Cytology, Histology and Embryology I course

***Course studying*:** I course
Semester: I semester
Exam: at the end of I semester
Horarium: 75 hours - 30 hours lectures, 45 hours seminars (2/3)
Lecturers: Prof. Pepa Atanassova, M.D., Ph.D., Ass. Prof. I. Koeva, M.D., Ph.D.

SYLLABUS

Classes	*Horarium*						*Credits*
	Per week	*I sem.*	*IIsem.*	*III sem.*	*IV esm.*	*Total*	
Lectures	1	30				30	
Seminars	1	45				45	
Total	***5 h.***	***75h.***				***75h.***	

Cytology, Histology and Embryology

***Syllabus*:** I course, I semester, horarium: 75 hours – 30 h. lectures, 45 hours seminars (2/3)
Lecturers: Prof. Pepa Atanassova, M.D., Ph.D., Ass. Prof. I. Koeva, M.D., Ph.D.
MAIN PURPOSE: Gaining deep knowledge of the main morphological structures of the human body: cells, tissues, stages of the embryonal development (fertilization, early and late gastrulation, histogenesis, differentiation).
TASKS OF THE SUBJECT:

1. Cytology- studying the structure of the human cells – cell membrane, cell orgenelles and inclusions, cytophysiology.
2. Histology– studying the main tissues of the human body – histogenesis, light-microscopical, electronmicroscopical, histochemical and functional characteristics.
3. Embryology - studying the embryonal development and the initial stages of the fetal period.

Methods of teaching: Lectures, seminars – light microscopic observation, describing electron microphotographs, discussion, drawing pictures from the microscopic preparations.
TECHICAL EQUIPMENT: light microscopes, vidiofilms, multimedia, sets of microscopical preparations, native preparations of placenta and fetuses and **CD interactive atlas of Cytology, Histology and Embryology**, all made by the teachers of the Department of Anatomy, Histology and Embryology, MU-Plovdiv.
CONTROL AND EVALUATION: tests during the semester, preliminary examination in Cytology, final exam.
METHODS OF CONTROL: discussion, answering the questions in the PRACTICUM, drawing pictures from the preparations after observation by the light microscope, tests in the classes during the semester, preliminary examination in Cytology. Final exam: 1. Practical examination (identifying microscopical preparations and electronmicrophotographs); 2. Test on Cytology, Histology and Embryology; 3. Writing examination on one theme on Histology; 4. Oral examination.
OBLIGATORY COMPETENCY: deep knowledge of the structure of the cells and the tissues of the human body, the stages of the embryonal and fetal development.

I SEMESTER - (2/3)

SPECIFICATION:

a) horarium: 5 h. per week, 75 h. per semester.

b) lectures: 2 h. per week, 30 h. per semester.

c) seminars: 3 h. per week, 45 h. per semester.

d) final exam at the end of the I SEMESTER**.**

SCHEDULE:

Lectures on three subjects: Cytology – giving knowledge on the structure of the eukaryotic cell (cell membrane, cell organelles, inclusions, nucleus, cytophysiology). Hystology - giving knowledge on the main structural, ulrastructural, histochemical and functional characteristics of the tissues and their histogenesis. Embyology - giving knowledge on the human embryonal and fetal development (fertilization, early and late gastrulation, primitive organs, extra-embryonic layers, twins, anomalies in the human embryonal development).

Seminars: On a given theme, including observation preparations with light microscope, drawing pictures from them, answering the questions in the PRACTICUM, discussion , tests, differential counting of a blood smear.

Control: Tests every lesson, preliminary exam on Cytology.

Lectures: 2 h. per week

1.Introduction in Cytology, Histologu and Embryology – subject, methods of investigation, link with other subjects. **2. The cell - morphology. Cell membrane (plasmalema). Cytoplasm, cytosol .**

2. **Cell orgenelles. General organelles- structural, ultrastructural and functional characteristics.**

1.Endoplasmatic reticulum
2.Mitochondria
3.Golgi complex
4.Lysosomes

3. **Cytoplasm.**

1. Cytoskeleton
2. Specialized cell organelles

3. Cell inclusions

4. Nucleus in interphase and mitosis.

1. Interphase nucleus - structural, ultrastructural and functional characteristics.
2.Mitosis – phases

5. Cytophysiology

1.Phagocytosis
2.Acid phosphatase activity
3.Secretion
4.Mooving of cilia

6. Tissues – classification,properties

Epithelia. Unilayered epithelia. Multistratified epithelia.

1. Histogenesis

2. General characteristics
3. Classification

7. Connective tissue.
1. Histogenesis
2. General characteristics
3. Classification
4. Cells.
5. Intercellular substance
6. Fibrous connective tissue

8. **Connective tissue with solid intercellular substance.**
1. Cartilage
2. The bone tissue

9. **Blood tissue.**
1. Histogenesis
2. General characteristics
3. Classification
4. Cells

4.1.Erythrocytes
4.2.Leucocytes
4.3.Platelets

10. **Muscle tissue.**
1. Histogenesis
2. General characteristics
3. Classification
4. Cells
5. Myofibers, myofibrils

11. Nerve tissue.
1.Histogenesis
2.General characteristics
3.Classification
4.Cells – neurons, neuroglia
5. Nerve fibers
6. Myoneural synapse
7. Neuroglia

12. Reproductive tissue 1.Histogenesis
2.General characteristics
3.Classification
4.Cells
4.1. Oocytes
4.2. Spermatozoa

13. Early human embryonal development.
Fertilization
Clivage
Blastocyst
Implantation
Gastrulation
Primitive organs

14. Extra-embryonic layers

1. Chorion, amnion, yolk sack, alantoic diverticulum
2. Umbilical cord
3. Fetal sack
4. Placenta

15. Twins. Anomalies in the human embryonal development

Seminars: 3 h. per week

1. General Methods of Investigation in Histology.
The cell – morphology.
Cell membrane, plasmalema
Microscopical preparations:
1. Flatten cells
2. Spherical cells
3. Pyramidal cells

2. **Cytoplasma. Cell inclusions**
Microscopical preparations:
1.Lipid drops
2.Glycogen granules in hepatic cells
3.Pigment inclusions
Electron microphotographs:
1. Cell membrane Микровили
2. Microvilli
3. Desmosomes
4. Interdigitations
5. Protein granules
6. Lipid drops
7. Glycogen granules

3. Nucleus in interphase. Mitosis.
Microscopical preparations:
1. Nucleus in interphase
1.1 H-E staining
1.2 Foilgen staining
1.3 DNA synthesis (histoautoradiography)
2.Mitosis in cells of pea radix
Electron microphotographs:
1. Interphase nucleus

4. Cytoplasm. Cell organelles. *Microscopical preparations:*
1. Nissl substance (granules)
2. Mitochondria
3. SDH - activity
4. Golgi complex
Electron microphotographs:
1.Rough endoplasmatic reticulum
2.Smooth endoplasmatic reticulum
3.Ribosomes
4. Mitochondria

5.Golgi complex
6.Centrosome

5. Cytophysiology
Microscopical preparations:
1. Phagocytosis
2. Acid phosphatase activity
3. Secretion (secretory granulea)
4. Mooving of cillia – demonstration

Electron microphotographs:
Cilia
1.1 Longitudinal section
1.2. Transverse section
Secretory granules

6. Epithelia. Unilayered epithelia
Microscopical preparations:
1. Simple squamous epithelium
1.1. H-E staining
1.2. Impregnation
2. Cuboidal epithelium
3. Columnar epithelium
4. Unilayered (pseudostratified) ciliated columnar epithelium
5. Henle's epithelium

7.Colloquium (preliminary examination)
1. Practical part – 20 points
5 *microscopical preparations*
5 - *electron microphotographs*
2.Theoretical part – test **40 points**
60 points total
Discharge: 70% /14 p. + 28 p./

8. Epithelia. Multistratified epithelia. Secretory epithelia.
Microscopical preparations:
1. Stratified squamous epithelium
2. Stratified squamous keratinizing epithelium
3. Secretory epithelia
   3.1.Simple tubular glands
   3.2.Serous, mucous and compound alveolar (acinar) glands

9. Fibrous connective tissue
Microscopical preparations:
1.Loose connective tissue
2.Collagenous fibrous tiiue
3.Ellastic tissue
4.Pigment connective tissue
5.Adipose tissue – white and brown
a)Sudan III staining
b)H-E staining

Electron microphotographs:
1. Fibroblast
2. Mast cell

3. Plasma cell
4. Collagenfibers

Multilocular adipocyte

10. Connective tissue with solid intercellular substance.

1. Cartilage
2. The bone tissue

Microscopical preparations:

1. Hyaline cartilage
2. Elastic cartilage
3. Compact bone – decalcinated

4.Compact bone – Shliff

Electron microphotographs:

1. Osteocyte
2. Osteoclast

11. **Blood tissue.**

Microscopical preparations:

1. Blood smear - preparation
2. Blood smear - examination

Electron microphotographs:

1. Neotrophil granulocyte
2. Eosinophil granulocyte
3. Lymphocyte

Test – 30 p. and *preparations* –10 p./8+2/ on Epithelial and Connective tissues.
Total score – 40 p.

12. Muscle tissue.

Microscopical preparations:

1. Smooth (visceral) muscle tissue
2. Striated Skeletal muscle tissue
3. Striated Cardiac muscle tissue
4. Impulse conductive cardiac muscle tissue

Electron microphotographs:

1. Myofibril – skeletal

Cardiomyocyte – myofibril

13. Nerve tissue.

Microscopical preparations:

1. Multipolar neurons
2. Pear-like neurons
3. Pyramidal neurons
4. Myelinated nerve fibers

Electron microphotographs:

1. Myelinated nerve fiber

Myoneural synapse

14. Reproductive tissue.
General embryology. Gastrulation.

Microscopical preparations:

1. Oocyte
2. Spermatozoa
3. Early gastrulation

4. Late grastrulation

Electron microphotographs:

1. Oocyte
2. Spermatozoon

Test 40 p. and preparations -10 p./6+4/ on blood, muscle and nerve tissues
Total score - 50 p.

15. Extra-embryonic layers

Microscopical preparations:

1. Umbilical cord of 2-3 month old human embryo
2. Umbilical cord of newborn baby
3. Placenta

4.Fetal sack

Syllabus

in Cytology, General Histology and Embryology

for Students in Medicine

CYTOLOGY

1. Cell. Microscopic and ultrastructural components of the cell.
2. Biomembranes - structural, ultrastructural and chemical organization.
2. Plasma membrane (plasmalemma) - structural, ultrastructural and chemical organization.
3. Cell contacts - ultrastructure and function.
4. Specialization the cell surface - cilia, flagella, microvilli, basolateral folds.
5. Transport of the substances through the cell membrane. Endocytosis and exocytosis.
6. Endoplasmic reticulum – types, structural, ultrastructural and functional characteristics. Ribosomes.
8. Goigi apparatus (complex) - structural, ultrastructural and functional characteristics.
9. Mitochondria - structural, ultrastructural and functional characteristics.
10. Membrane bound vesicles. Lysosomes. Peroxisomes.
11. Cytoskeleton - microtubules. Centrioles. Cytocenter.
12. Cytoskeleton - microfilaments, intermediate filaments.
13. Specialized cell organelles. Structural, ultrastructural and functional characteristics.
14. Metabolic inclusions·in the cell. Types, structural, ultrastructural and functional characteristics.
15. Nucleus in interphase.
16. Cell division. Mitosis.
17. Synthesis and secretion in the cell.
18. Movement in the cell- role of the cilia, flagella and miofibrils.

GENERAL HISTOLOGY

1. Tissues- general characteristics. Histogenesis and classification.
2. Epithelial tissue. Histogenesis. General characteristics. Classification.
3. Unistratified epithelia. Structural, ultrastructural and functional characteristics. Examples.
4. Multistratified epithelia .Structural, ultrastructural and functional characteristics. Examples.
5. Gland epithelia. Structural, ultrastructural and functional characteristics. Examples.
6. Connective tissue. Histogenesis. General characteristics. Classification.

7. Intercellular substance of the connective tissue. Fibres - structural, ultrastructural, chemical and functional characteristics.
8. Ground substance of connective tissue. Structural, chemical and functional characteristics.
9. Histogenesis of the intercellular substance of the connective tissue – biosynthesis of collagen.
10. Connective tissue cells. Types, structural, ultrastructural and functional characteristics.
11. Fibrous connective tissue. Types, structural, ultrastructural and functional characteristics.
12. Cartilage. Types, structural, ultrastructural and functional characteristics.
13. Bone. Structural, ultrastructural and functional characteristics.
14. Osteogenesis (ossification). Types and structural characteristic.
15. .Specialized connective tissue: adipose tissue, reticular tissue, pigmentous tissue.
16. .Blood tissue. General characteristics. Classsification.
17. .Histogenesis of blood tissue. Scheme of the histogenesis.
18. Erythrocytes – structural, ultrastructural and functional characteristics. Erythropoiesis.
19. Granulocytes – types, structural, ultrastructural and functional characteristics. Ganulocytopoiesis.
20. Agranulocytes – types, structural, ultrastructural and functional characteristics. Lymphocyto - and monocytopoiesis.
21. Blood platelets (thrombocytes) - structural, ultrastructural and functional characteristics. Thrombocytopoiesis.
22. Interstitial (reactive blood) cells. Types, histogenesis. Structural, ultrastructural and functional characteristics.
23. Muscle tissue. Histogenesis. General characteristics. Classsification.
24. Smooth muscle tissue. Structural, ultrastructural, chemical and functional characteristics.
25. Cardiac striated muscle tissue. Structural, ultrastuctural, chemical and functional characteristics.
26. Skeletal striated muscle tissue. Structural, ultrastructural, chemical and functional characteristics.
27. Nervous tissue. Histogenesis. General characteristics. Classsification.
28. Nervous fibres. Types, structural, ultrastructural, chemical and functional characteristics.
29. Neuroglia. Types, structural, ultrastructural, and functional characteristics. Histogenesis.
30. Reproductive tissue. Spermatogenesis. Spermatozoa.
31. Reproductive tissue. Oogenesis. Oocytes.

GENERAL EMBRYOLOGY

32. Insemination. Fertilization. Factors that influence the processes.
33. Initial development of human embryo. Segmentation. Blastocysts. Morulla. Embryoblast. Trophoblast.
34. Implantation. Structural, ultrastructural and functional characteristics of the uterine endometrium during proliferative phase.
35. Early development (gastrulation) of human embryo. Formation of the germ layers. Embryonic disc. Chorion.
36. Late development (gastrulation) of human embryo. Formation of the mesoderm and the mesenchyme. Primitive organs.
37. Germ layers and their derivatives.
38. Yolk sac. Chorion. Alantoic diveiticulum. Vitelline haemopoiesis. Vitelline circulation.

39. Umbilical cord. Formation. Fetal circulation.
40. Placenta. Formation, structure, functions and blood circulation. Blood - placental barrier (placental membrane).
41. Amnion. Amniotic cavity. Amnio-chorionic membrane.
42. Twinning. Monozygotic. Dizygotic.
43. Abnormalities in the embryonic development. Teratogenic factors.

Textbooks

1. Junqueira, Carneiro. Histology, 4 edition, Springer, 1997
2. Stevens, Lowe, Human Histology, 2 edition, Chapman and Hall, 1997
3. Textbook of Human Histology, I. Singh
4. Human Embryology, I. Singh, 6 edition
5. Clinical and Functional Histology for Medical Students, R. Snell
6. Histology, Leeson&Leeson
7. Sobotta, Histology, Atlas, 6 edition
8. Practicum of Cytology, Histology and Embryology with CD interactive atlas , P. Atanassova, I. Koeva, E. Petrova, N. Penkova, V. Trichkova
9. Handbook in Cytology, Histology and Embryology, I. Koeva P. Atanassova, , E. Petrova, N. Penkova, V. Trichkova

The program is made by Prof. P. Atanassova, M.D., Ph.D.

HUMAN ANATOMY

Study course: 1st and 2nd year
Semesters to study: 1st, 2nd, 3rd and 4th semester
Exams: after 2nd semester – Anatomy 1, after 4th semester – Anatomy 2
Credit hours: 315 hours – 90 hours lectures, 225 hours practicals (6/15)
Lecturers: Prof. Sivkov, MD, PhD, Prof. Koeva, MD, PhD

TRAINING PLAN

Teaching method	*Credit hours*						*Credits*
	weekly	*1st sem.*	*2nd sem.*	*3rd sem.*	*4th sem.*	*total*	
Lectures	1, 2, 2, 1	15	30	30	15	90	27,5
Practical classes	3, 4, 4, 4	60	60	60	60	240	
Total	***19 ч.***	***60 ч.***	***90 ч.***	***75 ч.***	***90 ч.***	***330 ч.***	

ANATOMY – GROSS, MICROSCOPIC AND REGIONAL ANATOMY

Training plan: 1st and 2nd year; 1st, 2nd, 3rd and 4th semester, credit hours: 315 hours – 90 hours lectures and 225 hours practicals (6/15)

Lecturers: Prof. Sivkov, MD, Ph.D., Prof. Koeva, MD, Ph.D.

BASIC AIM: thorough knowledge of human anatomy by systems and organs at different levels of organization – from gross anatomy to ultramicroscopic structure.

OBJECTIVES OF THE SUBJECT:

1. Studying macroscopic structure of the organs and systems of human body
2. Studying microscopic structure of the organs of human body
3. Studying embryological development of the organs and systems of human body
4. Studying topography of the organs of human body

METHODS OF TEACHING: lectures, practical classes – self-made cadaver dissection, light microscopy, discussion, drawing.

TECHNICAL RESOURCES: slides, software (ADAM, Anatomist, How the body works), light microscope, videos, anatomy tables, models, native preparations.

CONTROL AND SCORING: midterm exams, final semester exam.

METHODS OF CONTROL: theoretical and practical discussions on specific subject every lesson, quizzes, presentation of self-made preparations, clinical case report. Final exams: after 2nd and 4th semester. Practical test and written exam including MCQ test and essay on a question from conspectus.

MANDATORY COMPETENCIES: thorough knowledge of gross and microscopic structure of human body as well as the topography of the organs and systems.

FIRST SEMESTER – LOCOMOTORY SYSTEM (1/4)

SPECIFICATION:

a) credit hours: 5 hours weekly; 75 hours per semester
b) lectures: 1 hour weekly; 15 hours per semester
c) practical classes: 4 hours weekly; 60 hours per semester
d) final exam after the 2nd semester

DESCRIPTION OF THE TRAINING COURSE

Lectures: Locomotary apparatus and circulatory system. Bone as an organ: structure, types of bone substance, growth and development of bones. Joints, Types of joints. Biomechanics. Muscles. General data. Structure of the muscle. Biomechanics.

Basic items from morphology of the circulatory system are included: heart, blood vessels, lymph vessels, lymph organs. Gross and microscopic structure as well as regional anatomy are discussed.

Practical classes: gross anatomy of bones, structure and biomechanics of joints, arrangement, attachments, innervation and function of the muscles are studied on cadaver preparations. The students make dissection of upper and lower limbs.
Control of knowledge: Theoretical and practical exams during the semester.

Lectures: 1 hour per week

1. Introduction to anatomy. Anatomy in the system of biological sciences. Development of anatomy. Relation to other medical sciences and medical practice.
2. Osteology. General data. Bone as an organ. Classification of bones. Growth of bone.
3. Joints. General data. Types of joints. Continuous joints. Synovial joints. Classification. Biomechanics.
4. Muscles. General data. Muscle as an organ. Structure of the muscle. Classification of the muscles. Supplementary structures of the muscle. Biomechanics.
5. Muscles, blood and nerve supply of the upper limb. Muscle groups. Main blood vessels. Innervation – brachial plexus.
6. Muscles, blood and nerve supply of the lower limb. Muscle groups. Main blood vessels. Innervation – lumbosacral plexus.
7. Topography of the upper limb. Regions. Boundaries. Content. In-depth anatomy
8. Topography of the lower limb. Regions. Boundaries. Content. In-depth anatomy.

Practicals: 4 hours weekly (2x2)

1. Introduction to anatomy and osteology. Vertebrae and vertebral column.
2. Bones of the thorax and shoulder girdle. Ribs, sternum. Bones of the shoulder girdle - scapula, clavicle.
3. Bones of the upper limb. Humerus. Radius and ulna. Bones of the hand.
4. Bones of the pelvis. Sacrum and coccyx. Hip bone. Pelvis as a whole.
5. Bones of the lower limb. Femur. Tibia, fibula, patella. Bones of the foot.
6. ***Midterm exam 1.***
7. Joints of the vertebral column. Joints between vertebrae. Joints between vertebral column and skull.
8. Joints of the thorax. Joints between ribs and vertebrae. Joints between ribs and sternum.
9. Shoulder and pelvic regions. Main blood and nerve supply of upper and lower limbs. Nerve plexuses – brachial, lumbar and sacral. Muscles, blood and nerve supply of the shoulder region.
10. Shoulder and pelvic regions. Muscles, blood and nerve supply of the pelvic region.
11. Shoulder and pelvic regions. Topographic regions of shoulder and pelvis.
12. Shoulder region. Joints of the shoulder girdle. Sternoclavicular, acromioclavicular joints. Humero-scapular joint.
13. Pelvic region. Joints of the pevis. Sacroiliac joint. Hip joint.
14. Arm and thigh. Muscles, blood and nerve supply.
15. Arm and thigh. Muscles, blood and nerve supply.
16. Arm and thigh. Muscles, blood and nerve supply.
17. Arm and thigh. Topographic regions.
18. Elbow and knee regions. Cubital fossa and popliteal fossa.
19. Elbow and knee regions**.** Elbow and knee joint.
20. ***Midterm exam 2.***
21. Forearm and leg. Muscles, blood and nerve supply of the forearm and leg.
22. Forearm and leg. Muscles, blood and nerve supply of the forearm and leg.
23. Forearm and leg. Topographic regions.
24. Forearm and leg. Joints of the forearm and the leg.
25. Wrist. Joints of the wrist. Topographic regions.
26. Hand. Muscles, blood and nerve supply.

