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 five-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. Мутев, А. Алексеев, Т. Николов, Биохимия в Интернет, Лекции по биохимия, 2010, второ допълнително и преработено издание (цветно), Централна медицинска библиотека, София.

Textbooks in English

Interactive resources
1. Косекова, Г. (1999) Биохимия в Интернет, Тестове по биохимия, Медицински университет, 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.

Lecture 2
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

Lecture 4
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**

**Lecture 5**

**Lecture 6**

**Lecture 7**

**Lecture 8**

**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-phosphate dehydrogenase deficiency.
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.

**Lecture 12**
Metabolism (synthesis and degradation) of phosphoglycerols. Biological role of phospholipases Ai, A2, C and D. Sphingolipids - types, structure and significance. Sphingolipidoses.

**Lecture 13**

**Lecture 14**
Derivatives of cholesterol (steroid hormones, vitamin D, bile acids) - structure and biologic role.
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
Structure of the prokaryotic and eukaryotic genes.

Lecture 3

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

Lecture 6
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**

**Lecture 10**

**Lecture 11**

**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 Zealand

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
Practice - Determination of total fats in blood serum.
Legalization of the semester.
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 AMINOACIDS - 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

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.


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.


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 $V_{\text{max}}$ 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.


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


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.


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.


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


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


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


42. Structure of the prokaryotic and eukaryotic genes.

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.


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

49. 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.


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


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


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