogenation of substrates - the main energy source for ATP synthesis. Reactions, enzymes and coenzymes of dehydrogenation. 10. Electron transport chain - location, biological significance. 11. Structure and oxidoreduction properties of major proton and electron acceptors (NAD^+, FAD, FMN, CoQ). Notions about the structure of cytochromes and Fe-S proteins. 12. Oxidation-Reduction Potential of Respiratory Chain Components. 13. Scheme of the electron transport chain. Enzymatic complexes. Electron transport chain inhibitors. 14. Oxidative phosphorylation. Phosphorylation points. Regulation of the intensity of the electron transport chain function. P/O coefficient. 15. Mechanism of oxidation with phosphorylation coupling (Mitchell hypothesis). ATP synthase. ATP-synthase inhibitors. Role of internal mitochondrial membrane in ATP biosynthesis. Transport of adenyl nucleotides and phosphate through the mitochondrial internal membrane. 16. Uncoupling of oxidation and phosphorylation processes. Uncoupling compounds, their mechanism of action. Examples of physiological and pathological uncoupling. 17. Microsomal oxidation. The role of cytochrome P450 in oxidoreduction reactions. 18. Oxidative stress. The oxygen reactive species: synthesis,

Objectives	Content units
of reactive oxygen species. 11. To be able to explain the biological role of antioxidant systems. 12. To present the connections between the main energy processes in the cell, as well as their impact on cell viability and homeostasis.	physiologic and pathologic effects. Antioxidant systems.
Chapter 3. Carbohydrates metabolism	
1. Define carbohydrates and appreciate their biomedical role. 2. Identify the stages of carbohydrates digestion, absorption and associated disorders. 3. To know the ways of carbohydrate metabolism under different physiologic and pathological conditions and the mechanisms involved. 4. Understand the connections between the carbohydrate and energy metabolism processes and the reciprocal regulatory influences. 5. Be able to calculate the energy output of anaerobic and aerobic oxidation of individual carbohydrates (glucose, galactose, fructose, sucrose, lactose). 6. To know the regulating enzymes of glycogeno-	1. The biological role of carbohydrates. 2. Classification and structure of carbohydrates: – monosaccharides (glucose, galactose, fructose, ribose, etc.); – disaccharides (maltose, lactose, sucrose); – homopolysaccharides (glycogen, starch, cellulose); – heteropolysaccharides. Their biological significance. Structure and role of hyaluronic acid and heparin. 3. Biochemical mechanisms of digestion and absorption of carbohydrates. Disaccharides intolerance. 4. Transport of blood glucose into tissues - glucose transporters (GLUT). Use of carbohydrates in tissues. 5. Metabolism of glycogen: glycogenogenesis and glycogenolysis. Reactions, enzymes, mutual regulation of processes. 6. Glycogenoses (von Gierke's disease, Pompe syndrome). 7. Glycolysis: reactions, enzymes. 8. Summary reaction of anaerobic glycolysis and energy output. 9. Aerobic oxidation of glucose and energy output. 10. Glycerol-phosphate and malate-aspartate shuttle systems of reducing equivalents transport from cytosol into mitochondria. Their importance. 11. Particularities of glucose oxidation in erythrocytes. 2,3-bisphospho-glyceride pathway (Rapoport-Luebering). 12. Gluconeogenesis - substrates, reactions, enzymes, overall reaction. Cori and glucose-alanine cycles. 13. Mutual regulation of glycolysis and gluconeogenesis.