27. Hand. Joints of the hand. Topographic regions.
28. Foot. Muscles, blood and nerve supply of the foot.
29. Foot. Joints of the foot. Topographic regions.
30. ***Midterm exam 3.***

SECOND SEMESTER – NERVOUS SYSTEM, SENSORY ORGANS (2/4)

SPECIFICATION:

a) credit hours: 6 hours weekly; 90 hours per semester
b) lectures: 2 hours weekly; 30 hours per semester
c) practical lessons: 4 hours weekly; 60 hours per semester
d) the final exam is after the 2nd semester

DESCRIPTION OF THE TRAINING COURSE

Lectures: nervous system and sensory organs. Basic principles in the structural pattern of the nervous system: nervous tissue, synapsis, neural chains, reflex arch. Internal and external features of the different parts of CNS. Peripheral nervous system. Structure of the sensory organs: eye and ear.

Practical classes: In the first half of the semester they are on CNS. On native preparations from human brain the students study the morphology of spinal cord and the parts of the encephalon. Next are the sensory organs like eye and ear and also the cranial nerves – their origin, course, branches and area of supply.

Control of knowledge: Theoretical and practical quizzes are held during the semester.

Lectures: 2 hours per week

1. Introduction to morphology of nervous system. Development of nervous system.
2. Spinal cord. Spinal nerves.
3. Brain. General description. Medulla oblongata.
4. Pons. Rhomboid fossa. Cerebellum.
5. Cerebellum.
6. Diencephalon. Thalamus, epithalamus, metathalamus.
7. Diencephalon. Hypothalamus, subthalamus.
8. Forebrain – general description. Brain cortex.
9. Forebrain – white matter. Basal ganglia.
10. Rhinencephalon. Limbic system.
11. Pathways in CNS.
12. Eye.
13. Ear.
14. Cranial nerves.
15. Autonomic nervous system.

Practicals: 4hours weekly (2x2)

1. Cranium. Frontal, parietal and occipital bones. Vault.
2. Skull – temporal and ethmoid bones.
3. Skull – sphenoid bone. Facial bones.
4. Skull. Nasal cavity. Paranasal sinuses. Orbit.
5. Skull – basis cranii externa and interna. Temporal, infratemporal and pterygopalatine fossae.
6. ***Midterm exam 1. Practical and theoretical quiz.***
7. Spinal cord. External features.
8. Spinal cord, spinal ganglion, autonomic ganglion, peripheral nerve – ***microscopic structure.***
9. Medulla. Pons. Rhomboid fossa.
10. Midbrain. Cerebellum. IVth ventricle.
11. Diencephalon. Thalamus, epithalamus, metathalamus.
12. Diencephalon. Hypothalamus, subthalamus. IIIrd ventricle.

13. ***Midterm exam 2.***
14. Telencephalon. Gross brain. Brodmann's areas.
15. Telencephalon – white matter, basal ganglia. Lateral ventricles.
16. Cerebral and cerebellar cortex – ***microscopic structure.***
17. Rhinencephalon. Limbic system.
18. Meninges. Blood supply of CNS.
19. Sensory organs. Receptors of general sensation – ***microscopic structure.***
20. ***Midterm exam 3.***
21. Eye. Visual system.
22. Ear. External and middle ear. Osseous labyrinth.
23. Inner ear. Auditory and vestibular systems.
24. Eye and ear – ***microscopic structure.***
25. Autonomic nervous system.
26. CN – general remarks. III, IV, VI, XI, XII.
27. CN – V, IX.
28. CN – VII, X.
29. ***Midterm exam 4.***
30. Pathways in the brain.

III SEMESTER –ANATOMY AND HISTOLOGY OF THE INTERNAL ORGANS (2/4)

SPECIFICATION:

a) teaching hours: 6 h.weekly; 90 h. for semester

b) lectures: 2 h.weekly; 30 h. for semester

c) practical classes: 4 h.weekly; 60 h. for semester

d) final examination: after the end of the IV semester

DESCRIPTION OF THE TEACHING COURSE:

Lectures: The main subject area of the lecture course is the macro- and microscopic structure and the embryonic development of the human internal organs. The purpose is to build up clear and logical notion about the normal morphology and development of the organs in systematic plan. The organs of the cardiovascular, immune, respiratory, digestive, endocrine, urinary, reproductive and integumental systems are examined in systematic aspect.

Practical classes: The basic teaching method in the practical course is the macro-and microscopic (study under light microscope) observation through which the students get a notion about the normal structure, function and development of the organs in the human body. During the semester there are examinations (tests) in the topic of each practical exercise and finally a total mark for the semester is summarized.

Control of the knowledge: Tests (3) and practical examinations (3).

PROGRAMME

OF THE LECTURES AND PRACTICAL CLASSES IN ORGAN ANATOMY FOR II MEDICAL COURSE

Lecturers: Assoc. Prof. Y. Koeva, MD, PhD, Assoc. Prof. P. Atanassova, MD, PhD

LECTURES– *2 h weekly*

1. Cardiovascular system. Heart–embryonic development, topography, macro-and microscopic anatomy.
2. Blood vessels - embryonic development, macro-and microscopic anatomy. Lymph system –principal structure. Lymph vessels and lymph.

3. Immune system–principal structure. Bone marrow, thymus, spleen and lymph nodes– embryonic development, macro-and microscopic anatomy.
4. Respiratory system- embryonic development and general structure of the organs of the respiratory system. Nasal cavity, larynx, trachea and lungs– macro-and microscopic anatomy.
5. Digestive system. Oral cavity-embryonic development, general structure.Tongue, salivary glands and teeth – embryonic development, macro-and microscopic anatomy.
6. Pharynx, oesophagus and stomach-embryonic development, macro-and microscopic anatomy.
7. Small, large intestines and appendix–embryonic development, macro-and microscopic anatomy.
8. Liver, gall bladder and pancreas–embryonic development, macro-and microscopic anatomy.
9. Urinary system-embryonic development and principal structure of the organs. Kidney, ureter and urinary bladder– macro-and microscopic anatomy.
10. Endocrine system- general characteristic and classification. Hypophysis and epiphysis. Peripheral endocrine organs-adrenal gland, thyroid and parathyroid glands- embryonic development, macro-and microscopic anatomy.
11. Male reproductive system-embryonic development and general characteristic. Testis– macro-and microscopic anatomy.
12. Male reproductive system–epididymis, prostate, seminal vesicles, penis and male urethra– macro- and microscopic anatomy.
13. Female reproductive system. Ovary–embryonic development, macro-and microscopic anatomy.
14. Female reproductive system – uterus, oviduct and vagina–embryonic development, macro-and microscopic anatomy.
15. Integumental system. The skin and its appendages- embryonic development, macro-and microscopic anatomy.

PRACTICAL CLASSES: 4 h weekly (2x2)

1. Principal structure of a tube and parenchymatous organs- 2 h.
2. Cardiovascular system- macro- and microscopic anatomy– 2 h.

Histological sections:

1. artery and vein- muscular type
2. aorta-orcein, H-E
3. arteriola, venula and capillaries
4. EM of capillaries

3. Heart- macro-and microscopic anatomy.- 2 h.

Histological sections:

1. heart wall
2 . Impulse-conducting system

4. Immune system- bone marrow, thymus and lymph nodes- macro-and microscopic anatomy.2h.

Histological sections:

1. bone marrow
2. thymus
3. lymph node

5. Immune system–spleen and tonsils – macro-and microscopic anatomy– 2 h.

Histological sections:
1. spleen
2. tonsilla palatina

6. Nasal cavity and the paranasal air sinuses - macro-and microscopic anatomy.– 2 h
Histological sections:
1.nasal mucosa

7. Larynx- macro-and microscopic anatomy.– 2 h
Histological sections:
1. epiglottis
2. larynx

8. Tarchea, bronchi and the lungs – macro-and microscopic anatomy.– 2 h
Histological sections:
1.trachea

9. The lungs and bronchi – macro-and microscopic anatomy.– 2 h
Histological sections:
1. lungs
2. small and middle-sized bronchi
3. embryonic lung
4. EM of alvelocytes and blood-air barrier

10. Digestive system. Oral cavity–macro-and microscopic anatomy- 2h.
Histological sections:
1. lips
2. cheeks
3. uvula

11. Teeth- – macro-and microscopic anatomy- 2 h.
Histological sections:
1. embryonic tooth
2. adult tooth- H-E
3. adult tooth– schliff

12. Test in cardiovascular, respiratory and immune systems

13. Tongue and salivary glands – macro-and microscopic anatomy- 2h.
Histological sections:
1. tongue ,papillae filiformes
2. tongue, papillae vallatae
3. parotid gland
4. submandibular gland
5. sublingual gland

14. Pharynx and oesophagus –macro-and microscopic anatomy– 2 h.
Histological sections:
1.oesophagus

15 .Stomach -macro-and microscopic anatomy.- 2h.
Histological sections:
1. stomach – fundus
2. stomach –pylorus
3. EM of parietal and chief cells

16. Small and large intestine (caecum, colon, rectum)- macro-and microscopic anatomy 2h.
Histological sections:
1. small intestine
2. duodenum
3. large intestine
4. appendix

5. EM of goblet cell

17. Liver and pancreas–macro-and microscopic anatomy- 2 h.

Histological sections:

1.liver

2. gall bladder

3. pancreas

4.EM of hepatocytes

18. Urinary system–kidney-macro-and microscopic anatomy. – 2 h

Histological sections:

1. kidney-H-E

2. kidney– kongorot

3. EM of blood-urinary barrier

19. Ureter and urinary bladder – macro-and microscopic anatomy – 2h.

Histological sections:

1. ureter

2. urinary bladder

3. urethra (male)

20. Test in digestive and urinary systems

21. Endocrine system-hypophysis, epiphysis and the islets of Langerhans - macro-and microscopic anatomy - 2h.

Histological sections:

1. hypophysis

2. epiphysis

3. islets of Langerhans

3.1 staining by H-E

3.2 by impregnation

22. Endocrine system–thyroid, parathyroid and adrenal glands - macro-and microscopic anatomy - 2h.

Histological sections:

1. thyroid gland

2. parathyroid glands

3. adrenal gland

4. EM of adrenocorticocytes

23. Male reproductive system –testis, epididymis- macro-and microscopic anatomy - 2 h.

Histological sections:

1.testis

2.epididymis

3.EM of Leydig cell

24. Prostate, seminal vesicles, penis and male urethra– macro-and microscopic anatomy. The external male genitalia - 2 h.

Histological sections:

1. prostate

2.ductus deferens

25. The external male genitalia - 2 h.

Histological sections:

1. penis

26. Female reproductive system. Ovary–macro-and microscopic anatomy - 2 h.

Histological sections:

1. ovary

27. Uterus, oviduct and vagina–-macro-and microscopic anatomy. - 2 h.

Histological sections:

1. uterus
2. oviduct
3. vagina

28. The external female genitalia- 2 h.

Histological sections:

1. mammary gland (lactating)
2. mammary gland (non-lactating)

29. Test in endocrine, male and female reproductive systems

30. The skin and its appendages- 2 h.

Histological sections:

1. skin
2. hair
3. nail

Literature:

Textbooks:

1. Junqueira, Carneiro. Histology, 4 edition, Springer, 1997
2. Stevens, Lowe, Human Histology, 2 edition, Chapman and Hall, 1997
3. Grey's Anatomy

Atlases

1. Sobotta. Atlas of Human anatomy, 14th edition, Urban & Fisher, 2006
2. Rohen, Yokochi, Luten-Drecoll. Human Anatomy, 4 edition, Springer, 1998
3. Krstic, Human Microscopic Anatomy, Springer, 1997

Made by Assoc. Prof. Yvetta Koeva, MD, PhD

FOURTH SEMESTER – REGIONAL ANATOMY OF BACK, NECK, THORAX, ABDOMEN AND PELVIS (1/4)

SPECIFICATION:

a) credit hours: 5 hours weekly;75 hours per semester
b) lectures: 1 hour weekly; 15 hours per semester
c) practical lessons: 4 hours weekly; 60 hours per semester
d) the final exam is after the 4th semester
e) how the exam is organized: practical and theoretical exam: quiz, written exam, oral exam.

DESCRIPTION OF THE TRAINING COURSE

Lectures: Topography of the internal organs. The discussion of the internal organs is continued. Regional anatomy of back, neck, thorax, abdomen and pelvis.

Practical classes: Cadaver dissection. During dissection the students examine the superficial landmarks and underlying structures of the back, head, neck, thoracic and abdominal wall. Topography of the organs in the neck, thorax, abdomen and pelvis is also studied.

Control of knowledge: Theoretical and practical quizzes are held during the semester.

Lectures: 1 hour weekly

1. Neck topography. Subcutaneous elements.Lateral neck region Infrahyoid region.
2. Neck topography. Carotid and submandibular region; root of the neck.
3. Topography of thorax. Thoracic cavity. Pleural cavity. Mediastinum.

4. Abdominal wall. Inguinal canal. Abdominal and peritoneal canal. Upper peritoneal region – organs, bursae, peritoneal structures.
5. Topography of the abdomen. Lower peritoneal region. organs, bursae, peritoneal structures. Retroperitoneum.
6. Topography of the pelvis. Peritoneal, subperitoneal and subcutaneous region. Organs, spaces, muscles, fasciae.
7. Topography of the head. Regions. Blood and nerve supply, lymph drainage. Epicranial and parotid regions.
8. Topography of the head. Temporal, infratemporal regions. Peripharyngeal space.

Practicals: 4hours weekly (2x2)

1. Introduction to cadaver dissections. Body regions. Back – subcutaneous elements superficial muscles.
2. Back – deep muscles.
3. Subcutaneous elements of the a/ neck, b/ thorax and c/ abdomen.
4. Fossa axilaris. Anterior wall. Fascia of the neck.
5. Fossa axillaris.
6. Lateral cervical region.
7. Anterolateral abdominal wall. Inguinal canal. M. rectus abdominis and its vagina.
8. Upper region of abdominal cavity. Omental bursa.
9. Lower region of the abdominal cavity.
10. Carotid triangle and sternocleidomastoid region.
11. ***Midterm exam 1.***
12. Vessles and nerves in the region of a.mesenterica superior.
13. Infrahyoid region. Vessels of a. mesenterica inferior.
14. Thoracic cavity.
15. Root of the neck. Submandibular triangle.
16. Superior mediastinum.Root of the lung.
17. Vessels and nerves in the region of the truncus celiacus. V. Portae.
18. Anterior and middle mediastinum.
19. Posterior mediastinum.
20. Intercostals spaces and thoracic diaphragm.
21. ***Midterm exam 2.***
22. Retroperitoneum – primary and secondary retroperitoneal organs - topography.
23. Retroperitoneum – vessels and nerves.
24. Pelvis - peritoneal region.
25. Pelvis – subperitoneal and subcutaneous regions. Vessels and nerves of the pelvis.
26. Muscles of facial expression. Vessels and nerves of the face. Temporomandibular joint – structure, biomechanics. Muscles of mastication.Regio parotideomasseterica.
27. Epicranial, temporal and infratemporal regions.
28. **Discussion on the dissection preparations.**
29. ***Midterm exam 3.***
30. Peripharyngeal space.

FIRST YEAR FINAL EXAM QUESTIONS

I. Locomotory system

1. Bone as an organ. Structure of mature bone: osseous (bone) tissue, compact and spongy bone tissue. Types of bones. The skeleton - definition, function.
2. Development and growth of the bones. Histogenesis - types of bone formation. Factors, influencing bone formation. Increase of the bones in length and thickness - the growth cartilage, periosteum - structure.

3. Joints between bones. Solid joints.
4. Synovial joints (diarthroses) - the structure of the synovial joints: basic and additional elements. The classification of the synovial joints.
5. Vertebral column. Joints of the vertebral column. The vertebral column as a whole. Biomechanics.
6. Skeleton of the thorax. Joints of the thorax. The thorax as a whole. Biomechanics.
7. Joints between the vertebral column and the skull. Biomechanics.
8. Joints between the skull bones. Temporomandibular joint.
9. Joints of the shoulder girdle. Shoulder joint.
10. Elbow joint. Joints between the bones of the forearm.
11. Joints of the hand. Carpometacarpal joints. Metacarpophalangeal joints. Interphalangeal joints.
12. Joints of the pelvic girdle. The pelvic girdle as a whole. Biomechanics.
13. Hip joint.
14. Knee joint.
15. Joints between the leg bones. Ankle joint.
16. Joints of the foot - subtalar joint and talo-calcaneo-navicular joint. Joints of the foot with limited movement. Interphalangeal joints. Arches of the foot. Biomechanics.
17. Structure of skeletal muscle: auxiliary structures, classification of muscles, biomechanics.
18. Muscles of the shoulder girdle - groups, attachments, action, and nerve supply.
19. Muscles of the upper arm - groups, attachments, action, and nerve supply.
20. Muscles of the forearm - groups, attachments, action, and nerve supply..
21. Muscles of the hand - groups, attachments, action, and nerve supply.
22. Synovial sheaths of the hand. Flexor and extensor retinacula.
23. Muscles around the hip joint - groups, attachments, action, and nerve supply.
24. Muscles of the femoral region - groups, attachments, action and nerve supply.
25. Muscles of the leg - groups, attachments, action and nerve supply.
26. Muscles of the foot - groups, attachments, action and nerve supply.
27. Topography of the upper limb – lateral (quadrangular) and medial (triangular) axillary space, cubital fossa.
28. Topography of the lower limb - suprapiriform foramen, infrapiriform foramen, vascular and muscular lacuna, obturator and femoral canal.
29. Topography of the lower limb – Femoral triangle, adductor canal, popliteal fossa, cruropopliteus canal.
30. The superficial veins of the upper and lower limbs.
31. The axillary artery. Position, parts, branches. Anastomoses around the shoulder joint.
32. The arteries of the upper limb - the brachial artery, the radial artery and the ulnar artery. Their position and branches.
33. The external and internal iliac arteries. Position, branches. Anastomoses around the hip joint.
34. The arteries of the lower limb - the femoral artery, the popliteal artery, the anterior and posterior tibial arteries. Position and branches.
35. Brachial plexus. The formation, position. Branches of the supraclavicular branches.
36. Median and ulnar nerve. Origin, position, branches. Areas of sensory and motor innervation.
37. Radial, axillary and musculocutaneous nerve.
38. Lumbar plexus. Formation, position, branches.
39. Sacral and coccygeal plexus. Formation, position, branches.
40. Sciatic nerve. Origin, position, branches. Branches supplying skin and muscles.

II. Nervous system and sensory organs

1. Skull (cranium) - facial cranium and neurocranium (cranial skull). Calvaria (calva, vault). The skull of the newborn.

2. External surface of the base of the skull - elements, passing through the openings and canals.
3. Internal surface of the base of the skull - elements, passing through the openings and canals.
4. Lateral aspect of the skull: temporal, infratemporal, and pterygopalatine fossae. Walls, boundaries, communications and elements passing through them.
5. Orbit. Walls, communications, and elements passing through them.
6. Skeleton of the nasal cavity. Walls, communications and elements passing through them.
7. Spinal cord - position, shape, size, segments. Meninges and blood supply.
8. Spinal cord. Grey matter - arrangement and structure.
9. Spinal cord. The white matter - ascending (sensory) and descending (motor) tracts. Intersegmental tracts.
10. Brain - development, shape, size. Anatomical and ontogenetic division. Brainstem - new and old parts. The reticular formation.
11. Medulla oblongata - position, size, the external view (aspect), the internal structure.
12. Pons - position, parts, external view, internal structure.
13. Cerebellum - position, shape, size, parts. General arrangement - grey and white matter. Archi-, paleo-, and neo-cerebellum. Nuclei. Cerebellar peduncles.
14. Cerebellar cortex - structure. Afferent and efferent tracts.
15. The fourth ventricle. Rhomboid fossa. Cerebrospinal fluid - formation, circulation, and drainage.
16. Midbrain - position, parts. External view and internal structure.
17. Diencephalon - thalamus, epithalamus, metathalamus. Position, parts, external view, internal structure.
18. Diencephalon - hypothalamus, subthalamic area. Position, external view , internal structure.
19. Cerebrum (forebrain) - position, shape, lobes. Exterior of the cerebral hemispheres - sulci and gyri. Important functional areas of the cerebral cortex.
20. Cerebral cortex - structure. Variations in the structure.
21. Basal nuclei of the cerebrum.
22. White matter. Internal capsule.
23. Olfactory apparatus (rhinencephalon). Olfactory pathway.
24. Limbic system.
25. The third ventricle. The lateral ventricle. Cerebrospinal fluid - formation and circulation, and darainage.
26. The meninges of the brain. Blood supply of the brain.
27. Ascending pathways for general sensation.
28. Ascending pathways for proprioception.
29. Efferent pathways from the cerebral cortex (the pyramid system).
30. The extrapyramid system.
31. Cranial nerves - number, names, groups. General principles of formation. Nuclei (motor, sensory, parasympathetic), ganglia.
32. Third, fourth, and sixth cranial nerves - nuclei, position, characteristics. Course of the nerve, branches, area of distribution.
33. Trigeminal nerve. Nuclei - position, characteristic. The ganglion of the nerve. The first branch of the nerve - course, branches, area of distribution.
34. Trigeminal nerve. Nuclei - position, characteristic. The ganglion of the nerve. The second branch of the nerve - course, branches, area of distribution.
35. Trigeminal nervee. Nuclei - position, characteristic. The ganglion of the nerve. The third branch of the nerve - course, branches, area of distribution.
36. Facial nerve. Nuclei - position, characteristic. The course, branches, area of distribution.
37. Glossopharyngeal nerve. Nuclei - position, characteristic. The course, branches, area of distribution.
38. Vagus nerve. Nuclei - position, characteristic. The course, branches, area of distribution.

