MEDICAL UNIVERSITY – SOFIA

FACULTY OF DENTAL MEDICINE

DEPARTMENT OF MEDICAL CHEMISTRY AND BIOCHEMISTRY

TEACHING PROGRAM

Name of the discipline: Medical Biochemistry

Educational degree: Master

Discipline type: obligatory

Duration of the course: 2semesters - II and III semester

Level of the course: Level M (master level)

Forms of assessment: formative assessment, participation in seminars, colloquiums, examination

What forms and educational methods are used in the course? -interactive problem-solving oriented learning is introduced: multimedia lectures, seminars, written and computer Web-based interactive tests, work with virtual patients - solving of Web-based interactive simulations of clinical cases

Semestrial examination: yes - after the III semester

LEADING LECTURER: Professor Ganka Kossekova, PhD, Dr.Sc.

DEPARTMENT: Medical Chemistry and Biochemistry

COURSE ANNOTATION: The course on Medical Biochemistry for Dental Medicine students gives them an opportunity to acquire knowledge and competence for the molecular organization of living matter, enzymology, bioenergetics, metabolism, molecular biology, molecular pathology, characteristic features of metabolism in different tissues and organs in norm and pathology, necessary for their complete medical training dental help.

DESCRIPTION OF THE COURSE: The course consists of 120 academic hours, as follows:
Lectures - 60 hours
Practical exercises - 60 hours, including 4 colloquiums (seminars) announced at the beginning of the course in the II semester and 3 colloquiums (seminars) in the III semester.

Formation of the rating - the assessment is comprehensive: formative assessment of the students during the course on the topic for a fiven week program, assessment at the colloquiums on one or more sections of the subject program, and result at the annual examination on the whole subject.

Aspects in formation of the rating: results from the formative assessment, check-up of self-prepared schemes of metabolic pathways, results from the colloquiums, participation in discussions, tests, solving of clinical cases (work with virtual patients) and result from the examination.

HELPFUL RESOURCES FOR TEACHING AND LEARNING: multimedia, schemes, cases for interpretation.

OBJECTIVES OF THE TEACHING PROGRAM: the students should acquire knowledge and competency for medical biochemistry to a level allowing them to understand the molecular bases of diseases in man and be able to organize and carry out competently a modern dental help in conformity with the contemporary European and World standards for healthcare: Global Standards in Medical Education, accepted by the World Federation for Medical Education (WFME).

PROGRAM TASKS: The program should ensure that the students:

- understand the molecular organization of the living matter, the links between the structure and function of proteins and nucleic acids, the intermolecular interactions;
- understand the principles of the enzyme action and the mechanisms, via which it is affected by different environmental factors, as well as to explain the importance of the enzymes for metabolism and regulation and application of enzymes in the medical practice;
- understand the principles of bioenergetics, explain the importance of environmental factors and the mechanisms via which they influence the bioenergetical processes in the cell;
- understand the basic metabolic pathways, the links between them, their regulation and the

environmental factors

- acquire basic knowledge about how the genetic information is stored, preserved and passed on to progeny, the effect of environmental factors on DNA replication, basic mechanisms for DNA damage and repair;
- understand the principles of molecular pathology, build conceptual understanding for the importance of genetic and other factors for the onset of pathology, importance of the molecular genetic heterogenity for understanding of most common diseases nowadays in man and their diagnostics and treatment;
- understand the characteristic features of metabolism and its disorders in liver, muscle, nerve tissue, adipose tissue, blood, bones and teeth.

PRELIMINARY REQUIREMENTS: Before starting Biochemistry, the students should have good basic knowledge in Biology and Chemistry and should have taken obligatory the examinations in the disciplines mentioned above.

EXPECTED RESULTS: At the end of the course the students should know and can interpretate:

- the molecular organization of the living matter, the links between the structure and function of proteins and nucleic acids, the intermolecular interactions;
- the principles of the enzyme action and the mechanisms, via which it is affected by different environmental factors, as well as to explain the importance of the enzymes for metabolism and regulation and application of enzymes in the medical practice;
- the principles of bioenergetics, explain the importance of environmental factors and the mechanisms via which they influence the bioenergetical processes in the cell;
- the basic metabolic pathways, the links between them, their regulation and the environmental factors which affect them;
- the mechanisms via which the genetic information is stored, preserved and passed on to progeny, the effect of environmental factors on DNA replication, basic mechanisms for DNA damage and repair;
- the principles of molecular pathology, build conceptual understanding for the importance of genetic and other factors for the onset of pathology, importance of the molecular genetic heterogenity for understanding of most common diseases nowadays in man and their diagnostics and treatment;
- the characteristic features of metabolism and its disorders in liver, muscle, nerve tissue, adipose tissue, blood, bones and teeth.