Objectives	Content units
lysis, glycogenogenesis, glycolysis, gluconeogenesis and glucose oxidation pentose phosphate pathways, their levels and types of regulation. 7. Can appreciate glucose metabolism disorders based on main biochemical investigations (physiological and pathological hypo- and hyperglycemia). 8. Demonstrate the pathogenic mechanisms responsible for the development of diabetes melitus.	14. Pentose phosphate glucose oxidation pathway. Biological role of the process, reactions of the oxidative step, enzymes, coenzymes. The overall reactions of stages I and II and of the whole process. 15. Fructose metabolism - hepatic and muscular pathways: reactions, enzymes, biological role. Hereditary disorders of fructose metabolism. 16. Metabolism of galactose - reactions, enzymes, biological role. Hereditary disorders of galactose metabolism. 17. Metabolism of lactose. Lactose biosynthesis - reactions, enzymes, regulation and biological importance of the process. 18. Synthesis of glucuronic acid - reactions, enzymes, regulation and biological importance of the process. Use of glucuronic acid. 19. Hormonal regulation of glucose metabolism: the influence of insulin, glucagon, catecholamines and glucocorticoids. 20. Regulation of carbohydrate metabolism in postprandial and in incipient stages. 21. Disorders of carbohydrate metabolism. Hyper- and hypoglycemia, glucosuria - physiological and pathological causes. Type I and II diabetes mellitus - causes, metabolic disorders, molecular mechanisms of complications. 22. Biochemical methods for glucose metabolism assessment - glycemia, glucose tolerance test, glycated hemoglobin, insulin, C-peptide
Chapter 4. Metabolism of lipids	
1. Define lipids and their biomedical role. 2. Identify the stages of lipid digestion, absorption, resynthesis and transport, and associated disorders. 3. Know ways to metabolize lipids in different tissues and the mechanisms involved. 4. Understand the connections between the processes of lipid, carbohydrate and energy metabo-	1. Food lipid digestion and absorption. Structure and role of bile acids. Cleavage of triglycerides, phospholipids, cholesterides: enzymes, hydrolysis products. 2. Absorption of food lipids hydrolysis products. Hormonal regulation (action of colecistokinin, secretin). Disorders of digestion and absorption of lipids. Pancreatic, hepatic and intestinal steatorrhea . 3. Resynthesis of lipids in enterocytes. Chylomicron formation. 4. Fatty acid biosynthesis - location, steps, reactions, enzymes, coenzymes, regulation: – saturated with even number of carbon atoms; – unsaturated with even number of carbon atoms; – arachidonic acid biosynthesis (general notions).

Objectives	Content units
lism and the reciprocal regulatory influences. 5. Demonstrate the ways of mutual transformations glucose ↔ lipids. 6. Be able to appreciate lipid metabolism disorders based on main biochemistry investigations (hypo- and hyperlipidemia, hypercholesterolemia, lipidemia). 7. Demonstrate the pathogenic mechanisms of tissue and organs disorders in lipid pathology (obesity, atherosclerosis, hereditary and aquired dislipidemias).	5. Triglycerides biosynthesis: localization, reactions, enzymes and coenzymes, regulation. 6. Catabolism of triglycerides - reactions, enzymes, hormonal regulation (action of catecholamines, glucagon, insulin, glucocorticoids). 7. Glycerol metabolism – ways of use; oxidation: reactions, enzymes, energy output. 8. Beta-oxidation of fatty acids: – saturated by even number of carbon atoms (location, stages, reactions, enzymes, coenzymes, energy output, regulation); – unsaturated and with odd number of carbon atoms (peculiarities); – in peroxisomes (peculiarities), the biological role. 9. Ketone bodies: – representatives, chemical structure; – biosynthesis (site, substrate, reactions); – use (tissues, reactions, end products, energy output); – ketonemia and ketonuria (causes, mechanism of occurrence). 10. Neuro-hormonal regulation of lipid metabolism (catecholamines, glucagon, insulin, glucocorticoids, thyroid hormones). 11. Cholesterol biosynthesis - steps, first step reactions (up to mevalonic acid), enzymes, coenzymes, regulation. Catabolism and excretion of cholesterol (general notions). 12. Biosynthesis of glycerophospholipids: localization, reactions, enzymes and coenzymes. Lipotrope substances, their role. 13. Biosynthesis of sphingophospholipids and glycolipids: precursors, main reactions, enzymes. 14. Tissue catabolism of glycerophospholipids, sphingomyelins and glycolipids (site, enzymes, hydrolysis products). 15. Hereditary tissue lipidoses (Neimann-Pick, Tay-Sachs) - causes, biochemical changes, clinical manifestations. 16. Blood transport of lipids. Plasma lipoproteins: structure, separation methods, types (chylomicrons, VLDL, LDL and HDL), chemical composition (lipids and apoproteins), metabolism, functions. 17. Dyslipidemias - causes, biochemical changes, clinical manifestations:

Objectives	Content units
	– primary hyperlipoproteinemias (familial hypercholesterol-emia, familial hyperchylomironemia). – secondary hyperlipidemias (in diabetes, alcohol consumption). – primary hypolipoproteinemias (general notions). Tangier disease - cause, biochemical changes. 18. Acquired lipidoses (obesity, atherosclerosis, in alcohol consumption) - causes, metabolic changes. 19. Normal plasma lipid values. The diagnostic significance of plasma triglycerides, total cholesterol, HDL- and LDL-cholesterol assay. 20. Relationship between energy, glucose and lipid metabolism. 21. The metabolic role of fat-soluble vitamins A, D, E, K. Hypo- and hypervitaminosis (causes and metabolic manifestations).
Chapter 5. Metabolism of simple proteins and cromoproteins.	
1. Identify the stages of protein digestion and absorption in GIT. 2. Define the types of nitrogen balance and describe the people for whom it is specific. 3. Be aware of the biomedical importance of the transamination process and enzymes. 4. Describe the main processes that generate ammonia and its toxicity mechanisms. 5. To know the ways of temporary and final detoxifycation of ammonia, elimination of the detoxification products and the diseases associated with the disturbances of these processes. 6. Explain the clinical	1. Daily requirements of dietary proteins. Biological value of food proteins. 2. Proteolytic enzymes. Activation mechanism. The specificity of proteases. 3. Digestion of proteins in the stomach. Gastric proteolytic enzymes. The role of hydrochloric acid. HCl secretion and its regulation (H^+, K^+-ATP-ase). The composition of gastric juice and its changes in pathology. Gastric secretion inhibitors. 4. Digestion of proteins in the intestine. Pancreatic and intestinal proteolytic enzymes, their specificity of action. Regulation of proteins digestion in the intestine. 5. Absorption of amino acids in the intestine. Active secondary and facilitated transport of amino acids. 6. Putrefation of the amino acids into the large intestine. The putrefaction products. Mechanisms of detoxification of toxic products in the liver (microsomal oxidation, conjugation). Conjugation agents, enzymes. 7. The fate of the absorbed amino acids. Transport of amino acids into cells. The gamma-glutamyl cycle. 8. Common metabolic pool of amino acids. The dynamic state of protein metabolism. The nitrogen balance. Protein deficiency. 9. Parenteral protein nutrition. 10. Transamination of amino acids: mechanism, enzymes,