39. Accessory nerve, hypoglossal nerve. Nuclei - position, characteristic. The course of the nerves, branches, area of distribution.
40. Spinal nerves - number, groups, formation. Functional or analysis of the spinal nerves. The spinal ganglion.
41. Autonomic nervous system - definition, criteria for division into sympathetic and parasympathetic divisions. Reflex arch. Analysis of its neurons. Autonomic ganglia. Differences between the autonomic and somatic nervous system.
42. Sympathetic division of the autonomic nervous system - nuclei, sympathetic trunk, prevertebral ganglia, nerves.
43. Parasympathetic division of the autonomic nervous system. Cranial and sacral parasympathetic outflow - nuclei, ganglia, nerves.
44. Plexuses of the autonomic nervous system in the thorax, abdominal and pelvic cavities - formation, position, organs receive their fibers.
45. Organ of vision - general remarks. The eyeball - shape, position, size. Outer (fibrous) coat.
46. The eyeball - middle (vascular) coat - parts, description.
47. Retina. Visual pathway.
48. Refracing media of the eye - cornea, lens, vitreous body, aqueous humour.
49. Extraocular muscles. Eyelids. Lacrimal apparatus. Conjunctiva. Orbital fat.
50. External ear.
51. Middle ear.
52. Internal ear. The bony labyrinth.
53. Internal ear. The membranous labyrinth - cochlear part. Organ of Corti. Pathway of hearing.
54. Internal ear. The membranous labyrinth - vestibular part. Organ of equilibrium. Pathway of equilibrium.

Recommend Resources for study:

1. *Gray's Anatomy*
2. *Human Anatomy – Regional and applied by B.D.Chaurasia*
3. *Neuroanatomy by William DeMyer*

SECOND YEAR FINAL EXAM QUESTIONS

I. Splanchnology

1. The circulatory system. Definition. Constituting elements. Major (or systematic) circulation. Lesser (or pulmonary) circulation. Fetal circulation.
2. Heart - position, surface projection on the chest wall. Cardiac size, shape and external features. Pericardium.
3. Cardiac chambers and internal features. The valves of the heart.
4. Cardiac wall (endocardium, myocardium, epicardium) - structure. Fibrous skeleton.
5. Cardiac nerve supply. Coordination of cardiac activities - the conducting system. Blood supply of the heart.
6. Arteries - definition, position in the body, structure of arterial wall. Types of arteries.
7. Veins - definition, position in the body, structure of arterial wall. Types of veins.
8. Microcirculatory blood system. Arterioles, capillaries and sinusoids. Venules. Arteriovenous anastomoses.
9. The lymphoid system. Definition, constituting Blood supply. Lymph capillaries - microstructure. The thoracic duct and its tributaries. The right lymphatic duct - formation. Movements of the lymph.
10. The spleen. Position, structure, blood supply and nerve supply.
11. The lymph nodes - position, groups, structure. The tonsils. The thymus.

12. Digestive system- the major organs of the digestive system. The vestibule of the mouth. Lips. Cheeks. Blood supply and nerve supply.
13. Oral cavity proper - walls. The hard and soft palate. The oropharyngeal isthmus. The mucous membrane. Blood supply and nerves.
14. Teeth. Deciduous and permanent dentition. Structure of the tooth.
15. Tongue - parts, surfaces. The mucous membrane - papillae. The lingual tonsil. The lingual muscles. Blood supply, nerves, and lymph drainage.
16. The major salivary glands. Position, structure. Blood supply, lymph drainage, and nerves.
17. Pharynx - position, shape, parts, description. Structure of the pharyngeal wall. Blood supply, lymph drainage, and nerves.
18. Esophagus - position, parts, description. Structure of the pharyngeal wall. Blood supply, lymph drainage, and nerves.
19. Stomach - position, shape, size. Peritoneal relation of the stomach.Blood supply, lymph drainage, and nerves.
20. Stomach - parts. Structure of the wall. Glands of the stomach.
21. Small intestine. Duodenum - position, parts, description, peritoneal relation of the duodenum. Structure of the wall. Blood supply, lymph drainage, and nerves.
22. Small intestine - jejunum and ileum. Position, peritoneal relation. Structure of the wall. Blood supply, lymph drainage, and nerves.
23. Large intestine - parts, position. External features of the large intestine. Peritoneal relation. Blood supply, lymph drainage, and nerves.
24. Large intestine - the colon. Parts, position, peritoneal relation. Structure of the wall. Blood supply, lymph drainage, and nerves.
25. Caecum. The vermiform appendix - position, shape, size. Structure of the wall. Peritoneal relation. Blood supply, lymph drainage, and nerves.
26. Rectum - position, shape, size. Peritoneal relation. Structure of the wall. Blood supply, lymph drainage, and nerves.
27. Liver - position, shape, size, lobes. Peritoneal connection of the liver.
28. Structure of the liver - the liver lobule, the portal lobule, the liver acinus, microcirculation. Blood supply, lymph drainage, and nerves of the liver.
29. The biliary system. The gall bladder. Structure, description, peritoneal connection of the gall bladder. Blood supply, lymph drainage, and nerve supply.
30. Pancreas - shape, position, description, peritoneal relation. Structure. Blood supply, lymph drainage, and nerves.
31. Respiratory system. The major organs of the respiratory system -principle structure.The nose.
32. Nasal cavity - division, description, mucous membrane. Paranasal air sinuses. Blood supply, lymph drainage, and nerve supply.
33. Larynx - position, shape. Laryngeal cartilages, vocal folds, layngeal muscles - nerve supply.
34. Larynx - the cavity of the larynx, mucous membrane. Blood supply, lymph drainage, and nerve supply.
35. Trachea - position, parts, size. The principal bronchi. The tracheobronchial tree. Structure of the wall.
36. Lungs - shape, position, description, surface marking. Lobes, segments, lobules.
37. Respiratory spaces of the lungs. Structure of a lung lobule - acinus, blood-air barrier.
38. Urinary system. Components. Kidneys - position, shape, and size. Topography of the kidneys. Capsules of the kidney.
39. Kidneys. Internal structure. Blood supply and microcirculation.
40. Excretory structures - minor and major calyces, pelvis, ureter.
41. Urinary bladder. Position, shape, and size. Peritoneal relations. Structure of the wall. Blood and nerve supply. Female urethra.
42. Endocrine system. Organs. Classification. General characteristics. Thyroid, parathyroid, and suprarenal glands - position and structure. Blood and nerve supply.

43. Male reproductive system. Organs. Testis - position, structure, and coats. Accessory ducts. Epididymis. Blood and nerve supply.
44. Accessory ducts - ductus deferens, ejaculatory duct. Seminal vesicles. Prostate gland - position, size and shape. Internal structure. Blood and nerve supply.
45. Penis. Male urethra. Blood and nerve supply.
46. Female reproductive system. Organs. Ovary - position, shape, size, peritoneal relations, suspensory ligaments. Internal structure. Blood and nerve supply, lymph drainage.
47. Uterus - position, shape, size, peritoneal relations. Suspensory ligaments.
48. Uterus. Uterine cavity. Structure. Blood and nerve supply, lymph drainage.
49. Uterine tubes - position, parts, peritoneal relations. Structure. Blood and nerve supply, lymph drainage.
50. External genital organs. Vagina - position, shape, size, peritoneal relations. Structure. Blood and nerve supply, lymph drainage.

II. Regional anatomy

51. Scalp.
52. Muscles of facial expression - groups, blood and nerve supply.
53. Blood and nerve supply of the face.
54. Muscles of mastication - action , nerve supply.
55. Joints between the skull bones. Temporomandibular joint.
56. Parotid region.
57. Temporal region.
58. Infratemporal region.
59. Lateropharyngeal and retropharyngeal spaces.
60. Digastric triangle.
61. Carotid triangle.
62. The carotid system of arteries. The common carotid artery - begining, position and branches. External and internal carotid arteries - position and branches.
63. Infrahyoid region.
64. Posterior cervical triangle.
65. Antescalenus, interscalenus, and scalenovertebral spaces.
66. The subclavian artery. Position and branches. Anastomoses around the shoulder joint.
67. Cervical plexus. The formation, position, branches. Subcutaneous structures in the cervical, thoracic, and abdominal regions.
68. Cervical fascia.
69. Muscles of the neck - groups, attachments, action, and nerve supply.
70. Muscles of the back - groups, action, nerve supply.
71. Chest wall. Muscles and intercostal spaces. Topography of the chest wall.
72. Axilla. Shape, walls, and contents.
73. Thoracic cavity. Pleura. Pleural cavity.
74. Diaphagm.
75. Superior mediastinum.
76. Posterior mediastinum.
77. Anterior and middle mediastinum.
78. The aorta. Position and division in parts. The ascending aorta, the arch of the aorta, the thoracic aorta - branches.
79. Anterior abdominal wall. regions, muscles, fasciae. Topography of the abdominal wall. Sheath of the rectus abdominis muscle.
80. Inguinal canal. Linea alba.
81. Abdominal cavity. Walls, regions. Peritoneum - gross anatomy, blood and nerve supply.
82. Peritoneal cavity. Upper region - organs, peritoneal structures, and recesses.
83. Peritoneal cavity. Lower region - organs, peritoneal structures, and recesses.

84. Omental bursa. Greater omentum.
85. The unpaired visceral branches of the abdominal aorta - the coeliac trunk, the superior and inferior mesenteric arteries. Position and branches.
86. The hepatic portal system - constituting veins. Position of the portal vein. Anastomoses between the portal and systematic circulation.
87. Retroperitoneal space.
88. The abdominal aorta. Parietal (lateral) and paired visceral branches.
89. The superior and inferior vena cava. Position. Main tributaries. Anastomoses between the two caval veins.
90. Peritoneal cavity. Pelvic region - organs, peritoneal structures, and recesses.
91. Subperitoneal space - organs, and spaces.
92. Subcutaneous pelvic region. Perineum. Ischioanal fossa.

Recommend Resources for study:

1. *Gray's Anatomy*
2. *Human Anatomy – Regional and applied by B.D.Chaurasia*

MEDICAL UNIVERSITY - PLOVDIV

FACULTY OF MEDICINE

PROGRAMME

IN

HUMAN BIOLOGY

Approved by the Departmental Council on 6 June, 2012

Confirmed by the Faculty Council on……., 2012

MEDICAL UNIVERSITY – PLOVDIV

FACULTY OF MEDICINE

COURSE NAME

Human Biology

TYPE OF COURSE ACCORDING TO THE UNIFORM STATE REQUIREMENTS

Mandatory

LEVEL OF EDUCATION:

Master degree /M/

FORM OF EDUCATION:

Lecture courses, practical courses, self-training.

SEMESTERS OF EDUCATION:

1st and 2nd semesters

AUDITORIUM CLASSES:

60 hours of lecture courses, 55 hours of practical courses

TECHNICAL EQUIPMENT APPLIED IN THE TRAINING:

microscopes, permanent and temporary microscopic preparations, cell cultures, audiovisual equipment, tools and technical devices for illustration and performance of molecular, cellular and immunological methods, laboratory protocols, test books.

TRAINING METHODS: lecture courses, practical courses, seminars, individual work with excellent students.

CONTROL AND EVALUATION:

- ✓ *Ongoing evaluation* – weekly tests, oral examinations, colloquia on different syllabus sections.
- ✓ *Final evaluation* – combined written test, oral examination.

Score assessment

Participation in seminars, weekly tests, essay preparation and presentation

Semester exam:

Yes / written and oral examination/

State Exam

No

Lecturer
Full Professor from the Department of Biology

Department:
Biology

ANNOTATION

The discipline Biology allows students to acquire knowledge and skills in the following basic biological concepts:

- Molecular foundations of life – biological macromolecules
- Realization of genetic information
- Genetic code
- Organization of the genetic material in the cell
- Karyotype
- Heredity and variability
- Human hereditary diseases
- Genetic engineering
- Biology of the cell
- Reproduction
- Individual development
- Immunological homeostasis
- Population genetics.
- Theory of evolution.
- Molecular evolution.
- Interactions between organisms in biocenosis.
- Human interactions with nature environment.

COURSE OBJECTIVES: The objective of the biology course is to develop:

1. The understanding that living systems, including humans, have hierarchically ordered levels of organization with their own specificity and rules that determine biological features and functions.
2. The notion that humans, as a product of biological evolution, are ecologically connected to the development of nature and of the biosphere as a whole.
3. The ability to apply biological rules as scientific theory and methodology of medicine.

4. Practical skills and knowledge of basic biological techniques with medical application.

COURSE TASKS

Proficiency in the most important properties and manifestations of the organismal world and humans in particular:

- cellular basis of life;
- heredity and variability;
- reproduction and individual development of organisms;
- immunological homeostasis;
- biology and genetics of populations;
- evolutionary theory;
- anthropogenesis;
- basic ecology;
- morphology and biological cycle of medically important parasites.

OBLIGATORY COMPETENCIES:

1. *Theoretical knowledge* – mastering and analysis of:
   - ✓ hierarchical levels and structural organization of the human organism (molecular, cellular and systemic)
   - ✓ genetic structures and processes of transfer of genetic and epigenetic information
   - ✓ mechanisms of immunological homeostasis
   - ✓ ontogenesis and phylogenesis
2. *Practical skills:*
   - ✓ preparation of temporary and permanent microscopic slides
   - ✓ light microscopy
   - ✓ karyotyping
   - ✓ genetic cases
   - ✓ basic immunological reactions
   - ✓ blood typing
   - ✓ basic molecular biology methods
   - ✓ basic cellular biology methods
   - ✓ fingerprinting and dermatoglyphics
   - ✓ populational variation analysis

CURRICULUM

Type of courses	***Course hours***				***Credits***
	weekly	***I semester***	***II semester***	***All***	
Lecture courses	2	30	30	60	***9,9***
Practical courses	2	20	25	45	
All	***4 hours***	***50 hours***	***55 hours***	***105 hours***	

PROGRAMME IN HUMAN BIOLOGY

FIRST SEMESTER

№	LECTURE COURSES	HOURS	DATE
1.	Human biology – task and objects. General parasitology. Parasites and parasitism.	2	
2.	Nucleic acids. Replication.	2	
3.	Transcription.	2	
4.	Translation.	2	
5.	Regulation.of transcription and translation. Genetic code.	2	
6.	Modern concept of the gene structure and function. Mobile genetic elements. Oncogenes.	2	
7.	Organisation of genetic material in eucariotic cell. Structure of the chromosomes.	2	
8.	Chromosome charting. Mutations.	2	
9.	Genetic disorders.	2	
10.	Genetic and molecular engineering. Recombinant DNA technology.	2	
11.	Genetic engineering. Gene therapy.	2	
12.	Cell-cell interactions. Eukaryotic cell cycle. Apoptosis.	2	
13.	Cell reproduction. Control of cell growth. Tumor growth.	2	
14.	Meiosis and gametogenesis. Fertilization.	2	
15.	Stages of embryonic development. Genetic mechanism of embryogenesis.	2	

TOTAL - 30 hours

SECOND SEMESTER

№	LECTURE COURSES	HOURS	DATE
1.	Immunity. Immune homeostasis. Innate immunity.	2	
2.	Antigens – definition, structure, features. Types of antigens.	2	
3.	Transfusion immunology. Blood group antigens. Alloantigens – blood group antigens. System AB0(H). Genetics of the AB0(H) system. Rhesus system. Principles of haemotransfusion.	2	
4.	Immune system. Antigen processing and presentation. Immunological network interactions.	2	
5.	Cells participating in the immune response - types, characteristic, functions. Immune response.	2	
6.	Kinetics of the immune response. Immunological memory and tolerance. Primary and secondary immune response – phases. Kinetics of the humoral immune response.	2	
7.	Immunoglobulin classes – structure, properties and functions. Complement	2	
8	Genetic control of antibody synthesis.	2	
9.	Major histocompatibility complex. Transplantation immunology.	2	
10.	Tumor immunology.	2	
11.	Mechanisms of immune tolerance. Types of immune tolerance. Adoptive tolerance. Reproductive immunology.	2	
12.	Hypersensitivity. Molecular biology and immunology of HIV.	2	
13.	Population genetics. The Hardy-Weinberg equation. Factors affecting gene frequencies.	2	
14.	Theory of evolution..		
15.	Molecular evolution	2	

TOTAL - 30 hours

PROGRAMME IN HUMAN BIOLOGY

FIRST SEMESTER

№	PRACTICAL COURSES	HOURS	DATE
1.	Microscope. Microscopy rules and techniques.	2	
2.	Subkingdom Protozoa. Subphylum Sarcodina. Phylum Ciliophora.	2	
3.	Subkingdom Protozoa. Subphylum Mastigophora.	2	
4.	Subkingdom Protozoa. Phylum Apicomplexa. Class Sporozoa.	2	
5.	Phylum Platyhelmintes. Class Trematoda \Flukes\. General characteristics of Class Trematoda.	2	
6.	Phylum Platyhelmintes. Class Cestoda.	2	
7.	Phylum Nemathelmintes. Class Nematoda.	2	
8.	Phylum Arthropoda. Class Arachnoidea. General structural features.	2	
9.	Phylum Arthropoda. Class Insecta. General characteristics.	2	
10.	Colocquium in parasitology	1	

TOTAL - 19 hours

SECOND SEMESTER

№	PRACTICAL COURSES	HOURS	DATE
1.	Nucleic acids. DNA replication	2	
2.	Transfer of genetic information. Transcription. Translation. Genetic code.	2	
3.	Organization of the genetic material in the cell.	2	
4.	Karyotype. Pathological karyotype	2	
5.	Genetic disorders.	2	
6.	Cell division. Mitosis. Apoptosis. Tumor biology. *Coloquium in molecular biology*	2	
7.	Sexual reproduction. Meiosis. Gametogenesis. Fertilization.	2	
8	Immunity. Antigens. Blood group antigens.	2	
9.	Immune system. Immunocompetent cells. Types of immune response.	2	
10.	Humoral immune response. Antibodies. Genetics of the immune response. Complement.	2	
11.	Major histocompatibility (MHC) complex. Transplantation.	2	
12.	Immunological tolerance. Tumoral immunity. Hypersensitivity reactions.	2	
13.	Population genetics. The Hardy – Weinberg equation.	2	
14.	Coloquium in immunology		

TOTAL - 26 hours

LECTURE COURSE SYLLABUS

LECTURE №1 – 2 hours. Human biology. Basic biological concepts.

Basic of human biology – tasks, definitions.Biology in science system. Biology – a basic theory of medicine.

General parasitology. Parasites and parasitism.

Parasites – hosts interactions. Ecology of parasitism. Natural focal infections. Basic clinical parasitology. Prevention and control.

LECTURE №2 – 2 hours. Nucleic acids. Replication.

Chemical structure of nucleic acids. Double-stranded DNA. RNA – types. DNA replication – elements, stages, replication fork. Circular DNA replication. DNA repair and regulation of replication.

LECTURE №3 – 2 hours. Realization of genetic information. Transcription

Transcription in pro- and eukaryotes. Necessary elements for transcription. RNA - polymerase. Stages of transcription.

LECTURE №4 - 2 hours. Translation.

Protein synthesis program: elements, stages. Ribosomal structure. Role of tRNA. Termination of translation. The effect of antibiotics on translation.

LECTURE №5 – 2 hours. Regulation of transcription and translation. Genetic code. Gene structure and function. Mobile genetic elements.

Regulation of transcription and translation. The main dogma of transfer of genetic information. Genetic code and decoding the genetic code. Decoding the genetic code.

LECTURE №6 – 2 hours. Contemporary notion of the gene. Classes of mobile genetic elements – IS and transposones. Oncogenes.

Contemporary notion of the gene – definition, types. Mobile genetic elements – definition, types, functions. Oncogenes - definition, types, activation

LECTURE №7 - 2 hours. Organization of the genetic material. Chromosome structure and function.

Nucleosome model. Levels of organization of the genetic material. X chromosome inactivation.

LECTURE №8 – 2 hours. Chromosome charting. Karyotype.

Chromosome identification methods. Normal and pathological karyotype – major clinical syndromes. Human chromosomes identification by banding methods.