RECOMMENDED TEXTBOOKS:

Textbooks in Bulgarian

1. Косекова, Г., В. Митев, А. Алексеев, Т. Николов, Биохимия в Интернет, Лекции по биохимия, 2010, второ допълнително и преработено издание (цветно), Централна медицинска библиотека, София.
2. Ангелов, А., Е. Гачев, К. Даичева, А. Кръшкова, Т. Николов, Л. Сираков (1995), Биохимия за медици и стоматолози, Университетско издателство „Св. Климент Охридски“, София.

Textbooks in English

1. Devlin, T. M. (ed.) (2006) Textbook of Biochemistry with Clinical Correlations, Wiley-Liss, New York, 6th ed.
2. Murray, R., D. Bender, K. Botham, P. Kennely, V. Rodwell, P. Well (2009) Harper's Illustrated Biochemistry, McGraw-Hill Medical, New York, 28th edn.
3. Harvey, A., R. Ferrier, 2011, Lippincott’s Illustrated Reviews. Biochemistry, 5th ed, Philadelhia.

Interactive resources

1. Косекова, Г. (1999) Биохимия в Интернет, Тестове по биохимия, Медицински университет, София.
3. Косекова, Г., „Тестове по биохимия” , 2004, CD, Централна медицинска библиотека, София.
4. Косекова, Г., ред. „Интерактивни учебни материали по медицинска биохимия” , 2011, DVD, Централна медицинска библиотека, София.

Web-site

http://biochemistry.mu-sofia.bg

PROGRAM OF THE LECTURES
IN MEDICAL BIOCHEMISTRY

FOR THE STUDENTS IN DENTAL MEDICINE

SPRING SEMESTER: 15 weeks x 2 hours = 30 hours
(All the lectures use multimedia and include animations and other interactive resources)

Lecture 1.
Contemporary Biochemistry - basis for understanding metabolism in health and disease. Subject, objectives and scope of Biochemistry. Relationship between Biochemistry and other biomedical disciplines stimulates mutual advances. Biochemical investigations - necessary for diagnosis, prognosis and therapy. Examples: Galactosemia, Myocardial Infarction.
Proteins: significance, amino acid composition, classification of amino acids based on the chemical structure and polarity of the side chains. Covalent bonds and noncovalent interactions in the protein molecule. Characteristic features of the polypeptide chains. Primary structure. Differences in the primary structure of hemoglobin A and S. Primary structure of insulin in different species. Charge properties of the amino acids and proteins. Electrophoresis. Electrophoretic profiles of serum proteins, role for diagnostics. Chomatographic techniques. Methods for determination of amino acid composition and primary structure. Phenylketonuria.

Lecture 2
Secondary, tertiary and quaternary structure of proteins. Globular and fibrous proteins. Structure and function of hemoglobin. Glycated hemoglobin. Denaturation and renaturation. Sickle Cell Anemia. Prion Diseases.
Relationship between protein structure and function. Structural similarities between a hemoglobin subunit and myoglobin, important for oxygen binding. Differences in the oxygen saturation curves of myoglobin and hemoglobin. Difference between HbA and HbF. Changes in collagen structure when vitamin C is deficient.

Lecture 3
Nucleic acids - types and biologic role. Chemical composition, chemical bonds within nucleotides and between them. Free nucleotides with important biologic action. Characteristic features of the polynucleotide chains. Purine and pyrimidine analogs as anticancer and antimicrobial agents. Primary structure of nucleic acids. Sickle cell anemia and phenylketonuria - examples for molecular diseases. Conformation of DNA and different RNAs. Types of RNA and their biological significance.

Lecture 4
Characteristics of the enzymes as biologic catalysts. Coenzymes and prosthetic groups. Nomenclature and classification of enzymes. Mechanism of enzyme catalysis. Enzyme-substrate complex. Active cite. Enzyme specificity.
Enzyme kinetics. Michaelis-Menten equation - effect of the substrate concentration and the enzyme concentration on the velocity of the enzyme-catalyzed reaction. Enzyme units. Evaluation of the kinetic parameters V_{max} and K_m via the Lineweaver-Burk plot. Kinetic characteristics of phosphorybosyl pyrophosphate synthase in cases of gout. Increased sensitivity to ethanol due to increased K_m of acetaldehyde dehydrogenase.