Objectives	Content units
importance of urea assay in urine and blood. 7. Know the pathways of each amino acid use, the sources and mechanisms of synthesis of the non-essential ones and the ways of their metabolism. 8. Differentiate the main types of jaundice (prehepatic, hepatic and posthepatic) by the level of bile pigments in blood, urine and stool. 9. Know the pathway of hemoglobin biosynthesis and differentiate the main types of porphyrias 10. Differentiate the main types of anemias by laboratory markers.	coenzymes, process significance. Diagnostic value of blood transaminase activity (ALT and AST). 11. Amino acid deamination. Types. Direct deamination of amino acids. Oxidative deamination of glutamic acid (reaction, enzyme, coenzymes, process importance). 12. Indirect amino acid deamination. Stages. Enzymes, coenzymes. The biological role. 13. Metabolism of alpha-ketoacids obtained by deamination of amino acids. Ketogenic and glucogenic amino acids. 14. Biosynthesis of non-essential amino acids (transreamination, biosynthesis from essential amino acids). 15. Biochemical mechanisms of ammonia toxicity. 16. Ammonia detoxification: carbamoylphosphate synthesis, reductive amination of alpha-ketoglutarate. Synthesis and role of glutamine. Kidney glutamase. Formation of ammonium salts. 17. Biosynthesis of urea. Reactions, enzymes, overall reaction. Enzymatic deficiencies of the urea synthesis cycle. Clinical importance of urea assay in urine and blood. 18. Hyperammonemia and uremia (causes, clinical manifestations, treatment principles). 19. Decarboxylation of amino acids (reactions, enzymes, coenzymes). Biosynthesis of histamine, serotonin, dopamine, gamma-aminobutyric acid, their biological role. Neutralization of biogenic amines. 20. Tetrahydrofolic acid. Structure and metabolic role. Its role in the synthesis of serine, methionine, glycine, purine and pyrimidine nucleotides. Megaloblastic anemia. 21. Metabolism of methionine and cysteine. Synthesis and use of S-adenosylmethionine. Synthesis and role of creatine-phosphate. Hyperhomocysteinemia. 22. Metabolism of glycine, serine and threonine (biosynthesis, metabolic role, catabolism). Hyperoxaluria. 23. Role of arginine in NO synthesis: reaction, enzymes, biological role. 24. Metabolism of phenylalanine and tyrosine. The role of these amino acids in the synthesis of other biologic important compounds. Hereditary pathology of phenylalanine and tyrosine metabolism (phenylketonuria, alcaptonuria, albinism).

Objectives	Content units
	25. Metabolism of tryptophan. His role in the synthesis of biologically active substances (serotonin, melatonin). 26. Metabolism of dicarboxylic amino acids - Glu, Gln, Asp, Asn. Synthesis, metabolic role, catabolism. 27. Metabolism of branched amino acids (notions). 28. Relationships of protein, carbohydrate and lipid metabolisms. The role of liver in metabolism integration. 29. Digestion and absorption of chromoproteins. 30. Iron metabolism. 31. Hemoglobin biosynthesis: site, substrates, first two reactions, process regulation. Porphyria (general notions). 32. Catabolism of hemoglobin. Bilirubin: formation, conjugation, biliary excretion, metabolism in the intestine, urine excretion. 33. Hyperbilirubinemia. The main types of jaundice (prehepatic, hepatic and posthepatic). The importance of blood, urinary and faecal pigments assay in the diagnosis and differentiation of the jaundices.
Chapter V. Metabolism of nucleoproteins and nucleic acids. Biosynthesis of proteins	
1. Know the pathways of the metabolic use of nucleotides in general, their sources and mechanisms of synthesis and metabolism. 2. Present the molecular biochemical mechanisms and identify the similarities and differences of the replication, transcription and translation processes. 3. Explain the clinical importance of uric acid assay in urine and blood. 4. Be able to differentiate the types of hyperuricemia according to laboratory results. 5. Identify the major pathogenic mechanisms of gout.	1. Digestion and absorption of nucleic acids. 2. Purine nucleotide biosynthesis: purine ring atoms sources, phosphoribosylamine synthesis reactions, IMP structure, AMP and GMP synthesis reactions, synthesis of nucleoside diphosphates and triphosphates. Regulation of the process. 3. Pyrimidine nucleotide biosynthesis: sources of atoms in the pyrimidine ring, UTP and CTP biosynthesis. Biosynthesis of deoxyribonucleotides. Biosynthesis of thymidine nucleotides. Regulation 4. Salvage pathway of purines and pyrimidines metabolism. 5. Catabolism of purine nucleotides (uric acid synthesis). Gout - causes, clinical manifestations, treatment principles. 6. The final products of pyrimidine nucleotide catabolism, their fate. 7. Structural analogs of purines and pyrimidines as antiviral and antitumoral medicines. 8. Replication of DNA in prokaryotes (E. coli) - matrix, substrates, enzymes and proteic factors. Biochemical mechanism and stages of DNA biosynthesis. Replication inhibitors - mechanism of action and biomedical role (acyclovir, foscarnet, doxorubicin).