Nonmendelian inheritance. Basic principles and characteristics

LECTURE №9 – 2 hours. Heredity and variation. Mutations.

Heredity variation. Norm of reaction.

Mutations alter the DNA sequence. Major types of mutations. DNA rearrangements. Mutagenesis hot spots. Chromosomal mutations – structural and numerical. Adaptive phenotype modifications. Achievements and perspectives.

Nonmendelian inheritance

LECTURE №10 - 2 hours. Genetic engineering

Principles of genetic engineering at the level of the population, organism and sell.

LECTURE №11 – 2 hours. Molecular engineering. Gene therapy.

Methods on recombinant DNA technology. Principles of molecular engineering. DNA cloning. Restriction enzymes. Vectors. Recombinant DNA – production, introduction in host cells.Monitoring of gene expression.

Gene therapy for molecular diseases. Achievements and perspectives.

LECTURE №12 – 2 hours. Eukaryotic cell cycle. Control of cell growth. Apoptosis. Regulation.

Cell cycle regulation – checkpoints, cyclins, cdk.

Programmed cell death. Characteristics and mechanisms. Dysregulation and diseases. Apoptosis vs. necrosis.

LECTURE №13 – 2 hours. Cell reproduction. Regulation of cell growth. Tumor growth.

Mitosis. Definitions. Interphase. Mitotic cycle. Regulation of cell cycle.

Tumor growth. Mechanisms of cellular proliferation. Growth factors. Growth inhibition. Tumor growth.

LECTURE №14 – 2 hours. Meiosis and gametogenesis. Fertilization.

Mammalian and human fertilization – basic characteristics. Capacitation. Acrosome reaction. Cortical reaction. Zona reaction. Prenatal diagnosis.

Meiosis – characteristics. Genetic results of meiosis. Gametogenesis – stages. Spermatogenesis vs. oogenesis. The menstrual cycle – hormonal control.

LECTURE №15 – 2 hours. Molecular mechanisms of embryogenesis.

General characteristics - biogenetic law. Embryonic period - stages. Causes and factors of embryonic development. Embryonic induction.

Cellular differentiation. Molecular mechanisms of cell differentiation. Regulation of gene activity during embryogenesis - factors and mechanisms.

LECTURE №16 – 2 hours. Immunity. Immune homeostasis – innate immunity.

Immune homeostasis. Mechanisms of innate immunity.

LECTURE № 17 – 2 hours. Antigens.

Antigens – definition, structure, features. Antigen determinants. Types of antigens.

Epitopes. Haptens.

LECTURE №18– 2 hours. Human alloantigenes.

Alloantigens – blood group antigens. System AB0(H). Genetics of the AB0(H) system. Chemical structure of the A, B and H antigens. Biosynthesis of the H, A and B antigens. Rhesus system. Principles of haemotransfusion.

LECTURE №19 – 2 hours. Immune system.

Primary and secondary immune organs –sitructure and function.

LECTURE № 20 – 2 hours. Cells participating in the immune response. Immune response.

Lymphocytes. T cells – types, functions. TCRs and CDs. B cells – types, functions. Other cells of the immune response. Phagocytes and phagocytosis.

Kinetics of the immune response. Immunological memory and tolerance.

Primary and secondary immune response – phases. Kinetics of the humoral immune response.

LECTURE №21 – 2 hours. Antigen processing and presentation. Immunological network interactions. Cytokines.

Antigen recognition. Processing and presentation of different types of antigens. APC. Antigen receptors on lymphocytes. Cell-mediated immune response. Immunological network. Co-stimulation, secretion of cytokines and expression of cytokine receptors.

LECTURE №22 – 2 hours. Humoral immune response. Immunoglobulin classes. Allotypes and idiotypes

Immunoglobulin classes – structure, properties and functions. Antigenic markers of antibodies – isotype, allotype, idiotype spcificity. Complement – pathways of activation.

LECTURE №23 – 2 hours. Genetic control of antibody synthesis.

Genetic control of antibody synthesis. Gene pools. Somatic recombination. Genetics of immune cell differentiation.

LECTURE №24 – 2 hours. Major histocompatibility complex.

MHC-gene complex. MHC class I and MHC class II antigens – structure, functions. MHC interaction with CDs and TCRs. Antibodies – humoral immune response. Structure – basic structural units and regions. Opsonization and phagocytosis. Antibody-dependent cellular cytotoxicity (ADCC). Complement – pathways of activation.

Transplantation immunology.

Modes of rejection. Transplantation formula. Types of transplantation. Genetic control mechanisms. Host vs. graft reaction. Graft vs. host reaction.

LECTURE №25 – 2 hours. Tumor immunology.

Tumor antigens. Immune response against tumors – mechanisms. Evasion of immune response by tumors. Role of antibodies, NK cells, macrophages and spontaneous cytolytic activation.

LECTURE №26 – 2 hours. Immune tolerance. Reproductive immunology.

Mechanisms of immune tolerance. Types of immune tolerance. Adoptive tolerance. Autoimmunity.

Immunology of reproduction

LECTURE №27 – 2 hours. Hypersensitivity. Molecular biology and immunology of HIV.

Mechanism of hypersensitivity. Types of allergic reactions. Production of IgE antibodies. Activation of mast cells. Clinical symptoms.

General presentation of AIDS. The human immunodeficiency virus (HIV). Retroviruses. HIV genome and life cycle. HIV infection – mode of transmission. Immune response to AIDS. Opportunistic infections and cancer associated with HIV-infection.

LECTURE №28 – 2 hours. Population genetics. The Hardy-Weinberg equation. Factors affecting gene frequencies.

Population genetics – main features and terminology. Matching types. Hardy-Weinberg equation. Mutation, selection, migration, isolation – effects on gene frequency.

LECTURE №29 – 2 hours. Theory of evolution. Molecular evolution.

The concept of evolution. Darwin´s contemporary theory of evolution – microevolution, macroevolution. Types of natural selection. Genetic factors and mechanisms of evolution.

LECTURE №30 – 2 hours. Human evolution

Anthropogenesis. Paleonthologic history of human evolution.

PRACTICAL COURSE SYLLABUS

PRACTICAL №1 – 2 hours. Microscope. Rules for microscopy. Microscopic techniques.

Structure of the microscope. Rules for microscopy: a) dry system; b) oil immersion system. Preparation of temporary and permanent microscopic slides. Observation of a temporary microscopic slide of basal epidermis of a leaf of Tradescantia. Observation of a permanent slide of blood smear with oil immersion.

PRACTICAL №2 – 2 hours. Interspecies relations. Subkingdom Protozoa. Subphylum Sarcodina. Phylum Ciliophora.

Parasites and hosts. Origin of parasitism. Adaptation of the parasite to the host. Parasite-host interactions. Ecology of parasitism. Classification of zooparasites. Subphylum Sarcodina – general characteristic. Genus Entamoeba: Entamoeba histolytica; Entamoeba coli. Genus Balantidium: Balantidium coli. Observation of permanent microscopic slides.

PRACTICAL №3 - 2 hours. Subkingdom Protozoa. Subphylum Mastigophora.

Order Kinetoplastida – general characteristic. Genus Trypanosoma: Trypanosoma gambiense, Trypanosoma rhodiense, Trypanosoma cruzi. Genus Leishmania: Leishmania

donovani, Leishmania tropica. Genus Trichomonas: Trichomonas vaginalis, Trichomonas tenax, Trichomonas hominis. Observation of permanent microscopic slides.

PRACTICAL №4 - 2 hours. Subkingdom Protozoa. Phylum Apicomplexa. Class Sporozoea.

Class Sporozoa – general characteristic. Genus Plasmodium: Plasmodium vivax; Plasmodium malarie; Plasmodium falciparum; Plasmodium ovale. Observation of the ring trophozoite, schizont, merozoites, gametocytes in blood smears (permanent microscopic slides). Toxoplasma gondii.

PRACTICAL №5 – 2 hours. Phylum Platyhelminthes. Class Trematoda (flukes).

Class Trematoda (flukes) – general characteristic. Genus Fasciola – Fasciola hepatica. Genus Dicrocoelium – Dicrocoelium dendriticum. Genus Opistorchis – Opistorchis felineus. Genus Schistosoma – Schistosoma haematobium; Schistosoma japonicum; Schistosoma mansoni. Observation of eggs and adult individuals in permanent microscopic slides.

PRACTICAL № 6 – 2 hours. Phylum Platyhelminthes. Class Cestoda.

Class Cestoda – general characteristic. Genus Diphyllobothrium: Diphyllobothrium latum. Genus Taenia: Taenia saginata; Taenia solium. Genus Echinococcus: Echinococcus granulosus. Genus Hymenolepis: Hymenolepis nana. Observation of eggs of Taenia sp. and embryonal capsules of Echinococcus granulosus in permanent microscopic slides.

PRACTICAL №7 – 2 hours Phylum Nemathelminthes. Class Nematoda.

Class Nematoda – general characteristic. Genus Ascaris: Ascaris lumbricoides. Genus Enterobius: Enterobius vermicularis. Genus Trichuris: Trichuris trichiura. Genus Trichinella: Trichinella spiralis. Genus Ancylostoma: Ancylostoma duodenale. Genus Strongyloides: Strongyloides stercoralis. Genus Dracunculus: Dracunculus medinensis. Genus Wuchereria: Wuchereria bankrofti. Larva migra visceralis. Toxocara canis. Toxocara cati. Observation of eggs in permanent microscopic slides.

PRACTICAL №8 – 2 hours. Phylum Arthropoda. Class Arachnoidea.

Phylum Arthropoda – general characteristic, distribution, classification, medical importance. Class Arachnoidea – general characteristic. Order Scorpiones. Order Araneida (spiders). Order Acarina – кmorphology, life cycle, medical significance. Parasitic tacks: family Ixoidae; family Argasidae. Parasitic mites: family Sarcoptidae. Sarcoptes scabiei. Observation of tick capitulum, tick eggs and whole Sarcoptes scabiei individual in permanent microscopic slides.

PRACTICAL №9 – 2 hours. Phylum Arthropoda. Class Insecta.

General characteristics of class Insecta. Order Anoplura: Pediculus capitis; Pediculus hominis; Phthirius pupis. Order Aphaniptera: Pulex irritans. Order Heteroptera: Cimex lectularius. Order Diptera: genus Culex; genus Anopheles; genus Phlebotomus. Phlebotomus

papatasii. Comparison of eggs, maggots, pupae, wings and positions of imagoes between malarial and non-malarial mosquitoes. Observation of imaginal forms.

PRACTICAL №10 – COLLOQUIUM IN PARASITOLOGY.

RACTICAL №11 - 2 hours. Nucleic acids. DNA replication.

Theoretical background: DNA structure; RNA structure; mitochondrial DNA; DNA replication; DNA repair mechanisms. Schematic representations of: a) DNA structure; b) replication of linear DNA molecules; c) replication of circular DNA molecules.

PRACTICAL №12 - 2 hours. Transfer of genetic information. Transcription. Translation. Genetic code.

Theoretical background: transfer of genetic information; transcription – general characteristics, necessary elements, mechanism; transcription of prokaryotic and eukaryotic genes; the genetic code – characteristics; primary transcript maturation. Schematic representation of: a) the central dogma of genetic transfer; b) structure of a prokaryotic gene; c) structure of an eukaryotic gene.

PRACTICAL №13 - 2 hours. Organization of the genetic material in the cell.

Theoretical background: structure of eukaryotic chromosomes; submicroscopic structure - levels of DNA packaging; microscopic structure – structural elements, types of chromosomes; eu- and heterochromatin; epigenetic control of gene expression – X chromosome inactivation, genomic imprinting; polythene and lampbrush chromosomes; linear differentiation and banding patterns of human chromosomes;

PRACTICAL №14 - 2 hours. Karyotype. Pathological karyotype.

Theoretical background: karyotype analysis; structural and numerical chromosomal mutations; human karyotype pathology. Microscopic observation of polythene chromosomes. Schematic representation of: a) types of chromosomes according to the position of the centromere; b) Barr body in epithelial cells from buccal mucosa; c) Barr body in neutrophils. Comparative table listing the main features of different pathological karyotypes: Down syndrome, Patau syndrome, Edwards syndrome etc.

PRACTICAL №15 – 2 hours. Genetic disorders.

Theoretical background: Methods of genetic analysis a) cytogenetic method - principle b) polymerase chain reaction (PCR) - generally c) Southern blot - principle and application. Schematic representation of a) Main types of human's inheritance; b) Chromosomal disorders; Molecular diseases - schemes: a) hemoglobinopathies b) inherited diseases of metabolism c) pharmacogenetic disorders; d) inherited immunodeficiency diseases.

PRACTICAL №16 - 2 hours. Cell biology. Cell division. Mitosis. Apoptosis. Tumor biology.

Theoretical background: cell division: interphase, phases of mitosis, cytokinesis; amitosis – definition and characteristics; asexual reproduction of organisms; apoptosis – definition and characteristics; tumor biology – oncogenes and tumor-suppressor genes, mechanisms of tumor growth, characteristics of tumor cells. Microscopic observation of: a) mitosis in cells from Allium cepa; b) embryology of fish, animal mitosis; c) moulding in yeast. Schematic representation of the differences between apoptosis and necrosis. Comparative table listing the main features of apoptosis and necrosis.

COLLOQUIUM IN MOLECULAR BIOLOGY

PRACTICAL №17 - 2 hours. Sexual reproduction. Meiosis. Gametogenesis. Fertilization.

Theoretical background: meiosis; gametogenesis – oogenesis and spermatogenesis; fertilization; biological importance of sexual reproduction. Schematic representation of crossing-over. Microscopic observation of: a) meiosis in Lilium; b) rabbit ovary – follicles in various stages; c) testis – spermatogenesis; d) human spermatozoa. Comparative table listing the main features of oogenesis and spermatogenesis.

PRACTICAL №18 - 2 hours. Immunity. Antigens. Blood group antigens.

Theoretical background: immunological homeostasis; innate and adaptive immunity; antigens – types and characteristics; human alloantigens – ABO(H) and Rhesus systems; immune system – central and peripheral lymphoid organs. Agglutination reaction. Haemagglutination reaction for blood typing.

PRACTICAL №19 - 2 hours. Immune system. Immunocompetent cells. Types of immune response.

Theoretical background: cells of the immune response; stages in the differentiation of immunocompetent cells; cellular interactions during the immune response; immunological network – cells and cytokines; primary and secondary humoral immune response. Comparative table listing the main features of T- and B-cells. Comparative table listing the differences between different cytokines. Reaction – precipitation in solution (ring-precipitation). Precipitation in agarose gel. Single diffusion and immunoprecipitation. Double diffusion and immunoprecipitation (Oucherlony method). Radial immunodiffusion (Mancini method).

PRACTICAL №20 - 2 hours. Humoral immune response. Antibodies. Complement.

Theoretical background: cellular and humoral immunity; humoral immune response - definition: antibodies – properties and streucture; major immunoglobulin classes; Complement. Immunoelectrophoresis – definition, mechanism and stages, and application. Immunoanalysis on “solid phase” (ELISA method). Comparative table of the major immunoglobulin classes.

PRACTICAL №21 - 2 hours. Genetics of the immune response. Transplantation. Major histocompatibility (MHC) complex.

Theoretical background: gene pools for immunoglobulin light and heavy chains; somatic recombination and allelic exclusion; gene pools for TCR; antibody-class switching; transplantation – types, basic principles and laws of transplantation; graft versus host reaction; genes and antigens od the MHC. Comparative table listing the main features of MCH class I and MHC class II molecules. Immunohistochemical methods for visualization of antigen, antibody or antigen-antibody complexes in tissue sections. MHC typing.

PRACTICAL №22 - 2 hours. Immunological tolerance. Tumoral immunity. Hypersensitivity reactions.

Theoretical background: mechanism of immunological tolerance; tumoral immuniry – tumor-associated antigens (TAAs), defense mechanism of the host against tumor antigens, defense mechanism of tumor cells; hypersensitivity reactions. Methods of molecular immunology: Western blot, flowcytometry (FACS). Comparative table listing the main features of the four different types of hypersensitivity reactions.

PRACTICAL №23 - 2 hours. Population genetics. The Hardy-Weinberg equation. Quantitative traits.

Theoretical background: phenotype, genotype and gene frequency; types of cross-breeding; the Hardy-Weinberg equation – conditions for validity and application. Model of a panmixed population at a given gamete frequency.

COLLOQIUM IN IMMUNOLOGY

SYLLABUS IN HUMAN BIOLOGY

1. Subject and tasks of human biology. Interactions with other basic sciences and relation to medical theory and practice.
2. Chemical structure and molecular organization of living nature. Water, mineral salts, carbohydrates, lipids, proteins.
3. Nucleic acids. DNA - localization, structure, the double helix model, Chargaff's rules, conformations.
4. Nucleic acids. DNA – linear and circular, DNA functions. mtDNA – characteristics, functions.
5. Nucleic acids. RNAs – structure and types, functions, differences between RNAs and between RNA and DNA.
6. Replication of DNA. Necessary elements and mechanism. Replication of linear DNA molecules. Fidelity of replication. DNA repair.
7. Replication of circular DNA molecules. Differences in the replication in prokaryotes and in eukaryotes.
8. Transcription. Necessary elements, stages and mechanism. Reverse transcription.
9. Transcription in prokaryotes and in eukaryotes – comparison. Processing and splicing. Inhibition of transcription.
10. Translation. Necessary elements, stages and mechanism. Posttranslational modifications. Inhibition of translation.
11. DNA sequence organization and regulation.

12. Transfer of genetic information. The Central dogma. The genetic code-characteristics. Effect of mutations on the genetic code. Control of gene expression.
13. DNA recombinant biotechnology. Clinical applications.
14. Molecular diagnostics – DNA analysis: Southern blot, PCR, DNA sequencing, allele-specific oligonucleotide analysis, DNA electrophoresis.
15. Gene therapy – vectors, principles and ethical considerations.
16. Gene therapy – therapeutic strategies and clinical application.
17. Genetic linkage. Gene mapping. Genetic heterogeneity. The human genome project.
18. Mutations – characteristics and types; mutagenic factors. Gene rearrangements and point mutations. Transcriptional and translational mutations.
19. RNA mutations. Dynamic mutations. Dominant negative mutations. Ethnic distribution of mutations.
20. Genetic engineering at the level of the population and the organism – hybridization, artificial insemination, pre- and postzytogic selection, in vitro fertilization.
21. Genetic engineering at the level of the cell – cellular hybridization, fusion of embryos (hymeras), transplantation of somatic cell nuclei into eggs, animal cloning.
22. Molecular engineering. Recombinant DNA technologies, vector systems, transfer of foreign genes into somatic cells.
23. Submicroscopic structure of chromosomes. Chromatin, levels of organization. Euchromatin and heterochromatin
24. Microscopic structure of chromosomes. Chromosome types and analysis.
25. Chromosome classification. The normal human karyotype and its evolution.
26. Epigenetic control of gene expression. X-chromosome inactivation. Genomic imprinting.
27. Chromosomal and genomic mutations – types. Numerical alterations. Trisomy.
28. Numerical alterations. Monosmy, mosaic aneuploidy, uniparental disomy, polyploidy.
29. Structural alterations – deletions, duplications, isochromosomes.
30. Structural alterations – inversions, translocations, fragile X.
31. Prenatal diagnosis – diagnostic techniques, genetic counseling.
32. The eukaryotic cell cycle. Cell division – mitosis and amitosis. Stages of mitosis – characteristics. Cell cycle regulation – cyclins and cdk.
33. Apoptosis. Characteristics – apoptosis vs necrosis. Genetic control, mechanisms, detection.
34. Biology and genetics of cancer. Malignancy as a genotype - tumor-suppressor genes and oncogenes.
35. Meiosis. Stages of meiosis – characteristics. Differences between mitosis and meiosis.
36. Gametogenesis. Spermatogenesis. Differences with oogenesis.
37. Gametogenesis. Ovogenesis. Menstrual cycle and pregnancy.
38. Fertilization. Stages of human embryonic development.
39. Developmental mechanisms – determination, differentiation. Establishing multicellularity. Fates of embryonic germ layers.
40. Innate and acquired immunity. Characteristics of the immune response. Clonal selection theory.
41. Humoral and cellular immunity. Characteristics and mechanisms.
42. Natural (innate) immunity – mechanisms.
43. Acquired immunity. Circulation of lymphocytes. Fate of the antigen.
44. The immune system. Central and peripheral lymphoid organs.
45. Antigens – characteristics, classes. Haptens. Crossreactivity.
46. Human alloantigens – blood group antigens ABO(H), Se and Rhesus.
47. Cells of the immune response. B cells – characteristics and functions.