Lecture 4

Effect of pH and temperature on the velocity of enzyme-catalyzed reactions. Changes in the pH optimum of alcohol dehydrogenase. Competitive and noncompetitive inhibitors. Activators. Conversion of proenzymes into active enzymes.

Antimetabolites - competitive inhibitors towards substrates and coenzymes. Examples: puromycin, acycloguanosine (acyclovir), 3'-azido-3'-deoxythymidine (AZT), sulfonamides, methotrexate, allopurinol.

Lecture 5

Allosteric regulation. Case of gout due to mutation in an allosteric center. Orotic aciduria. Regulation of enzyme action via phosphorylation - dephosphorylation. Cascade for regulation of glycogen phosphorylase and glycogen synthase.

Importance of enzymes for the clinical practice. Isozymes. Electrophoresis of lactate dehydrogenase isozymes. Increases in the levels of nonfunctional plasma enzymes (in myocardial infarction and hepatitis). Changes in functional plasma enzymes. Genetically determined enzymopathies (cases of gout, Lesch-Nyhan syndrome). Enzymes in therapy (in Myocardial Infarction).

Lecture 6

Short data about the organization of animal cells. Compartmentalization of metabolic processes. Metabolic pathways - types, biomedical importance.

Characteristics of living organisms as open chemical systems. Coupling of endergonic and exergonic processes via high-energy compounds. Types of high-energy compounds. Central role of the system ATP/ADP in energy transfer.

Characteristics of biologic oxidation. Substrates of biologic oxidation and ultimate acceptors of hydrogen. Oxido-reductases, important redox-systems: NAD^+/NADH, $NADP^+$/NADPH, FMN/$FMNH_2$, FAD/$FADH_2$, KoQ/$KoQH_2$, hemes of cytochromes, lipoate, ascorbate.

Lecture 7

Oxidative phosphorylation at substrate level: synthesis of ATP in the oxidation of glyceraldehyde-3-phosphate, enolase reaction, oxidative decarboxylation of a-keto acids (pyruvate dehydrogenase complex, role of the cofactors TPP, lipoate, CoA, FAD and NAD^+). Beri-beri.

Respiratory chain - localization, function and molecular structure. Sites for proton translocation. Coefficient of oxidative phosporylation (P/O). Respiratory control, phosphate potential. Inhibitors of electron transfer: barbiturates, antimycin A, KCN. Dangerous combination of barbiturates and alcohol.

Lecture 8

Chemiosmotic theory for the mechanism of the oxidative phosphorylation in the respiratory chain. ATP synthase. Effect of uncouplers (2,4-dinitrophenol). Natural uncouplers. Inhibitors of oxidative phosphorylation (oligomycin).

Uncoupled oxidation. Heat production. Role of thermogenin in mitochondria of brown adipose tissue. Electron transfer in the endoplasmic reticulum. Formation and detoxifying of reactive oxygen intermediates: superoxide, H_20_2 and free hydroxyl radical.

Citric acid cycle - importance for catabolism and anabolism. Chemical reactions. Metabolic and energy balance. Mechanisms of regulation. Pyruvate dehydrogenase deficiency.

Lecture 9

Glycolysis - importance, chemical reactions, energy balance at anaerobic and aerobic conditions. Tissue specificity of glycolysis. Relationship between glycolysis and respiratory chains - shuttle mechanisms for transfer of hydrogen from the cytosol into mitochondria (malate and

glycerophosphate shuttles). Links with the citric acid cycle. Lactic acidosis.
Gluconeogenesis. Importance. Circumvention of the three irreversible steps in glycolysis. Regulation of gluconeogenesis. Fructose-1,6-bisphosphatase deficiency.

Lecture 10

The pentose phosphate pathway. Importance. Oxidative, isomerase and transferase reactions. Glucose-6-phospate dehydrogenase deficiency.
Metabolism of galactose. Galactosemia. Metabolism of fructose. Fructose intolerance. Glycogenolysis and glycogenesis. Role of cAMP. Regulation. Glycogen storage diseases.

Lecture 11

Lipids - classification. Oxidation of fatty acids with an even and odd number of carbon atoms. Energy balance.
Biosynthesis of fatty acids. Role of acetyl-CoA carboxylase. Fatty acyl synthase - multifunctional enzyme. Synthesis of triacylglycerols. Obesity. Catabolism of triacylglycerols. Metabolism of glycerol.

Lecture 12

Metabolism (synthesis and degradation) of phosphoglycerols. Biological role of phospholipases Ai, A2, C and D. Sphingolipids - types, structure and significance. Sphingolipidoses.
Ketogenesis. Utilization and oxidation of ketone bodies in extrahepatal tissues. Ketonemia and ketonuria. Ketoacidosis in starvation and in Diabetes Mellitus.