Objectives	Content units
6. Prescribe pathogenetic treatment in gout.	9. Peculiarities of eukaryotic replication. Telomeres and telomerase. Telomerase structure. The biomedical role of telomerase. 10. Biochemical mechanisms of DNA repair. Enzymes involved. 11. The biochemical mechanisms of the single nucleotide mutations. The biomedical role of mutations. Disease caused by mutations (sickle cell anemia, phenyl ketonuria). 12. The peculiarities of the gene structure in prokaryotes and eukaryotes. Structural and regulatory genes. 13. Prokaryote transcription (E. coli): matrix, substrates, enzymes, biochemical mechanism. Transcription inhibitors (rifampicin, nalidixic acid, α-amanitin). 14. Peculiarities of transcription in eukaryotes. Post-transcriptional modifications of mRNA. 15. Biochemical mechanisms that regulate gene expression in prokaryotes and eukaryotes. 16. Reverse transcription. Biochemical mechanism and biomedical role. 17. The composition and structure of ribosome in pro- and eukaryotes. 18. Biochemical bases of the genetic code. Its properties. 19. Protein biosynthesis in prokaryotes. Steps: activation of amino acids; translation - initiation; elongation; termination. 20. Particularities of protein biosynthesis in eukaryotes - translational factors and post-translational modifications of synthesized proteins. Folding of synthesized proteins. 21. Regulation of protein biosynthesis in prokaryotes and eukaryotes. Translation inhibitors (tetracycline, chloramphenicol, erythromycin, streptomycin, diphtheria toxin). The medical role. 22. Polymorphism of proteins (hemoglobin variants, blood groups). 23. Biochemical bases of hereditary diseases. Biochemical diagnostic approaches.
Chapter VI. Hoemones.	
1. Define the notion of hormones and know their general properties. 2. Know the biomedical importance of hormonal	1. Hormones – definition, general properties and role of in the body. 2. Hormone classification. 3. Mechanisms of hormones synthesis, secretion and action regulation – the concept of feed-back regulation systems and hormonal biorhythms.

Objectives	Content units
regulation. 3. Describe the main mechanisms of action of hormones. 4. Identify the particular steps of different structure hormones mechanisms of action . 5. Know the individual hormones, their role, mechanism of action and the effects on the main metabolic processes. 6. Be able to distinguish the main disorders of hormonal secretion. 7. Present the biochemical mechanisms responsible for the effects of various secretion abnormalities for each individual hormone. 8. Can appreciate hormonal disturbances based on biochemistry investigations.	4. Structure of membrane and nuclear receptors. Interactions between hormone and receptor. 5. Mechanisms of action of hormones: – membrane-intracellular mediated by AMP-cyclic, GMP-cyclic, calcium ions, diacylglycerols, inositol phosphates; – the cytosolic-nuclear mechanism. 6. Hypothalamic hormones: releasing and release-inhibiting hormones. Their role. 7. Adenopituitary hormones: – hormones derived from pro-opiomelanocortin; – somatomamotropic hormones; – glycoproteic hormones. Chemical nature, mechanism of action, biological effects, secretion regulation and disorders. Practical use. 8. Posterior pituitary hormones: vasopressin (antidiuretic hormone) and oxytocin. Mechanism of action, biological effects. Diabetes insipidus. 9. Hormones that regulate calcium and phosphate metabolism (parathyroid hormone, calcitonin, calcitriol): structure, biosynthesis, secretion control, mechanism of action, target tissues, effects. Abnormalities of parathyroid hormone secretion. 10. Pancreatic hormones. Structure, biosynthesis and secretion regulation. Mechanisms of action and metabolic effects of insulin and glucagon. Metabolic disorders in diabetes. 11. Thyroid hormones (T3 and T4): structure, biosynthesis, secretion regulation, transport, metabolism, mechanism of action and metabolic effects. Disorders of thyroid function (hyperthyroidism and hypothyroidism). 12. Adrenal medulla hormones (adrenaline and noradrenaline): chemical structure, biosynthesis, storage and secretion, metabolism. Mechanism of action and metabolic effects of catecholamines. Pheochromocytoma. 13. Adrenal cortex hormones: structure, biosynthesis, secretion and transport, metabolism. 14. Glucocorticoids: regulation of secretion, mechanism of action, metabolic effects, disorders of secretion (Addison's disease: suprarenometabolic syndrome).