48. Cells of the immune response. T cells – characteristics and functions.
49. Cells of the immune response. APC, NK – characteristics and functions.
50. Cellular cooperation in the immune response. Activation of T and B cells.
51. T-independent responses. Immunological network interactions. Cytokines.
52. Kinetics of the immune response. Primary and secondary immune response. Immunological memory.
53. The Complement system – characteristics and functions. Classical, alternative and lectin pathways.
54. Antibodies – structure and function; types and characteristics.
55. Immunoglobulin classes – types and characteristics. Allotypes and idiotypes.
56. Biological properties of immunoglobulin classes.
57. Genetic control of antibody synthesis. Immunoglobulin gene structure, somatic recombination, allelic exclusion.
58. Immunoglobulin class switch. Generation of antibody diversity.
59. MHC – complex. Genes and antigens – structure and function. MHC-associated diseases.
60. MHC restriction. Activation of Tc cells.
61. Transplantation immunology. Types and lows of transplantation. Immune response in graft rejection. Graft versus host reaction.
62. Tumor immunology. Types of tumor antigens. Tumor escape mechanisms.
63. Tumor immunology. Immune response to tumors. Immunodiagnostics and immunotherapy.
64. AIDS. HIV characteristics. Mechanisms of HIV infection. Diagnosis, therapy and vaccination.
65. Hypersensitivity – general characteristics. Type I reactions.
66. Hypersensitivity. Type II, III and IV reactions.
67. Self tolerance. Control of the immune response to foreign antigens. Role of APC, B and T cells.
68. Mechanisms of acquired immune tolerance.
69. Antigen-antibody reactions. Agglutination, precipitation, immunodiffusion, immuno-electrophoresis, Western blotting, direct binding immunoassays - principles and application.
70. Antigen-antibody reactions. ELISA, immunofluorescence, flowcytometry, monoclonal antibodies.
71. Population genetics – major terms and principles. The Hardy-Weinberg equation and its application.
72. Factors affecting gene frequencies. Nonmendelian characters.
73. Theory of evolution. Natural selection. Species – general characteristics. Molecular evolution.
74. Parasites and parasitism. Parasite-host interactions. Origin of parasitism.
75. Type Protozoa. Class Sarcodina. *E. histolytica, E. coli, E. gingivalis*.
76. Type Protozoa. Class Infusoria. *B. coli*. Class Flagellata. *G. lamblia*.
77. Type Protozoa. Class Flagellata. *T. vaginalis, T. hominis, T. tenax*.
78. Type Protozoa. Class Flagellata. *T. gambienze.* Tsetse Flies.
79. Type Protozoa. Class Flagellata. *T. rhodesiense. T. cruzi.*
80. Type Protozoa. Class Flagellata. *L. donovani.* Sandfies.
81. Type Protozoa. Class Flagellata. *L. tropica.* Type Protozoa. Class Sporozoa. Genus Plasmodium – general characteristics.
82. Type Protozoa. Class Sporozoa. Genus Plasmodium – schizogony.
83. Type Protozoa. Class Sporozoa. Genus Plasmodium – sporogony,

84. Type Protozoa. Class Sporozoa. Genus Plasmodium – pathogenesis, clinics, diagnostics.
85. Type Protozoa. Class Sporozoa. *T. gondii*.
86. Type Plathelmintes. Class Cestoidea. *D. latum*.
87. Type Plathelmintes. Class Cestoidea. *T. solium, T. saginata*.
88. Type Plathelmintes. Class Cestoidea. *E. granulosus*.
89. Type Plathelmintes. Class. Trematoda. *O. felineus, F. hepatica*.
90. Type Plathelmintes. *S. haematobium, S. japonicum, S. mansoni*.
91. Type Nemathelmintes. Class Nematoda. *T. spiralis.*
92. Type Nemathelmintes. Class Nematoda. *A. lumbricoides*.
93. Type Nemathelmintes. Class Nematoda. *A. duodenale*.
94. Type Nemathelmintes. Class Nematoda. *E. vermicularis, T. trichiurus.*
95. Type Nemathelmintes. Class Nematoda. *W. bancrofti. Larva migrans*.
96. Type Nemathelmintes. Class Nematoda. *D. medinensis*.
97. Type Arthropoda. Class Arthropoda. Class Arachnoidea: Order Araneina (spiders), Order Scorpiones.
98. Type Arthropoda. Class Arthropoda. Order Acarina – general characteristics. *S. scabiei*. Parasitic mites.
99. Type Arthropoda. Class Insecta. Order Anoplura. Sucking lice – *P. capitis, P. vestimenti, Pht. pubis.*
100. Type Arthropoda. Class Insecta. Fleas – *P. irritans*. Bugs – *C. lectularius*.
101. Type Arthropoda. Class Insecta. Flies and mosquitoes.

Recommended literature:

1. Molecular Biology of the Cell. 4th edition. Alberts Br., Al. Johnson, J. Lewis, M. Raff, K. Roberts, P. Walter. Garland Science, New York. 2002.
2. Molecular Biology. D. Clark. Elsevier. 2005.
3. Cell and Molecular Biology. Concepts and Experients. Third edition. Gerald Karp
4. Basic and Clinical Immunology, Ed Daniel Stites, Abba Terr, Tristran Parlsrow. VIII edition.
5. Medical Immunology, Tristan Parslow, Daniel Stites, Abba Terr, John Imboden. 2005.
6. Immunobiology. The immune system in health and disease. V-th edition. Ed Janeway Jr. Garland Publishing. 2001.
7. BIOS Instant Notes Immunology, Immunology, Third Edition, Peter Lydyard, Alex Whelan, Michael Fanger, Garland Science, ISBN: 978-0-415-60753-72011, 2011
8. Manual in Medical Biology. Selected and adapted by M. Kazakova, V. Sarafian. 2008.
9. Manual in Parasitology. Selected and adapted by M. Kazakova, A. Milchev, V. Sarafian. 2008.

MEDICAL UNIVERSITY OF PLOVDIV

FACULTY OF PHARMACY

PROGRAMME

IN

BIOORGANIC CHEMISTRY

(Course in English)

Accepted by the Departmental Council on 4 July 2012

Approved by the Faculty Board on 16 July 2012

MEDICAL UNIVERSITY-PLOVDIV

FACULTY OF PHARMACY

Name of the course
„Bioorganic chemistry**”**

Type of course according to the Uniform State Requirements
Mandatory

Level of education
Master's degree **/MS/**

Forms of education:
Lecture course, laboratory classes, self-study

Duration of the course:
One semester

Auditorium classes:
Lectures 45 hrs, laboratory classes 45 hrs

Technical equipment applied in the training:
Multimedia presentations, UV-VIS spectrophotometer, HPLC system, GC system, other tools and technical devices for demonstration of the application of modern methods of quantitative chemical analysis in medicine, practical classes in chemistry

Control and evaluation:
Ongoing evaluation –tests, oral examinations, writing papers based on the studied topics.
Final evaluation – examination

Formation of the final grade The current average grade for the semester is formed based on the tests and papers

Aspects in the formation of the final grade:
Participation in discussions, tests and evaluation of the written papers

Term exam:
Entrance test, written and oral examination

State final certification examination
No
Lecturer:
Professors and associated professors of the Department of Chemistry and Biochemistry

Department:
Chemistry and Biochemistry

COURSE DESCRIPTION

The course takes place in the first year and lasts one semester. The major objective of the course is to prepare the students for subjects studied in the following years of tuition such as biochemistry, pharmacology, clinical medicine and physiology. During the course of training modern means of equipment are used.

COURSE OBJECTIVE

Master the basic concepts related to the chemical characteristics of metabolic processes in the body including: buffers, enzymes, biological oxidation, chemical aspects of carbohydrate, amino acid and lipid metabolism; basic types of heterocyclic compounds and biologically active derivatives. Introduction to instruments for the analysis of biological objects.

OBLIGATORY COMPETENCIES

At the end of course students must have the following knowledge and skills:

- To understand the meaning and content of such concepts as: concentration of solutions, pH and its definition, and the meaning and effect of buffer systems in the human body.
- To be acquainted with the classification of enzymes, their structure and action.
- To know the nature of redox processes in the body (biological oxidation) and the basic principles of biological metabolism
- To have a basic knowledge of high energy compounds and their place in the metabolism of substances in the human body
- To have a basic knowledge of carbohydrate, amino acid and lipid metabolism
- To have an understanding of basic types of heterocyclic compounds and mostly their biologically active derivatives: enzymes, vitamins and hormones.
- To be acquainted with the analytical equipment used during the practical classes and the possibilities it provides for studying biological objects.

CURRICULUM

Class	Examination	Auditorium hours			Hours per week						
	semester	Total	Lectures	Laboratory classes	I	II	III	IV	V	VI	X
Bioorganic chemistry	I	90	45	45	3/3						

LECTURE COURSE IN BIOORGANIC CHEMISTRY FOR STUDENTS IN MEDICINE

I year, I semester

№	TOPIC	HOURS	DATE
1.	**Bioorganic chemistry – introduction. Self-ionization of water. The pH scale. Buffers. Buffers in the human body**	**3**	
2.	**Solutions. Colligative properties of the solutions. Acids and basis**	**3**	
3.	**Colloids. Chemical kinetics. Activation energy diagram. Arrhenius Equation**	**3**	
4.	**Catalysis. Biocatalysis. Chemical equilibrium**	**3**	
5.	**Oxidation-reduction reactions, biological oxidation. Chemical thermodynamics. Bioenergetics**	**3**	
6.	**Coordination compounds. Chelates**	**3**	

7.	**Hydroxyl derivatives of hydrocarbons - alcohols and phenols**	**3**	
8.	**Carbonyl compounds**	**3**	
9.	**Carboxylic acids. Aliphatic and aromatic mono carboxylic acids. Dicarboxylic acids. Hydroxy- and keto acids.**	**3**	
10.	**Amines – chemical properties. Biogenic amines. Alpha amino acids: physical and chemical properties. Chemical aspects of amino acid metabolism.**	**3**	
11.	**Peptides. Proteins**	**3**	
12.	**Carbohydrates –chemical properties. Chemical aspects of carbohydrate metabolism**	**3**	
13.	**Lipids. Basic concepts of lipid metabolism**	**3**	
14.	**Five membered heterocyclic compounds – furan, thiophene, pyrrole, pyrazole, imidazole, thiazole and their biologically active derivatives.**	**3**	
15.	**Heterocyclic compounds with six-membered ring and fused rings. Carbonic acid**	**3**	

Total: 45 hrs

PRACTICAL CLASSES PROGRAMME

I year, I semester

№	TOPIC	HOURS	DATE
1.	Concentration of solutions. Preparation of solutions	3	
2.	Coordination compounds. Coordination chemistry of some biological metal ions	3	
3.	Solutions of electrolytes. Acids and bases according to the Theory of Bronsted-Lowry. Ionic product of water. pH and methods for its measurement. Buffers	3	
4.	Oxidation-reduction reactions. Biological oxidation and reduction. Redox potentials	3	
5.	Fundamentals of UV-visible spectroscopy	3	
6.	Isomerism of organic compounds. Alcohols and phenols – essential properties and biological activity	3	
7.	Carbonyl compounds. Ketone bodies in human pathology	3	
8.	Carboxylic acids and Hydroxycarboxylic acids. Quantification of residual salicylic acid in aspirin tablets	3	
9.	Amines. Derivatives of carbonic acid: urea, creatine	3	
10.	Amino acids and proteins. Dialysis	3	

11.	**Biocatalysis. Enzymatic hydrolysis of proteins**	**3**	
12.	**Carbohydrates – stereochemistry and properties of mono-, di-, and polysaccharides**	**3**	
13.	**Heterosyclic compounds. Low molecular weight bioregulators: vitamins and alkaloids**	**3**	
14.	**Principle of chromatography – column, paper, thin-layer and high-performance liquid chromatography. Application to biomedical science**	**3**	
15.	**Solving problems on bioorganic chemistry**	**3**	

Total : 45 hrs

LECTURES – THESES

LECTURE 1 – 3 hrs

BIOORGANIC CHEMISTRY –INTRODUCTION

1. Bioorganic chemistry –introduction.
2. Water – structure, properties and functions. Self-ionization of water. Ionic product of water.
3. The pH scale. Physical sense of pH.
4. Buffers. Calculation of the pH of the buffers. Buffers in the human body

LECTURE 2 – 3 hrs

SOLUTIONS. COLLIGATIVE PROPERTIES OF THE SOLUTIONS. ACIDS AND BASIS

1. Solutions: the nature of solutions; types of solvents and solutes. Types of concentration – percent concentration, molarity, normality.
2. Colligative properties of the solutions. Vapor pressure – Raoult's law. Principals of the diffusion, osmosis and dialysis.
3. Brønsted-Lowry theory of acids and bases. Acid ionization constant. Base ionization constant. Lewis theory of acids and bases.

LECTURE 3 – 3 hrs

COLLOIDS. CHEMICAL KINETICS. ACTIVATION ENERGY DIAGRAM. ARRHENIUS EQUATION COLLOIDS.

1. Classification of colloidal systems. Properties of colloids. Solutions of high molecular weight compounds – general characteristic.
2. Chemical kinetics – factors affecting the rate of reaction. Order of reaction - zero, first and pseudo-first order.
3. Activation energy diagram. Arrhenius Equation

LECTURE 4 – 3 hrs

CATALYSIS. BIOCATALYSIS. CHEMICAL EQUILIBRIUM

1. Catalysis – principals and types – homogeneous and heterogeneous; chemical intermediates. Promoters and inhibitors of the catalysis. Catalysts and reaction energy.
2. Biocatalysts: structure of enzymes; rate of enzymatic reaction – Michaelis-Menten constant. Specificity and regulation of enzyme activity
3. Chemical equilibrium - basic conceptions, principle of Le Chatelier's. Factors, influencing on the chemical equilibrium.

LECTURE 5 – 3 hrs

OXIDATION-REDUCTION REACTIONS, BIOLOGICAL OXIDATION. CHEMICAL THERMODYNAMICS. BIOENERGETICS

1. Oxidation-reduction reactions, biological oxidation and reduction, redox potentials. Redox pair in biological oxidation and reduction. Respiratory chain.
2. Chemical thermodynamics. The first and second laws of thermodynamics.
3. Bioenergetics – principals. Energy, enthalpy, entropy, free energy.
4. Endergonic and exergonic reactions. Compounds with high-energy bonds – ATP, creatine phosphate, phosphoenolpyruvate

LECTURE 6 – 3 hrs

COORDINATION COMPOUNDS. CHELATES

1. Coordination compounds – structure and classification. Stability constant of coordination compounds. Biologically active coordination compounds.
2. Chelates – structure. Chelates formed by polyhydroxy alcohols, amino acids, peptides, protoporphyrins (hemoglobin, cytochrome, vitamin B_{12}).

LECTURE 7 – 3 hrs

HYDROXYL DERIVATIVES OF HYDROCARBONS – ALCOHOLS AND PHENOLS

1. Alcohols and phenols – types, isomers and chemical properties.
2. Physical properties, hydrogen bonds.
3. Synthesis of ethanol and production by fermentation. Partial oxidation of alcohols to aldehydes, ketones and carboxylic acids.
4. Phenols – electronic structure, chemical properties, ring reactions.
5. Biological oxidation of alcohols. Thioalcohols, coenzyme A – biological functions.

LECTURE 8 – 3 hrs

CARBONYL COMPOUNDS – ALDEHYDES AND KETONES

1. Aldehydes and ketones – chemical properties.
2. Biologically active quinons – coenzyme Q, vitamin K.
3. Glycerol aldehyde – configuration

LECTURE 9 – 3 hrs

CARBOXYLIC ACIDS. ALIPHATIC AND AROMATIC MONO-CARBOXYLIC ACIDS. DI-CARBOXYLIC ACIDS. HYDROXY- AND KETO ACIDS.

1. Carboxylic acids-classification.
2. Chemical properties of mono-carboxylic acids, pKa.
3. Biological oxidation of long chain carboxylic acids (β-oxidation).
4. Esters of phosphoric acid and esters of nitric acid. ATP-significance in biological metabolism. Phosphoenol pyruvate-significance in biological metabolism.
5. Saturated and unsaturated dicarboxylic acids – oxalic, malonic, glutaric and adipic acids. Fumaric and maleic acid.
6. Hydroxy- and keto acids.

LECTURE 10 – 3 hrs

AMINES – CHEMICAL PROPERTIES. BIOGENIC AMINES. ALPHA AMINO ACIDS: PHYSICAL AND CHEMICAL PROPERTIES. CHEMICAL ASPECTS OF AMINO ACID METABOLISM.

1. Amines – definition and structure and
2. Important chemical properties of amines. Sulfonamides. Biogenic amines.
3. Alpha amino acids – classification. Important physical and chemical properties.
4. Chemical aspects of amino acid metabolism.

LECTURE 11 – 3 hrs

PEPTIDES. PROTEINS

1. Peptides – structure, disulphide bridges.
2. Proteins –primary structure.
3. Enzymes as protein molecules

LECTURE 12 – 3 hrs

CARBOHYDRATES – CHEMICAL PROPERTIES. CARBOHYDRATE METABOLISM – CHEMICAL ASPECTS

1. Carbohydrates. Monosaccharides – structure, configuration, and cyclic forms; examples of monosaccharides.
2. Glycolysis – basic concept.
3. Disaccharides. Polysaccharides. Heteropolysaccharides

LECTURE 13 – 3 hrs

LIPIDS. BASIC PRINCIPLES OF LIPID METABOLISM

1. Lipids – classification. Fatty acids – saturated, nonsaturated.
2. Triacylglycerols. Fats and oils. Chemical aspects of fat burning. Phospholipids. Waxes
3. Lipids – classification. Terpenes and steroids – structure and biosynthesis. Lipid soluble vitamins.

LECTURE 14 – 3 hrs

HETEROCYCLIC COMPOUNDS WITH FIVE-MEMBERED RINGS – FURAN, THIOPHENE, PYRROLE, PYRAZOLE, IMIDAZOLE, THIAZOLE AND THEIR BIOLOGICALLY ACTIVE DERIVATIVES.

1. Heterocyclic compounds – classification.
2. Five-membered ring heterocyclic compounds with one heteroatom (pyrrole, furan and thiophene) – structure (π-sextet), acid-base and chemical properties.
3. Important biological molecules containing pyrrole ring – heme, hemoglobin, bilirubin, cytochrome, proline, hydroxyproline
4. Heterocyclic compounds with five-membered ring and two heteroatoms (pyrazole, imidazole, and thiazole) – structure and important chemical properties. Reduction of pyrazole.

5. Important biological molecules containing pyrazole, imidazole, and thiazole ring – histidine, antipyrin, pyramidone, analgin.
1. Classification of lipids.

LECTURE 15 – 3 hrs

HETEROCYCLIC COMPOUNDS WITH SIX-MEMBERED RING AND FUSED RINGS. CARBONIC ACID

1. Heterocyclic compounds with six-membered ring and one heteroatom. Pyridine – structure and major chemical properties.
2. Important biological molecules containing pyridine ring – nicotine, nicotinamide
3. Carbonic acid – dissociation, biological importance. Carbonates.
4. Derivatives of carbonic acid – urea, barbituric acid, guanidine, creatine, and arginine
5. Biomolecules containing pyrimidine ring – nucleotides, vitamins, drugs.
6. Purine and its derivatives. Uric acid. Nucleic acids

LABORATORY CLASSES –THESES

LABORATORY CLASS 1 -3 hrs

CONCENTRATION OF SOLUTIONS. PREPARATION OF SOLUTIONS

1. Ways of expressing concentration
2. Solving problems concerning solution concentration
3. Preparation of solutions

LABORATORY CLASS 2 – 3 hrs

COORDINATION COMPOUNDS. COORDINATION CHEMISTRY OF SOME BIOLOGICAL METAL IONS

1. Structure of coordination compounds
2. Stability of coordination compounds
3. Chelates. Structure and functions of biologically significant chelates
4. Preparation of coordination compounds

LABORATORY CLASS 3 – 3 hrs

SOLUTIONS OF ELECTROLYTES. ACIDS AND BASES ACCORDING TO THE THEORY OF BRONSTED-LOWRY. IONIC PRODUCT OF WATER. PH AND METHODS FOR ITS MEASUREMENT. BUFFERS

1. Discussion on the concepts “acid” and “base” according to existing theories. Buffers
2. Demonstrating different ways of measuring pH
3. Testing the action of a given buffer solution

LABORATORY CLASS 4 – 3 hrs

OXIDATION-REDUCTION REACTIONS. BIOLOGICAL OXIDATION AND REDUCTION. REDOX POTENTIALS

1. Discussion on principles of redox reactions, types of redox reactions
2. Biological oxidation
3. Experiments demonstrating redox processes with inorganic and organic compounds

LABORATORY CLASS 5 – 3 hrs

FUNDAMENTALS OF UV-visible spectrophotometry

1. Discussion on Fundamentals of UV-visible spectrophotometry
2. Demonstration of cytochrome c redox cycle

LABORATORY CLASS 6 – 3 hrs

ISOMERISM OF ORGANIC COMPOUNDS. ALCOHOLS AND PHENOLS – ESSENTIAL PROPERTIES AND BIOLOGICAL ACTIVITY

1. Isomerism – definition, types, examples
2. Experiments demonstrating the essential chemical properties of alcohols and phenols
3. Qualitative reactions for testing alcohols and phenols.

LABORATORY CLASS 7 – 3 hrs

CARBONYL COMPOUNDS. KETONE BODIES IN HUMAN PATHOLOGY

1. Experiments demonstrating nucleophilic and redox properties of aldehydes and ketones.
2. Some tests for detection of aldehydes and ketones.
3. Tests for ketone bodies in biological samples

LABORATORY CLASS 8 – 3 hrs

CARBOXYLIC AND HYDROXY CARBOXYLIC ACIDS. QUANTIFICATION OF RESIDUAL SALICYLIC ACID IN ASPIRIN TABLETS

1. Comparing the degree of ionization of carboxylic acids in water solution; pH of solutions of some derivatives of carboxylic acids
2. Demonstration of some chemical properties of carboxylic acids
3. Determination of the concentration of salicylic acid in aspirin tablets.