Lecture 13

Transport of lipids in the organism. Composition, origin and functions of lipoproteins (chylomicrons, VLDL, LDL, HDL. Receptors for lipoproteins. Familiar hypercholesterolemia. Metabolism of cholesterol. Chemical reactions in the synthesis of cholesterol. Excretion from the body. Regulation. Atherosclerosis.

Lecture 14

Derivatives of cholesterol (steroid hormones, vitamin D, bile acids) - structure and biologic role.
General reactions of amino acid catabolism: oxidative deamination, transamination,
transdeamination. Clinical importance of aminotransferases. Decarboxilation of amino acids. Biological amines. Parkinson's disease.

Lecture 15

Detoxification of ammonia - synthesis of glutamine, urea cycle and ammoniogenesis.
Catabolism of the carbon skeletons of amino acids. Glycogenic and ketogenic amino acids. Nutritionally essential and nonessential amino acids. One-carbon units - types, sources, importance. Role of S-adenosyl-L-methionine and folate derivatives.
Metabolic disorders of amino acids catabolism (phenylketonuria, alkaptonuria, methylmalonic aciduria.

AUTUMN SEMESTER: 15 weeks x 2 hours = 30 hours

All the lectures use multimedia and include animations and other interactive resources

Lecture 1

Biosynthesis and degradation of purine nucleotides. Regulatory enzymes in the biosynthesis. Hyperuricemia due to enzyme defects (gout, Lesch-Nyhan syndrome). Inhibition of xanthine oxidase.

Biosynthesis and degradation of pyrimidine nucleotides. Regulatory enzymes in the biosynthesis. Allosteric modulation and orotic aciduria.

Integration of metabolism. Links between metabolic pathways of carbohydrates, lipids, amino acids and nucleotides at molecular level. Role of common metabolites and key enzymes.

Lecture 2

Biosynthesis of DNA. General characteristics. DNA polymerases in prokaryotes. DNA polymerase complex in eucaryotes. Steps of replication. Repair mechanisms. Biosynthesis of different types of RNA. General characteristics. RNA polymerases in prokaryotes and eukaryotes. Steps of transcription. Processing of RNA molecules.

Structure of the prokaryotic and eukaryotic genes.

Lecture 3

Genetic code. Biosynthesis of proteins. Role of different types of RNA. Steps of the protein synthesis. Postsynthetic modifications. Inhibitors of protein synthesis.

Lecture 4

Regulation of gene expression in prokaryotes (operon model) and in eukaryotes: at the level of DNA, at the level of transcription, at the level of translation and posttranslational regulation.

Lecture 5

Recombinant DNA techniques. Recombination of DNA. Role of restriction endonucleases, reverse transcriptase and chemical methods. Identifying of DNA sequences - electrophoresis, Southern blot. Dideoxynucleotide method of Sanger for DNA sequencing. Amplification of DNA: cloning, polymerase chain reaction (PCR).

Use of recombinant DNA techniques in medicine. DNA polymorphisms. Detection of mutations by allele-specific probes and by PCR. Detection of a variable number of tandem repeats. Genetic consultations. Production of vaccines and therapeutic proteins. Gene therapy. Solving of cases in forensic medicine. Transgenic animals. DNA chips in diagnostics.

Lecture 6

Signal transduction through membranes. Types of signal molecules. Classifications of hormones. Receptors.

Molecular mechanisms of hormones which bind to intracellular receptors.

Lecture 7

Molecular mechanisms of hormones which bind to receptors on the cell surface. Example - effect on glycogen phosphorylase and glycogen synthase. Role of cyclic SMP and other second messengers. Kinase cascades as second messengers.

Diabetes mellitus - changes in metabolism in type I and type II. Type I as autoimmune disease. Mechanism of insulin action. Pathobiochemistry of diabetes mellitus type I and type II.

Complications.

Lecture 8
Biochemistry of liver. Inactivation and detoxification of xenobiotics. Ethanol metabolism.

Lecture 9
Biochemical characteristics and metabolism of red and white blood cells. Hemoglobinpathies. Biosynthesis of porphyrins. Types of porphyrias. Degradation of haemoglobin. Bile pigments. Enterohepatic urobilinogen cycle. Jaundices.

Lecture 10
Water-soluble vitamins. Metabolic role. Lipid-soluble vitamins. Metabolic role.
Biochemistry of food digestion. Chemical composition and enzymes of the digestive fluids - saliva, gastric, pancreatic, and intestinal fluid. Degradation of food and uptake of the digested food.