Objectives	Content units
	15. Mineralocorticoids: regulation of secretion, mechanism of action, metabolic effects, disorders of secretion (Cohn's disease). 16. Sex hormones: structure, biosynthesis, secretion and transport, metabolism, regulation of secretion. 17. Mechanism of action and biological effects of androgens, estrogens and progesterone. 18. Eicosanoids (prostaglandins, thromboxanes, leukotrienes): precursor, chemical structure, synthesis pathways, enzymes, biomedical role.
Chapter VII. Biochemistry of the blood	
1. Know the main chemical compounds of the blood. 2. Define the structural-functional particularities of the main nitrogenous and non-nitrogen containing chemical compounds of the blood. 3. Define the structural-functional particularities of the main blood cells. 4. Explain the sequence of hemostasis phases. 5. Demonstrate the intrinsic and extrinsic mechanisms of coagulation. 6. Define fibrinolysis, the anticoagulant system and demonstrate their mechanisms. 7. Explain the mechanisms of blood gases transport and their role in the maintenance of blood pH. 8. Define the notion of hypoxemia and hypoxia. Explain the causes of their occurrence.	1. Blood chemical composition and functions. 2. Organic nitrogen-containing compounds of blood plasma. – Plasma proteins. Albumin and globulins (fibrinogen, transferrin, ceruloplasmin, haptoglobin, immunoglobulins). Methods of dosing and separation of proteins. Variations of protein fractions in pathology. – Plasma enzymes. Functional classification. Mechanisms of plasma disenzymia. The main plasma enzymes with diagnostic value. – Nonprotein nitrogen-containing compounds of blood plasma. Residual nitrogen, its fractions in normal state and pathology. 3. Non-nitrogen containing organic compounds of blood plasma (glucose, lipids, organic acids, ketone bodies). The importance of their determination. 4. Mineral plasma compounds. Their role. Blood ionogramm. 5. Hemostasis. The general characteristic of hemostasis phases (parietal, plasma and fibrinolytic time). 6. Coagulation of the blood. Plasma and platelets coagulation factors. The site of the synthesis, structural particularities, mechanism of activation of the main plasma factors. The role of vitamin K. Intrinsic and extrinsic coagulation mechanisms. Molecular mechanisms of clot formation and stabilization. Disorders of coagulation. 7. Fibrinolytic and anticoagulant systems: role, main factors, their chemical nature, mechanism of activation. Therapeutic applications. 8. Structural and functional features of platelets.

Objectives	Content units
9. Be able to explain the physiological and biochemical mechanisms of maintaining the blood acid-base balance (EAB). 10. Explain mechanisms of buffer systems and their biomedical role. 11. Use the main EAB indices to differentiate metabolic and respiratory acidosis and alkaloids. 12. Know the methods for the diagnosis of anemia, thrombocytopenia, and pathologies involving blood leukocytes.	Thrombocytopathies. 9. Regulation of the fluid status of the blood. Exploration of haemostasis and fibrinolysis. 10. Chemical composition of erythrocytes: hemoglobin, enzymes, non-hemoglobinic organic components and mineral components. 11. Particularities of mature red cell metabolism (glycolysis, 2,3-bisphosphoglycerate pathway, pentose phosphate pathway, antioxidant protection). Particularities of energy metabolism. ATP synthesis. Use of O_2 in erythrocytes. 12. Hemoglobin - as allosteric protein. Oxygenation/deoxygenation of hemoglobin. Conformational changes of hemoglobin during these processes. Oxygen curve. Bohr effect. Variants of physiological hemoglobins. Hemoglobinopathies. 13. O_2 and CO_2 transport by blood. Biochemical mechanism. The importance of hemoglobin in these processes and in the maintenance of constant blood pH. Hypoxemia and hypoxia. Causes of their occurrence. 14. Physiological and biochemical mechanisms acid-base balance (ABB) maintenance. Blood buffer systems. The main ABB indices. acidosis and alkaloids. 15. Chemical composition and metabolic peculiarities of the peripheral blood leucocytes population.