LABORATORY CLASS 9 – 3 hrs

AMINES. DERIVATIVES OF CARBONIC ACID: UREA, CREATINE

1. Some important chemical properties of amines and urea
2. Creatine function.

LABORATORY CLASS 10 – 3 hrs

AMINO ACIDS AND PROTEINS. DIALYSIS

1. Determination of pH of water solution of amino acids
2. Qualitative reactions for testing amino acids and proteins in a solution
3. Dialysis

LABORATORY CLASS 11 – 3 hrs

BIOCATALYSIS. ENZYMATIC HYDROLYSIS OF PROTEINS

1. Discussion on kinetics of enzyme reaction
2. Determination of proteolytic enzyme activity

LABORATORY CLASS 12 – 3 hrs

CARBOHYDRATES – STEREOCHEMISTRY AND PROPERTIES OF MONO-, DI-, AND POLYSACCHARIDES

1. Stereochemistry of carbohydrates
2. Chemical properties of carbohydrates
3. Some tests for monosaccharides and polysaccharides

LABORATORY CLASS 13 – 3 hrs

HETEROSYCLIC COMPOUNDS. LOW MOLECULAR WEIGHT BIOREGULATORS: VITAMINS AND ALKALOIDS

1. Discussion on heterocyclic compounds – structure and biological significance
2. Reactions for testing some vitamins, alkaloids and medicines

LABORATORY CLASS 14 – 3 hrs

PRINCIPLE OF CHROMATOGRAPHY – COLUMN, PAPER, THIN-LAYER AND HIGH-PERFORMANCE LIQUID CHROMATOGRAPHY. APPLICATION TO BIOMEDICAL SCIENCE

1. Principles of chromatography
2. Identification of medicines and alkaloids by means of TLC

LABORATORY CLASS 15 – 3 hrs

SOLVING PROBLEMS ON BIOORGANIC CHEMISTRY

RECOMMENDED TEXTBOOKS

1. Ouellette R J, Introduction to General, Organic and Biological Chemistry, Prentice-Hall 1997 and new editions

TOPICS FOR PAPERS

1. Enzymes – types and action
2. Lipids – types. Biologically active substances with lipid structure
3. Biologically active substances derived from heterocyclic compounds

Bioorganic chemistry syllabus for first year students of medicine

1. Water – structure, properties and functions. Self-ionization of water. The pH scale. Physical sense of pH. Buffers. Calculation of the pH of the buffers. Buffers in the human body
2. Solutions: the nature of solutions; types of solvents and solutes. Types of concentration – percent concentration, molarity, normality.
3. Brønsted-Lowry theory of acids and bases. Acid ionization constant. Base ionization constant. Lewis theory of acids and bases.
4. Colligative properties of the solutions. Vapor pressure – Raoult's law. Principals of the diffusion, osmosis and dialysis.
5. Colloids. Classification of colloidal systems. Properties of colloids. Solutions of high molecular weight compounds – general characteristic.
6. Chemical kinetics – factors affecting the rate of reaction. Order of reaction - zero, first and pseudo-first order. Activation energy diagram. Arrhenius Equation -
7. Catalysis – principals and types – homogeneous and heterogeneous; chemical intermediates. Promoters and inhibitors of the catalysis. Catalysts and reaction energy. Biocatalysts: structure of enzymes; rate of enzymatic reaction – Michaelis-Menten constant. Specificity and regulation of enzyme activity Chemical equilibrium - basic conceptions, principle of Le Chatelier's. Factors, influencing on the chemical equilibrium.
8. Oxidation-reduction reactions, biological oxidation and reduction, redox potentials. Redox pair in biological oxidation and reduction. Respiratory chain.
9. Chemical thermodynamics. The first and second laws of thermodynamics. Bioenergetics – principals. Energy, enthalpy, entropy, free energy. Endergonic and exergonic reactions. Compounds with high-energy bonds – ATP, creatine phosphate, phosphoenolpyruvate
10. Coordination compounds – structure and classification. Stability constant of coordination compounds. Biologically active coordination compounds.
11. Chelates – structure. Chelates formed by polyhydroxy alcohols, amino acids, peptides, protoporphyrins (hemoglobin, cytochrome, vitamin B_{12}).
12. Alcohols and phenols – types, isomers and chemical properties. Physical properties, hydrogen bonds. Synthesis of ethanol and production by fermentation. Partial oxidation of alcohols to aldehydes, ketones and carboxylic acids. Phenols – electronic

structure, chemical properties, ring reactions. Biological oxidation of alcohols. Thioalcohols, coenzyme A – biological functions

13. Aldehydes and ketones – chemical properties. Biologically active quinons – coenzyme Q, vitamin K. Glycerol aldehyde – configuration
14. Carboxylic acids – classification. Chemical reactions of saturated and aromatic carboxylic acids. Esters of phosphoric and nitric acids – biological significance.
15. Saturated and unsaturated dicarboxylic acids – oxalic, malonic, glutaric and adipic acids. Fumaric and maleic acid. Hydroxy- and keto acids.
16. Amines – definition, structure and important chemical properties. Sulfonamides. Biogenic amines.
17. Alpha amino acids – classification. Important physical and chemical properties. Chemical aspects of amino acid metabolism.
18. Peptides – structure, disulphide bridges. Proteins –primary structure. Enzymes as protein molecules.
19. Carbohydrates. Monosaccharides – structure, configuration, and cyclic forms; examples of monosaccharides. Glycolysis – basic concept.
20. Disaccharides. Polysaccharides. Heteropolysaccharides.
21. Lipids – classification. Fatty acids – saturated, nonsaturated. Triacylglycerols. Fats and oils. Chemical aspects of fat burning. Phospholipids. Waxes.
22. Lipids – classification. Terpenes and steroids – structure and biosynthesis. Lipid soluble vitamins.
23. Heterocyclic compounds – classification. Five-membered ring heterocyclic compounds with one heteroatom (pyrrole, furan and thiophene) – structure (π-sextet), acid-base and chemical properties. Important biological molecules containing pyrrole ring – heme, hemoglobin, bilirubin, cytochrome, proline, hydroxyproline.
24. Heterocyclic compounds with five-membered ring and two heteroatoms (pyrazole, imidazole, and thiazole) – structure and important chemical properties. Reduction of pyrazole. Important biological molecules containing pyrazole, imidazole, and thiazole ring – histidine, antipyrin, pyramidone, analgin.
25. Heterocyclic compounds with six-membered ring and one heteroatom. Pyridine – structure and major chemical properties. Important biological molecules containing pyridine ring – nicotine, nicotinamide.
26. Carbonic acid – dissociation, biological importance. Carbonates. Derivatives of carbonic acid – urea, barbituric acid, guanidine, creatine, and arginine.
27. Biomolecules containing pyrimidine ring – nucleotides, vitamins, drugs. Purine and its derivatives. Uric acid. Nucleic acids.

Questions for self-study

Topic 1

Concentration of solutions. Preparation of solutions

1. Definition of concentration of solutions
2. Ways of expressing solution concentration
   - percent concentration
   - molar concentration, molarity
   - molal concentration
   - osmole, osmolarity
   - normal concentration, normality
   - titer
3. Mixing of solutions
   - cross rule
   - mixing equation

Topic 2

Coordination compounds. Coordination chemistry of some biological metal ions

1. Coordination compounds – definition
2. Types of coordination compounds depending on:
   a) the electrical charge of the complex ion
   б) the type of ligands
3. Double salts. Chelates
4. Stability of coordination compounds, stability constant
5. Coordination compounds and chelates in the human body – biological significance and therapeutical role.

Topic 3

Acids and bases according to the Theory of Bronsted-Lowry. Ionic product of water. pH and methods for its measurement. Buffers

1. Theory of Bronsted-Lowry about acids and bases – principles, examples. Lewis' theory of acids and bases.
2. Ionic product of water. pH and methods for its measurement.
3. Buffers – definition and examples
   a) calculating the pH of buffers (Henderson-Hasselbalch equations)
   b) principles of buffer action when a strong acid/base is added to a buffer solution
   c) buffer capacity
4. Buffers in the human body

Topic 4

Oxidation-reduction processes. Biological oxidation and reduction. Redox potentials.

1. Nature of redox reactions
2. Types of redox processes.
3. Nernst equation. Direction of redox processes.
4. Specific features of biological oxidation and reduction. Respiratory chain

Topic 5

Fundamentals of UV-VIS spectroscopy

Principles of spectroscopy and its application in qualitative measurements

Topic 6

Isomerism of organic compounds. Alcohols and phenols –essential properties and biological activity

1. Isomerism
   a) definition
   b) types of isomerism, examples
2. Alcohols and phenols
   a) definition, classification
   b) structure and chemical properties: acid-base properties, esterification, etherification, oxidation, electrophilic substitution reactions (Es)
   c) alcohols and phenols with biological significance
3. Thioalcohols -coenzyme A

Topic 7

Carbonyl compounds: aldehydes and ketones – structure and reactivity. Biological significance of these substances

1. Carbonyl compounds – definition, types, structure
2. Reactivity of aldehydes and ketones
3. Addition reactions with nucleophiles: interaction with HCN, $NaHSO_3$, H_2O, alcohols.
4. Condensation reactions. Interaction with ammonia and compounds with $-NH_2$ group. Aldol addition.
5. Oxidation of carbonyl compounds
6. Biological significance of carbonyl compounds. Ketone bodies.

Topic 8

Carboxylic and hydroxycarboxylic acids.

1. Structure and properties of carboxylic and hydroxycarboxylic acids
2. Derivatives of hydroxycarboxylic acids with medical significance.

Topic 9

Amines. Derivatives of carbonic acid: urea and creatine

1. Amines – definition, classification, structure.
2. Chemical properties of amines –basicity, interaction with nitrous acid, alkylation reactions, acylation reactions, interaction with carbonyl compounds, deamination.
3. Derivatives of amines with biological significance – aminoalcohols, derivatives of p-aminophenol, derivatives of sulfanilic acid (sulfonamides). Biogenic amines.
4. Carbonic acid and its derivatives: urea, creatine

Topic 10

Amino acids and proteins

1. Amino acids – structure, chemical properties, examples
2. Peptides and proteins – structure and properties

Topic 11
Biocatalysis

1. Enzymes – classification, structure
2. Rate of enzyme catalyzed reactions
3. Specificity and regulation of enzyme action

Topic 12
Carbohydrates – stereochemistry and properties of mono-, di-, and polysaccharides

1. Carbohydrates – definition and classification
2. Monosaccharides – structure and chemical properties. Examples of aldoses and ketoses.
3. Optical isomerism
4. Glycolysis

Topic 13
Heterocyclic compounds. Vitamins and alkaloids

1. Heterocyclic compounds – classification, chemical properties.
2. Vitamins:
   a) definition, sources, biological significance
   b) classification
   c) examples
3. Alkaloids:
   a) overview
   b) general and specific properties
   c) examples containing pyridine-, piperidine-, quinine-, morphine- and purine ring
   d) biological significance

Topic 14
Chromatography

1. Chromatography
   a) principles of the method
   b) column chromatography
   c) thin-layer chromatography

Plovdiv Medical University

Faculty of Medicine

Program

in

Human Physiology

Approved at a meeting of the Department of Human Physiology – 21. 5.2012

Endorsed by the Faculty Board - 2012

Human Physiology

Study course: IInd year.
Semesters: IIIrd and IVth semester.
Examination: after the IVth semester.
Credit hours: 195 hours.
Lecturer: Associate professor Nikolay Petrov Boyadjiev, MD, DSc.

Course Study Plan

Form of instruction	**Credit hours**				**Credits**
	weekly	**IIIrd sem.**	**IVth sem.**	**Total**	
Lectures	2/4	30	45	75	
Practicals	3/4	60	60	120	**19.1**
Total	**5/8 hours**	**90 hours**	**105 hours**	**195 hours**	

Description: Cell physiology. The human body systems. Physiological functions and general principles of their regulation – cybernetic and physiological aspects. Homeostasis. General and specific properties of excitable cells. Synapse types. Chemical synapses. Neuro-reflex regulation of physiological functions. Functional morphology and main physiological properties of the autonomous nervous system. General principals of humoral regulation of physiological functions; physiological effects of the hormones released by the thyroid gland, adrenal glands, pituitary gland and pancreas. Functional morphology of the skeletal and smooth muscles. Blood physiology. The cardiovascular system – physiological characteristics of the working myocardium and the cardiac conduction system; electrical phenomena accompanying cardiac activity; registration and assessment of the ECG; heart sounds; regulation of cardiac activity; arterial pulse; nervous and humoral effects on vascular tone. Regulation of blood pressure. The respiratory system – regulation of respiration; lung volumes and capacities and gas exchange. Functions and regulation of the digestive system. Nutrition and metabolism of proteins, fats, sugars and energy. Excretory functions of the body. Water/electrolyte and acid/base balance. Sensory systems – somatosensory physiology, vision, hearing, smell and taste. Wakefulness and sleep. Higher nervous activity.
Objective: Learning the normal physiological functions of the body and their regulation so as to prepare the students for the clinical courses.

Aims:
1. Study of the normal physiological functions and their parameters.
2. Introduction to regulation of physiological functions.
3. Introduction to the body's capacity to respond to internal and external stimuli while preserving its uniqueness and integrity in achieving goals concerning oneself and one's surroundings.
4. Building a theoretical basis for uncovering pathophysiological processes as well as for the management of physical and drug therapies.
5. Learning the main medical and instrumental methods for evaluation of physiological parameters.
6. Introduction to the basic principles of experimental medicine.

Methods of instruction:
1. Lecture course.
2. Practical exercises.
3. Ongoing assessment tests.

4. Consultations.
5. Participation in experiments conducted in the department.
6. Homework, using textbooks and manuals recommended by the department.

Teaching tools and equipment used: Aspectomat; colour slides; overhead projectors; screens for overhear projectors; DVD-players; video monitors; disks with educational videos; computers; complete multimedia lecture course; the Schiller AT-104 Ergospirometric system; a three-channel ECG recorder (RFT, Germany); a multi-function patient monitor (Hewlett Packard, USA); a special external respiration spirometer ('Flowscreen', Jaeger, Germany); 'Oxymax'- a device for monitoring the metabolism of test animals (Columbus, USA); A Jaeger veloergometer (Germany); operation boards for small animals; a device for controlled breathing of small animals ('Hugo Sachks', Germany); a Leika capillary scope; microscopes; devices for registration of muscle contractions; rheograph; audiometers; colour perimeter; blood pressure measuring devices; compete multimedia lecture course (in Bulgarian and in English); complete multimedia lecture course in English for master programs in medical physics and engineering; seminar manuals for medical students (in Bulgarian and in English).

Assessment and evaluation:
Assessment of progress: Oral examination. Evaluation of each chapter: assessment test; oral exam.
Final evaluation: Assessment test of the final examination. Written exam topic drawn from the syllabus on the day of the final exam. Oral examination. Evaluation of practical skills.
Methods of knowledge assessment: Assessment tests of chapters, including evaluation tests and oral presentation.

Mandatory competencies:
1. Theoretical knowledge. Knowledge and interpretation of:
   - Physical and chemical basis of physiological processes.
   - The human body as a system. Physiological functions and general principles of neural and humoral regulation.
   - Functions of the nervous system – sensory, motor and autonomic nervous system control. Stress and distress. Higher nervous activity.
   - Telecrine and paracrine regulation of homeostasis.
   - Somatic functions. The locomotor (musculoskeletal) system and its regulation.
   - The sensory systems.
   - Functions – locomotor, cardiovascular, digestive, excretory, regulation of body temperature, reproductive systems and blood.
   - Physiological basis of nutrient and energy metabolism and of rational nutrition.
   - Changes in physiological systems during ontogeny and in the course of wakefulness and sleep.
2. Practical skills:
   - Registration of response gradation relative to stimulus strength or frequency.
   - Electroneurogram recording of mixed nerve.
   - Analysis of the reflex arc.
   - Examination of clinically important reflexes.
   - Examination of conditioned reflexes.
   - Determination of blood types ; principles of blood transfusion.
   - Chamber method for RBC and WBC count. Determination of the RBC indices . WBC differential count.
   - Methods for examining the pancreas, the thyroid gland and the adrenal glands – oral glucose tolerance test, Werner's test, radioiodine uptake test and the Thorn test. Hypoglycemic shock in rabbit.
   - Tests for early pregnancy.

- Perimetry. Colour vision test. Audiometry. Bone and air conduction test. Skin sensitivity.
- Measurement of muscle strength. The effect of loading on amplitude and performance.
- Physical examination of the lungs. Measuring pulmonary volumes and capacities with the Flowscreen spirometer.
- Measurement of oxygen consumption and carbon dioxide release at rest.
- Auscultation of heart sounds. Recording and analysis of the ECG. Registration and analysis of the ST-segment.
- Determining the stroke volume (SV) and cardiac output (C.O.) by the Fick method.
- Palpation of the arterial pulse. Arterial pulse evaluation. Sphygmography. Plethysmography. Capillaroscopy.
- Measuring the arterial blood pressure with the Riva-Rocci device by the Korotkoff method.
- The effect of bile on the filtration speed of vegetable oil (cooking oil) and the sedimentation of sulphur powder.
- Methods of determining the basal metabolic rate. Composing a meal plan.
- The effect of ADH on the diuresis of white mice. Calculation of the clearance of inulin (in), paraaminohippuric acid (PAH) and urea.
- Methods for investigating the attention span. Methods for measuring the reasoning abilities and for defining personality types.

LECTURES

Lecture № 1 - 2 acad. hours

Organization of the cell. Physical structure of the cell. Functional systems of the cell. Properties of the cell membrane and junctions between the cells. Intercellular signalization. Transport of substances through the cell membrane.

The human body. Homeostasis. General principles of the homeostatic regulation – regulatory systems and elements of the homeostatic regulatory system. Levels of physiological regulation.

Lecture № 2 - 2 acad. hours

Physiology of the excitatory tissues. Irritability and excitability. General and specific properties of the excitable cells. Membrane potential – ionic basis of the membrane potentials.

Measurement of excitability. Changes in the excitability during excitation. Inhibition. Conduction of the excitation.

Transmission of the excitation (inhibition) from an excitable cell to another. Synapses - types of synapses. Chemical synapses. Transmitters and modulators. Postsynaptic potentials. Summation of the postsynaptic potentials.

Lecture № 3 - 2 acad. hours

Functions of the nervous system – functional morphology of the nervous system. Physiology of the nerve cell. Glial cells. Neuronal circuits and processing of information form group of nerve cells – convergence, divergence, reverberating circuits, inhibition.

Lecture № 4 - 2 acad. hours

Reflex regulation of the physiological functions. Type of reflexes according to the mechanism of formation and the characteristics of the reflex arc.

Nerve centers. Types and properties. Cerebral blood flow. Cerebrospinal fluid.

Lecture № 5 - 2 acad. hours

The autonomic nervous system. General organization of the autonomic nervous system. Autonomic nerve centers, ganglia, transmitters and receptors in the autonomic nervous system.

Effects of sympathetic and parasympathetic stimulation on specific organs. Autonomic reflexes.

Role of the hypothalamus, reticular formation, cerebellum, basal ganglia and cerebral cortex in the control of the autonomic functions. Integration of the central nervous system in the adaptation processes of the body – "alarm" or "stress" response of the sympathetic nervous system.

Lecture № 6 - 2 acad. hours

General principles of the humoral control of the physiologic functions. Telecrinia and paracrinia. Classification, synthesis and mechanism of action of the hormones. Control on the hormone secretion.

Lecture № 7 - 2 acad. hours

Hypothalamic-neurohypophysial system. Neurosecretion. Hormones of the neurohypophysis. Physiologic effects and control of secretion.

Hypothalamo-adenohypophysial system. Hormones of the adenohypophysis. Physiologic effects and control of secretion.

Functional morphology of the thyroid gland. Iodine containing thyroid hormones. Physiologic effects and control of secretion. Hyperthyroidism and hypothyroidism.

Lecture № 8 - 2 acad. hours

Functional morphology of adrenal glands. Hormones of the adrenal medulla. Physiologic effects and control of secretion of adrenaline (epinephrine) and noradrenaline (norepinephrine).

Hormones of adrenal cortex – glucocorticoids. Physiologic effects and control of secretion. Pharmacologic effects of glucocorticoids.

Hormones of adrenal cortex – mineralcorticoids and adrenal androgens. Abnormalities of the adrenocortical secretion.

Lecture № 9 - 2 acad. hours

Physiology of reproduction. Male reproductive system. Spermatogenesis. Male sex hormones (androgens) – types, physiologic effects and control of secretion. Erection and ejaculation.

Physiology of reproduction. Female reproductive system. Ovogenesis. Female sex hormones (estradiol and progesterone) – types, physiologic effects and control of secretion. Regulation of the female monthly rhythm. Pregnancy and lactation. Tests for early pregnancy.

Lecture № 10 - 2 acad. hours

Endocrine functions of the pancreas – type of hormones, physiologic effects and control of secretion. Diseases of the endocrine pancreas.

Calcium and phosphate homeostasis. Parathyroid hormone, calcitonin, vitamin D - physiologic effects and control of secretion. Impairment of the calcium and phosphate homeostasis.