Lecture 11
Nerve tissue - metabolism and function. Regulation. Changes with aging, degeneration of neurons. Drug dependence. Neuromediators.

Lecture 12
Muscle tissue - metabolism and function. Molecular mechanisms of muscle contraction.

Lecture 13
Biochemical processes in epithelial and connective tissue. Elastins, collagens, heteropolysacharides. Defects.

Lecture 14
Metabolism of calcium and phosphorus. Regulation. Bone formation. Osteoporosis and hormone replacement therapy.

Lecture 15
Biochemical mechanisms for formation and maintaining of the tooth enamel **and** dentin. Defects.

Head of the Department of Medical Chemistry and Biochemistry:

Prof. Dr. V. Mitev, PhD, DSc.

MEDICAL BIOCHEMISTRY

PROGRAM FOR THE PRACTICAL EXERCISES IN MEDICAL BIOCHEMISTRY FOR STUDENTS IN DENTAL MEDICINE

I SEMESTER

Practical exercise 1
Proteins -aminoacid composition, properties. Protein conformation.
Practice - Determination of the protein concentration by biuret assay. Web-based illustrations.

Practical exercise 2
Proteins as polyelectrolytes. Structure and function of nucleic acids.
Practice - Electrophoresis of serum proteins. Virtual patient “Sandra”.

Practical exercise 3
BIOPOLYMERS (PROTEINS AND NUCLEIC ACIDS)
SEMINAR WITH FINAL MARK (test, written problems and oral discussion)

Practical exercise 4
Enzymes - structure, specificity and mechanism of action.
Practice - Prove of absolute and group specificity of the enzymes urease and acidic phosphatase. Web-based illustrations.

Practical exercise 5
Enzymes - kinetics. Michaelis constant. Inhibitors and activators. Regulation of enzymatic activity. Enzymatic units. Clinical importance of the enzymes.
Practice -Determination of Michaelis constant of the enzyme urease in the presence and in the absence of inhibitor using a computer program. Virtual patient “Vassil”.

Practical exercise 6
ENZYMES
SEMINAR WITH FINAL MARK (test, written problems and oral discussion)

Practical exercise 7
Principles of bioenergetics. Biological oxidation. High-energy compounds. Role of ATP.

Practical exercise 8
Respiratory chain and oxidative phosphorylation. Citric acid cycle.
Practice - oxidation and reduction of cytochrome c. Virtual models of electron transport and oxidative phosphorylation created by D.Norton, New Zeeland

Practical exercise 9
BIOENERGETICS
SEMINAR WITH FINAL MARK (test, written problems and oral discussion)

Practical exercise 10
Glycolisis and gluconeogenesis. Pentosophosphate metabolic pathway.

Practical exercise 11

Metabolism of glycogen, metabolism of galactose and fructose Virtual patients “Rumen” and ‘Charly

Practical exercise 12

Regulation of carbohydrate metabolism. Blood sugar. Sugar diabetis Bloodsugar curves

Practical exercise 13

GENERAL REVIEW OF CARBOHYDRATE METABOLISM
SEMINAR WITH FINAL MARK (test, written problems and oral discussion)

Practical exercise 14

General review of lipid metabolism. Lipid transport in the blood.
Practice - Determination of lipoproteins in blood serum.

Practical exercise 15

Degradation of fatty acids. Ketogenesis and ketolysis. Ketonemia.
Practice - Determination of total fats in blood serum.
Legalization of the semester.

MEDICAL BIOCHEMISTRY

PROGRAM FOR THE PRACTICAL EXERCISES
IN MEDICAL BIOCHEMISTRY
FOR STUDENTS IN DENTAL MEDICINE

II SEMESTER

Practical exercise 1

Metabolism of cholesterol and its derivatives

Practice - Determination of total cholesterol in blood serum.

Practical exercise 2

Lipogenesis. General review of lipid metabolism. Virtual patient “Vassil 2”.

Practical exercise 3

Atherosclerosis - molecular bases, heterogeneity, biochemical and molecular biological approaches for evaluation of the risk.

Practical exercise 4

LIPID METABOLISM AND ITS LINKS WITH CARBOHYDRATE METABOLISM.
SEMINAR WITH FINAL MARK.

Practical exercise 5

General reactions in the metabolism of aminoacids.

Practice - deamination of alanine. Transamination of aminoacids - serum ASAT and ALAT.

Practical exercise 6

End products of nitrogen metabolism. Biosynthesis of urea.

Practice - Determination of ammonia salts according to Malfaty. Virtual patients “Marina” and “Dimiter”.