VII. PROFESSIONAL (SPECIFIC (SC)) AND TRANSVERSAL (TC) COMPETENCES AND STUDY OUTCOMES

Professional (specific) (SC) competences

SC1. Knowledge, understanding and use of language specific to medical biochemistry.
SC2. General knowledge of key vital chemical compounds for the human body.
SC3. Explaining the outcome of major metabolic processes that ensure the viability of the body and the mechanisms of the most important disease-specific disorders.
SC4. Advanced knowledge of the peculiarities of chemical composition and organ metabolism under physiological conditions and in most important diseases.
SC5. Knowledge of the principles of biochemical laboratory methods, the diagnostic value of the main laboratory indices and the ability to interpret the results of basic laboratory investigations.
SC6. Ability to work at the main laboratory equipment (spectrophotometer, centrifuge, pipette).

Transversal competences (TC)

TC1. Communication skills, written and oral, in the field of medicine and biochemistry.
TC2. Individual and team work skills.

TC3. The ability to effectively apply information technology to medical activity as well as to identify sources of information and continuous education in the field of activity.

TC4. Understanding and the ability to apply the principles and values of general and professional ethics in action.

Study outcomes

Upon completion of the course the student will:

1. know the structure and physico-chemical properties of the main chemical compounds of medical interest (proteins, carbohydrates, lipids, nucleic acids and vitamins);
2. know the fundamental metabolic processes that ensure the viability and reproduction of the human body,
3. know the structural and metabolic peculiarities of different organs;
4. know the normal values and the physiological changes of the main biochemical markers;
5. assess the usefulness of certain biochemical investigations in the diagnosis of specific diseases and interpret correctly the results of biochemical investigations.
6. be able to determine independently some biochemical markers of general clinical and diagnostic utility;
7. solve individual case studies in medical biochemistry.

VIII. STUDENT'S SELF-TRAINING

No.	Expected product	Implementation strategies	Assessment criteria	Implementation terms
1.	Work with informa-tion sources	Selection of basic information and details regarding the study questions of the practical lesson by reading the lecture, the material in the textbook and additional information sources on the topic. Full reading of text and systematization of essential content. Wording of generalizations and conclusions regarding the importance of the theme/subject.	Level of information assimilation and volume of work	During the semester
2.	Work with on-line materials	Studying the teaching materials on the Chair and other relevant sites, completing and acquiring information on the studied	Level of information assimilation and volume of work	During the semester

		subject		
3.	Items for individual work and study cases solved	Self-solving of individual work items and study cases in accordance with the Practical Guide, with subsequent verification by the teacher in non-auditory hours.	Mark from 0-0.5 for each chapter. The ability to solve study cases for the particular cha pter is evaluated.	Each lesson
4	Self-asses-ment tests solved	Self-solving of the self-assament tests in accordance with the Practical Guide, with subsequent verification by the teacher in non-auditory hours.	Mark from 0-0.5 for each chapter. The ability to solve tests for the particular chapter is evaluated.	Each lesson
5	Paper on actual topic presented at the students scientific group of the chair and at national and international scientific conferences.	Selection of basic information and details on the current topics of biochemistry from scientific sources over the last 5 years.	Mark from 0-1.0 for each paper	During the year

IX. METHODOLOGICAL SUGGESTIONS FOR TEACHING-LEARNING-ASSESSMENT

Teaching and learning methods used

Biochemistry is taught in accordance with the classical academic standard: courses, laboratory lessons and seminars.