Lecture № 11 - 2 acad. hours

Physiology of skeletal muscles – functional morphology, mechanism and energy of muscle contraction. Types of muscle contractions. Types of muscle fibers. Muscle work and muscle fatigue. Electromyography.

Lecture № 12 - 2 acad. hours

Functional morphology of smooth muscles. Excitation, electrophysiologic characteristics and mechanism of contraction of smooth muscles.

Lecture № 13 - 2 acad. hours

Physiology of respiration. Lung ventilation. Functional organization of the airways, lungs and thoracic basket. Mechanics of breathing. Intrapleural and intrathoracic pressure. Role of the surfactant. Reflexes – cough and sneeze.

Rate and rhythm of breathing. Pulmonary and alveolar ventilation. Elastic and non-elastic resistance to breathing. Air flow during breathing. Work of breathing.

Static lung volumes and capacities and their functional concern. Anatomic and physiologic dead space. Estimation of the external respiration.

Lecture № 14 - 2 acad. hours

Physical basis of gas exchange. Solubility, diffusion coefficient and diffusion capacity of the gases. Composition of the gases in air, lungs and blood. Diffusion of gases across the alveolocapillary membrane. Ventilation-perfusion ratio.

Transport of O_2 in the blood. Oxyhemoglobin dissociation curves. Oxygen exchange in lungs and tissues.

Transport of CO_2 in the blood. Carbon dioxide exchange in lungs and tissues.

Lecture № 15 - 2 acad. hours

Control of respiration. Respiratory center and rhythm of breathing. Chemical control of respiration. Reflex control of respiration. Effects of the cerebral cortex on the respiratory functions.

Aviation, high altitude and space physiology, physiology of deep-sea diving.

Lecture № 16 - 3 acad. hours

Physical basis of gas exchange. Solubility, diffusion coefficient and diffusion capacity of the gases. Composition of the gases in air, lungs and blood. Diffusion of gases across the alveolocapillary membrane. Ventilation-perfusion ratio.

Transport of O_2 in the blood. Oxyhemoglobin dissociation curves. Oxygen exchange in lungs and tissues.

Transport of CO_2 in the blood. Carbon dioxide exchange in lungs and tissues.
Control of respiration. Respiratory center and rhythm of breathing. Chemical control of respiration. Reflex control of respiration. Effects of the cerebral cortex on the respiratory functions.

Lecture № 17 - 3 acad. hours

Cardiovascular system. Systemic and pulmonary circulation. Heart as an organ –functional morphology of the pericardium, endocardium and myocardium. Nerve supply. Myocardial blood supply.

Functional morphology and physiological characteristics of the excitatory and conductive system of the heart. Automaticity. Cardiac rhythm. Abnormalities of conductivity.

Physiological characteristics of the working myocardium. Excitation and contraction. Refractory periods**.** Extrasystoles**,** flutter and fibrillation**.** Myocardial metabolism.

Dynamics of the cardiac contractions – cardiac cycle. States of the valvular apparatus during different phases of the cardiac cycle.

Lecture № 18 - 3 acad. hours

Electrical events during cardiac performance. Origin, registration and evaluation of the electrocardiogram.

Functions of the heart valves of the heart. Heart sounds. Methods of examination. Stenosis and insufficiency of the valves. Correlation between a synchronous phonocardiographic and electrocardiographic record.

Heart rate. Stroke volume and cardiac output and their changes during different physiological conditions.

Control of the cardiac performance – intrinsic (self-control). Energetics of the heart pumping.

Extracardial neural regulation of the cardiac performance – characteristics of the sympathetic and parasympathetic effects. Humoral factors affecting cardiac performance.

Lecture № 19 - 3 acad. hours

Functional characteristics of blood vessels. Hemodynamic principles – characteristics of the vessels and the blood. Hemodynamic indices. Volume and linear velocity of the blood flow through the various parts of vascular system and factors determining them.

Blood pressure in the various parts of the cardiovascular system. Arterial blood pressure – methods of measurements and normal values. Factors determining the blood pressure levels.

Lecture № 20 - 3 acad. hours

Physiology of the microcirculation. Functional organization of the microcirculation unit.

Organ–related peculiarities of the capillaries. Control of the microcirculation.

Lecture № 21 - 3 acad. hours

Vascular tone. Basal tone of blood vessels. Local, neural and humoral regulatory mechanisms of the vascular tone.

Control of the circulation. Characteristic and localization of the receptors. Vasomotor center. Supramedular control of the circulation.

Control of the arterial blood pressure. Mechanisms of the quick short-term, quick ongoing, and long-term regulation.

Lecture № 22 - 3 acad. hours

Gastrointestinal system – functions. Digestion in the Mouth: processes of mastication, secretion, enzyme destruction and absorption. Swallowing – phases and regulation.

Motor functions of the Stomach – hunger contractions, storage function, mixing and propulsion of food. Emptying of the Stomach. Control of the Stomach motor activity. Vomiting.

Secretion, enzyme destruction and absorption in the Stomach. Gastric juice: composition, mechanism of secretion and functions. Gastric secretion and its control: cephalic, gastric and intestinal phases. Protective potentialities of the gastric barrier.

Lecture № 23 - 3 acad. hours

Small Intestine – motor activity: type of movements and regulation; secretion, digestion and absorption.

Colon – type of movements and their regulation; secretion, digestion and absorption. Defecation.

Pancreatic juice – composition and functions. Control of the pancreatic secretion.

Processes of formation and secretion of Bile. Composition and functions of the Bile. Regulation of the Bile secretion. Functions of the Liver.

Lecture № 24 - 3 acad. hours

Digestion and absorption of Proteins, Fats and Carbohydrates in the Gastrointestinal Tract. Absorption of Salts, Water and Vitamins.

Metabolism of the Nutrients in the organism. Metabolism of Carbohydrates: the level and regulation of Glucose in the circulating blood. Metabolism of Proteins and its control. Metabolism of Lipids and its control.

Energy metabolism in the organism. Energy values of the Nutrients. The Energy Equivalent of Oxygen. The measurement of the Metabolic Rate: Direct and Indirect Calorimetry. The Basal Metabolic Rate and the Daily Energy Requirements for different physiologic states.

Lecture № 25 - 3 acad. hours

Excretion functions of the organism and systems, accomplishing them. The Kidneys – functional structure. Peculiarities of the kidneys blood supply and innervation. Mechanism and control of glomerular filtration. Methods of glomerular function assesment.

Functions of renal tubules. Transport processes within the different parts of the tubules. Mechanisms for excretion of a dilute urine and a concentrated urine. Renal excretion.

Renal clearance tests. Volume of the urine and its components. Micturition. Endocrine and metabolic functions of the kidneys. Control of the renal functions.

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Lecture № 26 - 3 acad. hours

Temperature regulation. Body temperature and isothermia. Mechanisms of heat production and heat loss. Neurophysiologic bases of temperature regulation. Hyperthermia and hypothermia. Acclimatization. Regulation of body temperature within exsercise.

Lecture № 27 - 3 acad. hours

Water-electrolyte balance of the organism. Body fluids and electrolytes. Dynamics of body fluids volume and osmolality. Control of Water-Salts homeostasis. Thirst – physiologic mechanisms.

Acid-Base Balance of the organism. Buffer systems of the body fluids. Respiratory regulation of pH. Renal regulation of pH. Abnormalities in Acid-Base Balance.

Lecture № 28 - 3 acad. hours

Sensory systems. Functional morphology. General principles of sensory systems information coding and processing. Sensory systems adaptation.

General sensation. Somatosensory system – organization and modalities. Mechanisms of thermo- and mechanoreception. Pain sensation. Itch.

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Lecture № 29 - 3 acad. hours

States of brain activity and sleep. The role of the different neuronal structures in the maintenance of the brain activity. Physiologic changes within sleep. Electroencephalography.

Lecture № 30 - 3 acad. hours

Higher nerve activity – types and characteristics. Learning and memory: types and physiologic bases. Primary and secondary signalling systems. Communicative capabilities of man. Reading and writing speech. Auditory and visual gnosia.

LABORATORY EXERCISES

Laboratory exercise № 1 - 4 acad. hours

General physiology of excitable systems. The living organism. Homeostasis. Irritability and excitability of living organism. 1. Elaboration of a frog neuromuscular preparation. 2. Galvani's experiments. 3. Mateucci's experiment. 4. Types of stimuli. 5. Determination of the threshold of the stimulus (both direct and indirect) as applied to a muscle.

Laboratory exercise № 2 - 4 acad. hours

General physiology of excitable systems. Excitability and Excitation. Physiology of the Nerve Cells and Peripheral Nerves. Functions of the Nervous System. 1. Registration of response gradation relative to stimulus strength or frequency. 2. The effect of low temperature on the excitability of a frog sciatic muscle. 3. Electroneurogram (ENG) of a frog mixed nerve (the sciatic nerve). 4.

Determining the conduction velocity of different nerve fibres of the sciatic nerve. 5. Relatedness between stimulus intensity (I) and duration (t), and excitation (the Horveg-Weiss curve).

Laboratory exercise № 3 - 4 acad. hours

General physiology of excitable systems. Synapses. Reflex activity of the nervous system. Unconditioned reflexes. 1**.** Analysis of the reflex arc. 2. Measuring reflex time (after Turk).

3. Irradiation of excitation in the CNS. 4. The effect of Strychnine on the CNS. 5. Effect of narcosis on reflex activity.

Laboratory exercise № 4 - 4 acad. hours

General physiology of excitable systems. Nerve centres. Unconditioned reflexes. Clinically important reflexes. 1. Reflexes of a spinal frog. 2. Investigating of frog segmental reflexes. 3. Clinically important reflexes. 4. Examination of the papillary reflex to light, convergence and accommodation.

Laboratory exercise № 5 - 4 acad. hours

General physiology of excitable systems. Conditioned reflexes. The electroencephalography (EEG). 1. Conditioned reflexes in animals. 2. Conditioned reflexes in man. 3. The EEG – a method for registering summated bioelectric activity.

Laboratory exercise № 6 - 4 acad. hours

General physiology of excitable tissues. Review of 'General Physiology of Excitable Systems'.

Laboratory exercise № 7 - 4 acad. hours

Blood. Functions and Properties of Blood. Blood Constituents. Blood Types. 1. Taking blood. 2. Haematocrit determination. 3. The erythrocyte sedimentation rate (ESR) by the Westergren method. 4. Determination of blood types.

Laboratory exercise № 8 - 4 acad. hours

Blood. Red Blood Cells (RBC, Erythrocytes). Hemoglobin. 1. The chamber method for counting of erythrocytes. 2. Measurement of haemoglobin concentration of the blood. 3. Measurement of osmotic resistance of erythrocytes. 4. Measurement of erythrocyte indices.

Laboratory exercise № 9 - 4 acad. hours

Blood. White Blood Cells (WBC, Leucocytes). The Lymphatic System. 1. Chamber method for counting of leukocytes. 2. WBC differential count. 3. Platelet count. 4. Electronic methods for counting formed elements.

Laboratory exercise № 10 - 4 acad. hours

Blood. Haemostasis and coagulation. Review questions on Blood. Colloquium on the Chapter "Blood". 1. Bleeding time determination (Duke's method). 2. Thrombin (thromboplastin) time determination (Quick's method).

Laboratory exercise № 11 - 4 acad. hours

The Endocrine System. Hormonal Regulation. 1. Examination of the thyroid gland. 2. Methods for examining the adrenal gland. 3. Methods for examining the pancreas. 4. Hypoglycaemic shock in rabbit.

Laboratory exercise № 12 - 4 acad. hours

The Endocrine System. Hormonal Regulation (continued) – Sex Hormones.
Revision of 'Endocrine Physiology'. 1. The Galli-Mainini Test. 2 Immunologic pregnancy tests.

Laboratory exercise № 13 - 4 acad. hours

Sensory Systems. 1. Visual acuity. 2. Perimetry. 3. Color vision test. 4. Audiometry. 5. Acoumetry. 6. Aesthesiometry. 7. Skin sensitivity. 8. Kinaesthetic sensitivity.

Laboratory exercise № 14 - 4 acad. hours

The Locomotor System. Skeletal muscles. (Seminar question N 14 of the Examination Synopsis). **Smooth muscles**. (Seminar Question N 25 of the Examination Synopsis). **Practical Tasks**: 1. Recording of a single muscle contraction. 2. Recording of incomplete and complete tetanus. 3. Measurement of the absolute and specific strength of a frog muscle. 4. The effect of loading on amplitude and performance. 5. Myoneural transmission- the Claude Bernard test. 6. Recording of the muscle fatigue curve from an isolated frog muscle. 7. Measurement of muscle strength.

Laboratory exercise № 15 - 4 acad. hours

The Locomotor System. Skeletal Muscles (part II). Smooth Muscles. 1. Recording of the fatigue curve of an isolated frog muscle. 2. Measurement of muscle strength. 3. Ergography. 4. Demonstration of smooth muscle contractions using a section of the small intestine.

Laboratory exercise № 16 - 4 acad. hours

Respiratory system. External respiration. Lung volumes and lungs capacities. 1. Donders' model. 2. Physical examination of lungs. 3. Measurement of lung volumes and capacities.

Laboratory exercise № 17 - 4 acad. hours

Respiratory system. Exchenge and transport of oxygen and carbon dioxide. 1. Calculation of the partial pressure of oxygen in the air. 2. Calculation of the partial pressure of O_2 in alveolar air. 3. Calculation of the chemically bound O_2 in the blood. 4. Calculation of of the Ventiltion/Perfusion ratio in the different parts of the lungs in straight position at rest. 5. Calculation of the coefficient of utilization (UC) of O_2 in the tissues. 6. Measurement of O_2 consumption and CO_2 release.

Laboratory exercise № 18 - 4 acad. hours

Respiratory system. Regulation of Respiration. Review of 'Respiratory Physiology'.

Laboratory exercise № 19 - 4 acad. hours

The Cardiovascular System. The Heart. Physiological Features of the Cardiac Conduction System and of the Working Myocardium. 1. Mechanogram of a frog heart. 2. Effect of temperature on a frog venous sinus. 3. Stannius' ligatures. 4. Recording of ventricular extrasystoles.

Laboratory exercise № 20 - 4 acad. hours

Cardiovascular system. Cardiac Cycle. Electrical Phenomena Accompanying Cardiac Activity. Functions of the Heart Valves. 1. Auscultation of heart sounds. Recording and analysis of the ECG. 3. Registrasion and analysis of ST-segment. 4. Phonocardiography.

Laboratory exercise № 21 - 4 acad. hours

Cardiovascular system. Stroke Volume and Cardiac Output. Regulation of Cardiac Function. 1. Stroke Volume and Cardiac Output. Regulation of Cardiac Function. 2. Calculation of the stroke volume of the heart by Starr's formula. 3. Determining the cardiac output by the Fick method using data in a table. 4. Effects of vagal stimulation, epinephrine, acetylcholine and atropine on the cardiac activity of a warm-blooded test animal.

Laboratory exercise № 22 - 4 acad. hours

Cardiovascular system. Blood Vessels. Hemodynamic Indices. Arterial Pulse. Capillary Physiology. 1.Defying the characterictics of arterial pulse. 2. Sphygmography. Measurement of pulse wave velocity of conduction. 3. Plethysmography. 4. Capilliaroscopy. 5.Investigation of frogs' tongue capilliaries.

Laboratory exercise № 23 - 4 acad. hours

Cardiovascular system. Regulation of vascular tone. Arterial blood pressure and its control. 1. Claude-Bernard's experiment. 2. Measuring the arterial blood pressure with the Riva-Rocci device by the Korotkoff method. 3. Neural and humoral effects on the blood pressure of a warm-blooded animal.

Laboratory exercise № 24 - 4 acad. hours

Cardiovascular system. Review of 'Cardiovascular Physiology".

Laboratory exercise № 25 - 4 acad. hours

The Digestive System. 1. Demonstration of the motor activity of a frog's small intestine in situ.. 2. Demonstration of movements of the small intestine of a warm-blooded animal in vitro.
3. Effect of bile on the filtration speed of vegetable oil (cooking oil). 4. Effect of bile on the sedimentation of sulphur powder.

Laboratory exercise № 26 - 4 acad. hours

Digestion, Energy Metabolism and Nutrition. 1. Methods of determining the basal metabolic rate. 2. Measurement of loading providing maximal fat catabolism using indirect calorimetry. Principles of rational nutrition. Composing a meal plan.

Laboratory exercise № 27 - 4 acad. hours

The Excretory System and Water/Electrolyte Balance of the Body. 1. Effect of ADH on the diuresis of white mice. 2. Determining the effective filtration pressure (EFP) 3. Calculation of the clearance and transport maximum (Tm).

Laboratory exercise № 28 - 4 acad. hours

The Gastrointestinal System, Energy Metabolism and Nutrition. The Renal excretory System, Water-electrolyte and Acid-base Balance. (Review)

Laboratory exercise № 29 - 4 acad. hours

Body Changes during Physical Exercise. Assessment of the Body Condition by Function Tests. 1. Gas exchange changes during load testing. Spiroergometry. 2. Combined functional test of the cardiovascular system 3. Harvard step test. 4. Evaluation of the physical aerobic work capacity by the Sjostrand – PWC_{170} test.

Laboratory exercise № 30 - 4 acad. hours

Higher Nervous Activity. 1.Tachistoscopia. 2. Determination of types of higher nervous activity by the Sharankov test. 3. Bay Miller's visual memory test. 4. Raven's test.

EXAMINATION SYNOPSIS

1. Organization of the cell. Physical structure of the cell. Functional systems of the cell. Properties of the cell membrane and junctions between the cells. Intercellular signalization. Transport of substances through the cell membrane.
2. The human body. Homeostasis. General principles of the homeostatic regulation – regulatory systems and elements of the homeostatic regulatory system. Levels of physiological regulation.
3. Physiology of the excitatory tissues. Irritability and Excitability. General and specific properties of the excitable cells. Membrane potential – ionic basis of the membrane potentials.
4. Measurement of excitability. Changes in the excitability during excitation. Inhibition. Conduction of the excitation.
5. Transmission of the excitation (inhibition) from an excitable cell to another. Synapses - types of synapses. Chemical synapses. Transmitters and modulators. Postsynaptic potentials. Summation of the postsynaptic potentials.
6. Functions of the nervous system – functional morphology of the nervous system. Physiology of the nerve cell. Glial cells. Neuronal circuits and processing of information form group of nerve cells – convergence, divergence, reverberating circuits, inhibition.
7. Reflex regulation of the physiological functions. Type of reflexes according to the mechanism of formation and the characteristics of the involved reflex arc.
8. Nerve centers. Types and properties. Cerebral blood flow. Cerebrospinal fluid.
9. The autonomic nervous system. General organization of the autonomic nervous system. Autonomic nerve centers, ganglia, transmitters and receptors in the autonomic nervous system.
10. Effects of sympathetic and parasympathetic stimulation on specific organs. Autonomic reflexes.
11. Role of the hypothalamus, reticular formation, cerebellum, basal ganglia and cerebral cortex in the control of the autonomic functions. Integration of the central nervous system in the adaptation processes of the body – “alarm” or “stress” response of the sympathetic nervous system.
12. General principles of the humoral control of the physiologic functions. Telecrinia and paracrinia. Classification, synthesis and mechanism of action of the hormones. Control on the hormone secretion.
13. Hypothalamic-neurohypophysial system. Neurosecretion. Hormones of the neurohypophysis. Physiologic effects and control of secretion.
14. Hypothalamo-adenohypophysial system. Hormones of the adenohypophysis. Physiologic effects and control of secretion.
15. Functional morphology of the thyroid gland. Iodine containing thyroid hormones. Physiologic effects and control of secretion. Hyperthyroidism and hypothyroidism.
16. Functional morphology of adrenal glands. Hormones of the adrenal medulla. Physiologic effects and control of secretion of adrenaline (epinephrine) and noradrenaline (norepinephrine).
17. Hormones of adrenal cortex – glucocorticoids. Physiologic effects and control of secretion. Pharmacologic effects of glucocorticoids.
18. Hormones of adrenal cortex – mineralcorticoids and adrenal androgens. Abnormalities of adrenocortical secretion.
19. Endocrine functions of the pancreas – type of hormones, physiologic effects and control of secretion. Diseases of the endocrine pancreas.