Practical exercise 7

Metabolism of purine and pyrimidine nucleotides. Gout.

Practice - Determination of uric acid in blood serum. Virtual patient “Emil”.

Practical exercise 8

METABOLISM OF CARBOHYDRATES, OF LIPIDS AND OF AMONOACIDS - GENERAL REVIEW AND LINKS BETWEEN THE DIFFERENT METABOLISMS. REGULATION OF THE PROCESSES.
SEMINAR WITH FINAL MARK.

Practical exercise 9

Metabolism of nucleic acids and protein biosynthesis. Molecular diseases.

Virtual patient “Todor”.

Practical exercise 10

Metabolism of porphyrines and bile pigments. Types of jaundice.

Practice - Determination of bilirubin in blood serum Virtual patient “Kiril”.

Practical exercise 11

General regulation of metabolism at the level of the organism Hormones, growth factors, cytokines. Chemical nature and molecular mechanisms of their action Hormonal receptors. Transducing systems, oncogenesis:

Practical exercise 12

Molecular mechanisms of diabetes - pathogenesis of type I and type II. Mechanism of action of insuline. Pathobiochemistry of diabetes and its complications. Blood sugar curves in norme and diabetes. Web-based simulations of clinical case “Rositsa”.

Practical exercise 13

Biochemistry of the liver. Vitamines.

Practical exercise 14

Biochemistry of connective and bone tissue.

Practical exercise 15

Biochemistry of the muscular tissue. Determination of creatine in muscular tissue. Evaluation of the average annual mark.

Legalization of the semester.

MEDICAL BIOCHEMISTRY

SYLLABUS FOR STUDENTS IN DENTAL MEDICINE

1. Contemporary Biochemistry - basis for understanding metabolism in health and disease. Subject, objectives and scope of Biochemistry. Relationship between Biochemistry and other biomedical disciplines stimulates mutual advances. Biochemical investigations - necessary for diagnosis, prognosis and therapy. Examples: Galactosemia, Myocardial Infarction.

2. Proteins: significance, amino acid composition, classification of amino acids based on the chemical structure and polarity of the side chains. Covalent bonds and noncovalent interactions in the protein molecule. Characteristic features of the polypeptide chains. Primary structure. Differences in the primary structure of hemoglobin A and S. Primary structure of insulin in different species.

3. Charge properties of the amino acids and proteins. Electrophoresis. Electrophoretic profiles of serum proteins, role for diagnostics. Chomatographic techniques. Methods for determination of amino acid composition and primary structure. Phenylketonuria.

4. Secondary, tertiary and quaternary structure of proteins. Globular and fibrous proteins. Structure and function of hemoglobin. Glycated hemoglobin. Denaturation and renaturation. Sickle Cell Anemia. Prion Diseases.

5. Relationship between protein structure and function. Structural similarities between a hemoglobin subunit and myoglobin, important for oxygen binding. Differences in the oxygen saturation curves of myoglobin and hemoglobin. Difference between HbA and HbF. Changes in collagen structure when vitamin C is deficient.

6. Nucleic acids - types and biologic role. Chemical composition, chemical bonds within nucleotides and between them. Free nucleotides with important biologic action. Characteristic features of the polynucleotide chains. Purine and pyrimidine analogs as anticancer and antimicrobial agents.

7. Primary structure of nucleic acids. Sickle cell anemia and phenylketonuria - examples for molecular diseases. Conformation of DNA and different RNAs. Types of RNA and their biological significance.

8. Characteristics of the enzymes as biologic catalysts. Coenzymes and prosthetic groups. Nomenclature and classification of enzymes. Mechanism of enzyme catalysis. Enzyme-substrate complex. Active cite. Enzyme specificity.

9. Enzyme kinetics. Michaelis-Menten equation - effect of the substrate concentration and the enzyme concentration on the velocity of the enzyme-catalyzed reaction. Enzyme units. Evaluation of the kinetic parameters V_{max} and K_m via the Lineweaver-Burk plot. Kinetic characteristics of phosphorybosyl pyrophosphate synthase in cases of gout. Increased sensitivity to ethanol due to increased K_m of acetaldehyde dehydrogenase.

10. Effect of pH and temperature on the velocity of enzyme-catalyzed reactions. Changes in the pH optimum of alcohol dehydrogenase. Competitive and noncompetitive inhibitors. Activators. Conversion of proenzymes into active enzymes.

11. Antimetabolites - competitive inhibitors towards substrates and coenzymes. Examples: puromycin, acycloguanosine (acyclovir), 3'-azido-3'-deoxythymidine (AZT), sulfonamides,

methotrexate, allopurinol.