The course is held by the course holders.

Laboratory lesson is carried out in order to study the principles and methods for qualitative and quantitative biochemical analysis of the main laboratory markers; the work ends by completing the protocol and analyzing the results obtained.

Theoretical subjects according to practical guide are discussed, study cases and tests are solved. Interactive teaching and learning methods such as observation, analysis, comparison, classification / model / figure development, modeling, deduction and experiment are applied.

Applied teaching strategies / technologies

Teaching classical didactic strategies (inductive, deductive, analogous, algorithmic and heuristic) are applied in Biochemistry discipline teaching, which are achieved with the help of several teaching-learning methods (active-participative, individual study, verification and evaluation)

such as explanation and didactic conversation, work with the text-book, theoretical problem and laboratory work, case study, test solving, etc. For the implementation of the strategies and methods, a set of technical means of training are used both in the courses and seminars, as well as in the laboratory lessons.

Methods of assessment

Current: Various current assessment methods are used for each laboratory lessons and seminars: control papers, problem solving and testing, practical problem solving, etc.

There are 6 concluding tests during one year of Biochemistry study. The final mark of a concluding test consists of the computerized test mark and in the case of concluding tests II, III and IV – of the computerized test and the oral answer marks. To the final grade obtained is added the mark of the individual work assessment (0-0.5)

Concluding test I: "Enzymes"

Concluding test II: "Energy metabolism" and "Carbohydrates metabolism"

Concluding test III: "Lipids metabolism"

Concluding test IV: "Metabolism of simple proteins and chromoproteins".

Concluding test V: "Metabolism of nucleotides and nucleic acids. Biosynthesis of proteins ".

Concluding test VI: "Hormones" and "Biochemistry of blood"

Final: The final assessment is an computer based exam.

The final mark will consist of two parts. The first one – the average annual mark will consist of an average score of 6 concluding tests + (0-1.0) for attendance at conferences (share 0.5). The second one is the mark from the final SIMU-computer based test (share 0.5).

The average annual mark and the mark of final examination (computer assisted) - are expressed in numbers according to the mark scale (according to the table), and the final mark obtained is expressed in number with two decimals, which is transferred to student's record-book.

Marks at different assessment stages

Intermediate marks scale (annual average, marks from the exam)	National Assessment System	ECTS Equivalent
1,00-3,00	2	F
3,01-4,99	4	FX
5,00	5	**E**
5,01-5,50	5,5	
5,51-6,0	6	
6,01-6,50	6,5	**D**
6,51-7,00	7	
7,01-7,50	7,5	C

7,51-8,00	8	
8,01-8,50	8,5	**B**
8,51-8,00	9	
9,01-9,50	9,5	**A**
9,51-10,0	10	

NOTE. *Absence on examination without good reason is recorded as "absent" and is equivalent to 0 (zero). The student has the right to have two re-examinations.*

X. RECOMMENDED LITERATURE:

A. Compulsory:

1. Rodwell V.W., Bender D.A., Botham K.M. et al. HARPER´s illustrated biochemistry. 30th edition. Mc Graw Hill Education. 2014.
2. Champe P. C., Harvey R. A. Biochemistry. Lippincott's Illustrated Reviews. 6th edition, 2014.
3. Gavriliuc Ludmila. Biochemistry. Lectures for students of Medical Departments. 2009.

B. Additional

1. Bhagavan N. V., Ha Chung-Eun. Essentials of Medical Biochemistry with Clinical Cases. 2nd Edition. Academic Press. 2015
2. Bhagavan N.V., Ha Chung-Eun. Essentials of Medical Biochemistry: with Clinical Cases. Academic Press; 1st edition, 2011.
3. Lehninger A.L. Principles of Biochemistry The Johns Hopkins University School of Medicine, Worth Publishers Inc., 2007.