12. Allosteric regulation. Case of gout due to mutation in an allosteric center. Orotic aciduria. Regulation of enzyme action via phosphorylation - dephosphorylation. Cascade for regulation of glycogen phosphorylase and glycogen synthase.

13. Importance of enzymes for the clinical practice. Isozymes. Electrophoresis of lactate dehydrogenase isozymes. Increases in the levels of nonfunctional plasma enzymes (in myocardial infarction and hepatitis). Changes in functional plasma enzymes. Genetically determined enzymopathies (cases of gout, Lesch-Nyhan syndrome). Enzymes in therapy (in Myocardial Infarction).

14. Short data about the organization of animal cells. Compartmentalization of metabolic processes. Metabolic pathways - types, biomedical importance.

15. Characteristics of living organisms as open chemical systems. Coupling of endergonic and exergonic processes via high-energy compounds. Types of high-energy compounds. Central role of the system ATP/ADP in energy transfer.

16. Characteristics of biologic oxidation. Substrates of biologic oxidation and ultimate acceptors of hydrogen. Oxido-reductases, important redox-systems: NAD^+/NADH, $NADP^+$/NADPH, FMN/$FMNH_2$, FAD/$FADH_2$, K0Q/K0QH_2, hemes of cytochromes, lipoate, ascorbate.

17. Oxidative phosphorylation at substrate level: synthesis of ATP in the oxidation of glyceraldehyde-3-phosphate, enolase reaction, oxidative decarboxylation of a-keto acids (pyruvate dehydrogenase complex, role of the cofactors TPP, lipoate, CoA, FAD and NAD^+). Beri-beri.

18. Respiratory chain - localization, function and molecular structure. Sites for proton translocation. Coefficient of oxidative phosporylation (P/O). Respiratory control, phosphate potential. Inhibitors of electron transfer: barbiturates, antimycin A, KCN. Dangerous combination of barbiturates and alcohol.

19. Chemiosmotic theory for the mechanism of the oxidative phosphorylation in the respiratory chain. ATP synthase. Effect of uncouplers (2,4-dinitrophenol). Natural uncouplers. Inhibitors of oxidative phosphorylation (oligomycin).

20. Uncoupled oxidation. Heat production. Role of thermogenin in mitochondria of brown adipose tissue. Electron transfer in the endoplasmic reticulum. Formation and detoxifying of reactive oxygen intermediates: superoxide, H_20_2 and free hydroxyl radical.

21. Citric acid cycle - importance for catabolism and anabolism. Chemical reactions. Metabolic and energy balance. Mechanisms of regulation. Pyruvate dehydrogenase deficiency.

22. Glycolysis - importance, chemical reactions, energy balance at anaerobic and aerobic conditions. Tissue specificity of glycolysis. Relationship between glycolysis and respiratory chains - shuttle mechanisms for transfer of hydrogen from the cytosol into mitochondria (malate and glycerophosphate shuttles). Links with the citric acid cycle. Lactic acidosis.

23. Gluconeogenesis. Importance. Circumvention of the three irreversible steps in glycolysis. Regulation of gluconeogenesis. Fructose-1,6-bisphosphatase deficiency.

24. The pentose phosphate pathway. Importance. Oxidative, isomerase and transferase reactions. Glucose-6-phospate dehydrogenase deficiency.

25. Metabolism of galactose. Galactosemia. Metabolism of fructose. Fructose intolerance.

26. Glycogenolysis and glycogenesis. Role of cAMP. Regulation. Glycogen storage diseases.

27. Lipids - classification. Oxidation of fatty acids with an even and odd number of carbon atoms. Energy balance.

28. Biosynthesis of fatty acids. Role of acetyl-CoA carboxylase. Fatty acyl synthase - multifunctional enzyme. Synthesis of triacylglycerols. Obesity. Catabolism of triacylglycerols. Metabolism of glycerol.

29. Metabolism (synthesis and degradation) of phosphoglycerols. Biological role of phospholipases Ai, A2, C and D. Sphingolipids - types, structure and significance. Sphingolipidoses.

30. Ketogenesis. Utilization and oxidation of ketone bodies in extrahepatal tissues. Ketonemia and ketonuria. Ketoacidosis in starvation and in Diabetes Mellitus.

31. Transport of lipids in the organism. Composition, origin and functions of lipoproteins (chylomicrons, VLDL, LDL, HDL. Receptors for lipoproteins. Familiar hypercholesterolemia.

32. Metabolism of cholesterol. Chemical reactions in the synthesis of cholesterol. Excretion from the body. Regulation. Atherosclerosis.

33. Derivatives of cholesterol (steroid hormones, vitamin D, bile acids) - structure and biologic role.

34. General reactions of amino acid catabolism: oxidative deamination, transamination, transdeamination. Clinical importance of aminotransferases. Decarboxilation of amino acids. Biological amines. Parkinson’s disease.

35. Detoxification of ammonia - synthesis of glutamine, urea cycle and ammoniogenesis.

36. Catabolism of the carbon skeletons of amino acids. Glycogenic and ketogenic amino acids. Nutritionally essential and nonessential amino acids. One-carbon units - types, sources, importance. Role of S-adenosyl-L-methionine and folate derivatives.

37. Metabolic disorders of amino acids catabolism (phenylketonuria, alkaptonuria, methylmalonic aciduria).

38. Biosynthesis and degradation of purine nucleotides. Regulatory enzymes in the biosynthesis. Hyperuricemia due to enzyme defects (gout, Lesch-Nyhan syndrome). Inhibition of xanthine oxidase.

39. Biosynthesis and degradation of pyrimidine nucleotides. Regulatory enzymes in the biosynthesis. Allosteric modulation and orotic aciduria.

40. Integration of metabolism. Links between metabolic pathways of carbohydrates, lipids, amino acids and nucleotides at molecular level. Role of common metabolites and key enzymes.

41. Biosynthesis of DNA. General characteristics. DNA polymerases in prokaryotes. DNA polymerase complex in eucaryotes. Steps of replication. Repair mechanisms. Biosynthesis of different types of RNA. General characteristics. RNA polymerases in prokaryotes and eukaryotes. Steps of transcription. Processing of RNA molecules.

42. Structure of the prokaryotic and eukaryotic genes.

43. Genetic code. Biosynthesis of proteins. Role of different types of RNA. Steps of the protein synthesis. Postsynthetic modifications. Inhibitors of protein synthesis.

44. Regulation of gene expression in prokaryotes (operon model) and in eukaryotes: at the level of DNA, at the level of transcription, at the level of translation and posttranslational regulation.

45. Recombinant DNA techniques. Recombination of DNA. Role of restriction endonucleases, reverse transcriptase and chemical methods. Identifying of DNA sequences - electrophoresis, Southern blot. Dideoxynucleotide method of Sanger for DNA sequencing. Amplification of DNA: cloning, polymerase chain reaction (PCR).

46. Use of recombinant DNA techniques in medicine. DNA polymorphisms. Detection of mutations by allele-specific probes and by PCR. Detection of a variable number of tandem repeats. Genetic consultations. Production of vaccines and therapeutic proteins. Gene therapy. Solving of cases in forensic medicine. Transgenic animals. DNA chips in diagnostics.

47. Signal transduction through membranes. Types of signal molecules. Classifications of hormones. Receptors.

48. Molecular mechanisms of hormones which bind to intracellular receptors.

49. Molecular mechanisms of hormones wjiich bind to receptors on the cell surface. Example - effect on glycogen phosphorylase and glycogen synthase. Role of cyclic SMP and other second messengers. Kinase cascades as second messengers.

50. Diabetes mellitus - changes in metabolism in type I and type II. Type I as autoimmune disease. Mechanism of insulin action. Pathobiochemistry of diabetes mellitus type I and type II. Complications.

51. Biochemistry of liver. Inactivation and detoxification of xenobiotics. Ethanol metabolism.

52. Biochemical characteristics and metabolism of red and white blood cells. Hemoglobinpathies.

53. Biosynthesis of porphyrins. Types of porphyrias. Degradation of haemoglobin. Bile pigments. Enterohepatic urobilinogen cycle. Jaundices.

54. Water-soluble vitamins. Metabolic role. Lipid-soluble vitamins. Metabolic role.

55. Biochemistry of food digestion. Chemical composition and enzymes of the digestive fluids - saliva, gastric, pancreatic, and intestinal fluid. Degradation of food and uptake of the digested food.

56. Nerve tissue - metabolism and function. Regulation. Changes with aging, degeneration of neurons. Drug dependence. Neuromediators.

57. Muscle tissue - metabolism and function. Molecular mechanisms of muscle contraction.

58. Biochemical processes in epithelial and connective tissue. Elastins, collagens, heteropolysacharides. Defects.

59. Metabolism of calcium and phosphorus. Regulation. Bone formation. Osteoporosis and hormone replacement therapy.

60. Biochemical mechanisms for formation and maintaining of the tooth enamel **and** dentin. Destruction.