20. Calcium-phosphate homeostasis. Parathyroid hormone, calcitonin, vitamin D - physiologic effects and control of secretion. Impairment of the calcium and phosphate homeostasis.
21. Physiology of reproduction. Male reproductive system. Spermatogenesis. Male sex hormones (androgens) – types, physiologic effects and control of secretion. Erection and ejaculation.
22. Physiology of reproduction. Female reproductive system. Ovogenesis. Female sex hormones (estradiol and progesterone) – types, physiologic effects and control of secretion. Regulation of the female monthly rhythm. Pregnancy and lactation. Tests for early pregnancy.
23. Epiphysis, thymus and non-endocrine organs with endocrine functions. Tissue hormones – types, physiologic effects and control of secretion.
24. Physiology of skeletal muscles – functional morphology, mechanism and energetic of muscle contraction. Types of muscle contractions. Types of muscle fibers. Muscle work and muscle fatigue. Electromyography.
25. Functional morphology of smooth muscles. Excitation, electrophysiologic characteristics and mechanism of contraction of smooth muscles.
26. Physiology of the blood. Functions of the blood. Composition and volume of the circulating blood – regulation of the volume. Blood plasma – composition and its regulation. Hematocrit. Blood reservoirs.
27. Erythrocytes. Count and functions**.** Erythrocyte sedimentation rate**.** Hemoglobin**.** Erythrocyte indices. Iron metabolism. Hemolysis. Control of erythropoiesis and erythrocyte count in the bloodstream.
28. Blood types. Physiological and clinical significance. ABO and Rh blood type systems. Methods of analysis. Principles of blood transfusion.
29. Leukocytes. Count and functions of the different leukocyte types. Control of leukopoiesis and leukocyte count in the bloodstream. Immunity.
30. Hemostasis and hemocoagulation. Vascular-trombocyte and coagulation hemostasis. Fibrinolysis and anticoagulational mechanisms. Control of hemostasis.
31. Physiology of lymphatic system. Formation, composition and functions of lymph. Physiological role of the spleen.
32. Cardiovascular system. Systemic and pulmonary circulation. Heart as an organ – functional morphology of the pericardium, endocardium and myocardium. Nerve supply. Myocardial blood supply.
33. Functional morphology and physiological characteristics of the excitatory and conductive system of the heart. Automaticity. Cardiac rhythm. Abnormalities of conductivity.
34. Physiological characteristics of the working myocardium. Excitation and contraction. Refractory periods**.** Extrasystoles**,** flutter and fibrillation**.** Myocardial metabolism.
35. Electrical events during cardiac performance. Origin, registration and evaluation of the electrocardiogram.
36. Dynamics of the cardiac contractions – cardiac cycle. States of the valvular apparatus during different phases of the cardiac cycle.
37. Functions of the heart valves of the heart. Heart sounds. Methods of examination. Stenosis and insufficiency of the valves. Correlation between a synchronous phonocardiographic and electrocardiographic record.
38. Heart rate. Stroke volume and cardiac output and their changes during different physiological conditions.

39. Control of the cardiac performance – intrinsic (self-control). Energetics of the heart pumping.
40. Extracardial neural regulation of the cardiac performance – characteristics of the sympathetic and parasympathetic effects. Humoral factors affecting cardiac performance.
41. Functional characteristics of blood vessels. Hemodynamic principles – characteristics of the vessels and the blood. Hemodynamic indices. Volume and linear velocity of the blood flow through the various parts of vascular system and factors determining them.
42. Blood pressure in the various parts of the cardiovascular system. Arterial blood pressure – methods of measurements and normal values. Factors determining the blood pressure levels.
43. Arterial blood flow. Arterial pulse. Sphygmography. Characteristics of the arterial pulses. Venous blood flow. Venous pulse. Phlebography.
44. Physiology of the microcirculation. Functional organization of the microcirculation unit. Organ–related peculiarities of the capillaries. Control of the microcirculation.
45. Vascular tone. Basal tone of blood vessels. Local, neural and humoral regulatory mechanisms of the vascular tone.
46. Control of the circulation. Characteristic and localization of the receptors. Vasomotor center. Supramedular control of the circulation.
47. Control of the arterial blood pressure. Mechanisms of the quick short-term, quick ongoing, and long-term regulation.
48. Physiology of respiration. External respiration. Functional organization of the airways, lungs and thoracic basket. Mechanics of breathing. Intrapleural and intrathoracic pressure. Role of surfactant. Defense reflexes – cough and sneeze.
49. Rate and rhythm of breathing. Pulmonary and alveolar ventilation. Elastic and non-elastic resistance to breathing. Air flow during breathing. Work of breathing.
50. Static lung volumes and capacities and their functional concern. Anatomic and physiologic dead space. Estimation of the external respiration.
51. Physical basis of gas exchange. Solubility, diffusion coefficient and diffusion capacity of the gases. Composition of the gases in air, lungs and blood. Diffusion of gases across the alveolocapillary membrane. Ventilation-perfusion ratio.
52. Transport of O_2 in the blood. Oxyhemoglobin dissociation curves. Oxygen exchange in lungs and tissues.
53. Transport of CO_2 in the blood. Carbon dioxide exchange in lungs and tissues.
54. Control of respiration. Respiratory center and rhythm of breathing. Chemical control of respiration. Reflex control of respiration. Effects of the cerebral cortex on the respiratory functions.
55. Gastrointestinal system – functions. Digestion in the Mouth: processes of mastication, secretion, enzyme destruction and absorption. Swallowing – phases and regulation.
56. Motor functions of the Stomach – hunger contractions, storage function, mixing and propulsion of food. Emptying of the Stomach. Control of the Stomach motor activity. Vomiting.
57. Secretion, enzyme destruction and absorption in the Stomach. Gastric juice: composition, mechanism of secretion and functions. Gastric secretion and its control: cephalic, gastric and intestinal phases. Protective potentialities of the gastric barrier.
58. Small Intestine – motor activity: type of movements and regulation; secretion, digestion and absorption.

59. Colon – type of movements and their regulation; secretion, digestion and absorption. Defecation.

60. Pancreatic juice – composition and functions. Control of the pancreatic secretion.

61. Processes of formation and secretion of Bile. Composition and functions of the Bile. Regulation of the Bile secretion. Functions of the Liver.

62. Digestion and absorption of Proteins, Fats and Carbohydrates in the Gastrointestinal Tract. Absorption of Salts, Water and Vitamins.

63. Metabolism of the Nutrients in the organism. Metabolism of Carbohydrates: the level and regulation of Glucose in the circulating blood. Metabolism of Proteins and its control. Metabolism of Lipids and its control.

64. Energy metabolism in the organism. Energy values of the Nutrients. The Energy Equivalent of Oxygen. The measurement of the Metabolic Rate: Direct and Indirect Calorimetry. The Basal Metabolic Rate and the Daily Energy Requirements for different physiologic states.

65. Feeding: main principles in defining the physiologic standards– plastic and energy needs of the organism. Physiologic mechanisms of Starvation and Satiety.

66. Temperature regulation. Body temperature and isothermia. Mechanisms of heat production and heat loss. Neurophysiologic bases of temperature regulation. Hyperthermia and hypothermia. Acclimatization. Regulation of body temperature within exsercise.

67. Excretion functions of the organism and systems, accomplishing them. The Kidneys – functional structure. Peculiarities of the kidneys blood supply and innervation. Mechanism and control of glomerular filtration. Methods of glomerular function assesment.

68. Functions of renal tubules. Transport processes within the different parts of the tubules. Mechanisms for excretion of a dilute urine and a concentrated urine. Renal excretion.

69. Renal clearance tests. Volume of the urine and its components. Micturition. Endocrine and metabolic functions of the kidneys. Control of the renal functions.

70. Water-electrolyte balance of the organism. Body fluids and electrolytes. Dynamics of body fluids volume and osmolality. Control of Water-Salts homeostasis. Thirst – physiologic mechanisms.

71. Acid-Base Balance of the organism. Buffer systems of the body fluids. Respiratory regulation of pH. Renal regulation of pH. Abnormalities in Acid-Base Balance.

72. Sensory systems. Functional morphology. General principles of sensory systems information coding and processing. Sensory systems adaptation.

73. General sensation. Somatosensory system – organization and modalities. Mechanisms of thermo- and mechanoreception. Pain sensation. Itch.

74. Vision sensory system. Functional morphology of the eye – the optics of the eye; the mechanism of accommodation; errors of refraction. The pupillary reflex. Eyes movements and their control. Protective appliances of the eyes.

75. Detection, transmission and processing of the information in the retina. Central neurophysiology of vision. Light and dark adaptation. Visual acuity. Color vision.

76. The sense of hearing. Functional morphology of the external, middle and inner ear. Processing of the sound signal. Central auditory mechanisms. Vestibular apparatus. Central mechanisms of the maintenance of equilibrium. Vestibular reflexes.

77. Physiology of the chemical senses - taste and smell. Peripheral and central mechanisms of taste and smell sensations.

78. General characteristics of motor control. Muscle receptors – functions of the muscle spindles and tendon receptors. Spinal cord control of motor activity. The spinal cord reflexes. Motor control from higher levels of the brain.
79. States of brain activity and sleep. The role of the different neuronal structures in the maintenance of the brain activity. Physiologic changes within sleep. Electroencephalography.
80. Higher nerve activity – types and characteristics. Learning and memory: types and physiologic bases. Primary and secondary signalling systems. Communicative capabilities of man. Reading and writing speech. Auditory and visual gnosia.

Obligatory reading:

1. *Guyton, A. C. and Hall, J. E., Textbook of Medical Physiology, 12th ed., 2012.*
2. *Ganong's Review of Medical Physiology, 23rd ed., 2010.*
3. *Vander, A. G., Human Physiology, 6th ed., 1994.*
4. Seminar Manual of Human Physiology. A practical course for medical students - Edited by Nikolay Boyadjiev, 2012.

Recommended reading:

1. Vander A.G., Sherman J.H., Luchiano D.S. Human Physiology, 6th ed. McGraw Hill, Inc, 1994;
2. Guenard H. Physiology Humaine. 2e tiraje, Editions Paradel, Paris, 1995.

The Programme is approved at a Department meeting, protocol #29/21.05.2012.

AUTHOR OF THE PROGRAMME:

Nikolay Boyadjiev, MD,Phd,
Associate Professor

B I O C H E M I S T R Y

COURSE OF EDUCATION: 2-ND COURSE
SEMESTERS OF EDUCATION: III AND IV SEMESTER
EXAM: AFTER II SEMESTER
HOURS OF AUDITORIUM CLASSES: 180 HOURS
LECTURER: ASSOC. PROF. TATYANA VLAYKOVA, PhD

Curriculum

Form of classes	**Hours**				**Credits**
	w eekly	**I II semester**	**I V semester**	**otal**	
Lectures	3	45	45	90	
Practical exercises	3	45	45	90	**16.7**
Total	**6 hours**	**90 hours**	**90 hours**	**180 hours**	

THE PURPOSE OF THE COURSE is to study the function of human organism at intra- and intercellular level and the integration of the processes in the human organism in normal and pathological conditions.

THE TASKS OF THE COURSE ARE:

To introduce the students with the basic parts of medical biochemistry which include:

1. Structural aspects- biopolymers structure (proteins and nucleic acids), lipids, carbohydrates, nucleotides and porphyrins

2. Cell bioenergetics- characteristics of formation and use of energy in human organism

3. Enzymes as biocatalysts

4. Metabolism of carbohydrates, lipids, nucleotides and porphyrins in normal and pathological conditions

5. Regulation of gene expression at the level of replication, transcription and translation

6. Mechanism of intercellular interactions- signal transduction and cell adhesion

7. Change in the metabolism and in the mechanisms of cell regulation in the most common and socially significant diseases- diabetes, obesity, atherosclerosis and oncogenesis

8. Functional biochemistry- specificity of the metabolism and biological functions of the organs and tissues in human body

THE METHODS OF EDUCATION ARE: auditorium classes, practical exercises and individual and group consultation

TECHNICAL MEANS used in the education are: video materials, schemes, notebook for practical exercises, equipments for qualitative and quantitative analysis (centrifuges, spectrophotometers, etc.)

CONTROL AND EVALUATION:

Control	Mark	Portion of the final mark
Current	Average mark formed from 4 marks from 4 colloquiums	Very good 5 to exempt from the test on the exam
Exam- written	2 questions	Summary mark from written and oral exam
Exam- oral	2 questions and additional for the formation of the final mark	Summary mark from written and oral exam

METHODS OF CONTROL: current marks, tests after every part of exercises, test before the main exam, written exam on the main chapters of the questionnaire

COMPULSORY COMPETENCIES:

Theoretical knowledge:

- structural and functional characteristics of the biological macromolecules;
- the basis of human metabolism- characteristics of the metabolism
- integration of carbohydrates, lipids and proteins metabolism at cellular and organ level
- regulation of cell functions by a control of the enzymes activity, gene expression, signal transduction and mechanisms of cell adhesion
- disorders in the metabolism as causes for molecular diseases and main pathobiochemical mechanisms of atherosclerosis, diabetes, obesity and oncogenesis
- specific characteristics of the metabolism in different tissues and organs (functional biochemistry)

Practical skills:

- work with automatic pipettes
- introduction with spectrophotometric and immunoenzyme methods
- mastering of the work with universal diagnostic tests

LECTURE COURSE
IN BIOCHEMISTRY
FOR STUDENTS IN MEDICINE

	Winter term	
Week	Topic	Conspect
1	1. Protein functions. Hetero-, iso- and aloproteins. Peptides, polypeptides and proteins. Amino acids as structural units of the proteins. Classification according to the chemical nature of the radical and the polarity at pH 7.0. Levels of organization of the protein molecule. Primary structure of the proteins. 2. Conformation. Properties of the peptide bond. Secondary structure. α-Helix, β-sheet and random coil characterization. Supersecondary structures – motifs and domains. Tertiary structure – types of chemical bonds involved in it. Fibrous and globular proteins.	1,2
2	3. Quaternary structure – role in the regulation of the biological activity of the proteins. Maintaining mechanisms in the conformation of the proteins – involved enzymes and chaperons. Importance of the relation between structure and function of the proteins in Medicine. 4. Isoelectric point and protein precipitation. Denaturation. Electrophoresis. Electrophoretic profiles of serum proteins, role in diagnosis.	3,4
3	5. Nucleic acids – types and biological role. Chemical composition, chemical bonds in and between nucleotides. Free nucleotides with important biological meaning. Features of polynucleotide chains. Watson and Crick model. Purine and pyrimidine analogues as anticancer and antiviral agents. 6. Primary structure of nucleic acids. Conformation of DNA and different types of RNA. Nucleosomes. Importance of histone and nonhistone proteins for maintenance of the DNA conformation. Denaturation and renaturation of DNA. Hyperchromic effect and melting point. Ribozymes – role in the process of RNA maturation and their potential uses as inhibitors of gene expression.	5,6
4	7. Characteristics of enzymes as biological catalysts. Coenzymes and prosthetic groups. Enzyme names and classification. Mechanisms of enzyme catalysis. Enzyme–substrate complex.	7,8,9

	Active site. Specificity of enzyme action. 8. Enzymatic kinetics. Time-scale dependence of the enzyme reactions rates. Initial velocity. Dependence of the enzyme reaction rate on enzyme concentration. Enzyme units. Temperature and pH effects on enzyme reaction rates. 9. Enzyme reactions kinetics. Dependence of the enzyme reaction rate on substrate concentration. Michaelis – Menten equation about enzyme reaction velocity. Michaelis constant. Lineweaver – Burk plot (equation).	
5	10. Reversible and irreversible inhibition. Competitive and noncompetitive inhibitors. Vmax and Km in the presence of competitive and uncompetitive inhibitor. Enzyme activators. 11. Enzyme activity regulation. Regulation of absolute enzyme amount – constitutive and inducible enzymes. Factors affecting the half-life of enzymes. Regulation of catalytic activity by compartmentalization and shuttle mechanisms, polyenzymatic complexes, phosphorylation – dephosphorylation and allosteric control. Retroinhibition.	10,11
6	12. Clinical significance of enzymes. Intracellular enzymes in serum (myocardial infarction, hepatitis). Changes of the typical functional serum enzymes. Diagnostic significance of isoenzymes (creatine phosphokinase and lactate dehydrogenase). Hereditary enzyme diseases (Gout, Lesch-Nyhan syndrome). 14. Lipid-soluble vitamins. Biological functions. Avitaminoses and hypervitaminoses.	12,14
7	13. Water-soluble vitamins. Biological functions. Avitaminoses (diseases caused vitamin deficiencies)	13
8	15. Bioenergetics. Features of organisms as open chemical systems. The first and the second laws of thermodynamics and their application in living organisms. Coupling of endergonic with exergonic processes using macroergic compounds. Types of macroergic bonds and compounds. Central role of the system ATP/ADP. 16. Characteristics of biological oxidation. Substrates of biological oxidation and final hydrogen acceptors. Oxidoreductases. Important redox systems: NAD^+/NADH, $NADP^+$/NADPH, FMN/$FMN.H_2$, FAD/$FADH_2$, CoQ/$CoQH_2$, hem groups in cytochromes, lipoate, ascorbate.	15,16
9	17. Oxidative phosphorylation at substrate level: oxidative phosphorylation of glyceraldehyde-3-phosphate, enolase reaction, oxidative decarboxylation of α-keto acids (pyruvate dehydrogenase complex; role of the cofactors TPP, lipoate, CoA, FAD and NAD^+). 18. Respiratory chain – localization, function and molecular structure. Places for proton translocation. Oxidative phosphorylation coefficient (P/O). Respiratory control, phosphate potential.	17,18

	Inhibitors of electron transportation (barbiturates, antimicin A, KCN). Effect of barbiturates and alcohol combination. Mitochondrial diseases.	
10	19. Chemiosmotic theory for the mechanism of oxidative phosphorylation in the respiratory chain. ATP synthase. Effect of uncoupling agents (2,4-dinitrophenol). Natural uncoupling agents. Oxidative phosphorylation inhibitors (oligomicin). 20. Free oxidation. Heat production. Role of thermogenin in mitochondria of brown adipose tissue. Electron transport in endoplasmic reticulum. Generation and neutralization of superoxide, hydrogen peroxide and hydroxyl free radical.	19,20
11	21. Citric acid cycle – importance in catabolism and anabolism. Chemical reactions, metabolic and energetic balance. Regulation mechanisms. Pyruvate dehydrogenase deficiency. 22. Glucose metabolism – absorption in the intestinal tract and glucose transport systems. Glycolysis – importance, chemical reactions, energy production under anaerobic and aerobic conditions. Tissue specificity of glycolysis. Metabolic fate of NADH, lactate and pyruvate. Relationship between glycolysis and respiratory chain – hydrogen transfer shuttle systems from cytoplasm to mitochondria (malate-aspartate and glycerophosphate shuttle). Pasteur effect. Connection between glycolysis and citrate cycle. Lactic acidosis. Hemolytic anemia caused by pyruvate kinase deficiency. Cancer and glycolysis.	21,22
12	23. Gluconeogenesis. Cellular compartmentalization and tissue localization. Importance. Overcoming the irreversible steps of glycolysis. Gluconeogenesis regulation. Gluconeogenesis substrates. Role of gluconeogenesis in the kidney. Fructose-1,6-bisphosphatase deficiency, hypoglycemia and premature babies, hypoglycemia and alcohol toxicity. 24. Pentose phosphate pathway. Importance. Oxidative, isomerase and transferase reactions. Glucose-6-phosphate dehydrogenase deficiency.	23,24
13	25. Galactose and fructose metabolism. Galactosemia. Essential fructosuria. Fructose intolerance. 26. Glycogen metabolism - degradation and synthesis. Muscles and liver peculiarities. Regulation. Glycogenoses.	25,26
14	27. Regulation of carbohydrate metabolism and blood sugar level. Involvement of the different tissues and organs. Cori cycle. Regulatory enzymes and hormones. Features of carbohydrate metabolism in various tissues.	27
15	28. Lipids – classification. Lipid digestion – enzymes. Lipid transport in the body. Composition, origin and functions of lipoprotein complexes. Lipoprotein complexes receptors. Familial hypercholesterolemia.	28

	Summer term	
1	29. Cholesterol synthesis. Regulation. Removal from the body. 30. Cholesterol derivatives (steroid hormones, vitamin D, bile acids) – structure and biological role.	29,30
2	31. Triacylglycerol metabolism - degradation and biosynthesis. Hormone-sensitive adipocyte lipase. Glycerol metabolism. 32. Oxidation of fatty acids with even and odd number of carbon atoms. Energetic balance. Enzyme defects of the oxidation.	31,32
3	33. Ketogenesis. Utilization and oxidation of ketone bodies in extrahepatic tissues. Ketonemia and ketonuria. Ketoacidosis during fasting and diabetes. 34. Fatty acids biosynthesis. Citrate shuttle. Role of acetyl-CoA carboxylase. Acylsintase – multifunctional enzyme. Desaturation of fatty acids. Essential fatty acids deficiency.	33,34
4	35.Metabolism (synthesis and degradation) of glycerophosphatides. Biological role of phospholipases A_1, A_2, C and D. Eicosanoid synthesis and biological activity. Cyclic and linear pathways of formation. COX-1 and COX-2 inhibitors. Sphingolipids – types, structure and importance. Sphingolipidoses. 36. Lipid metabolism disorders. Atherosclerosis, tissue ischemia and myocardial infarction. Obesity. Role of leptin in obesity. Fatty liver	35,36
5	37. General reactions of amino acids degradation: oxidative deamination, transamination, transdeamination, decarboxylation, biogenic amines. Clinical significance of aminotransferases. 38. Ammonia detoxification by glutamate dehydrogenase reaction, glutamine synthesis, urea cycle and ammoniagenesis. Role of the liver, muscles and kidneys in the detoxification of ammonia.	37,38
6	39. General pathways for degradation of amino acid C-skeletons. Glucogenic and ketogenic amino acids. One-carbon-atom residues – types, sources, importance. Role of the S-adenosyl methionine derivatives and folic acid derivatives. Therapeutic application of folate analogues. Phenylalanine and tyrosine catabolism – phenylketonuria, tyrosinosis, albinism, alkaptonuria. Tryptophan catabolism – pellagra.	39
7	40. Amino acids synthesis. Nonessential and essential amino acids. Common reactions in the synthesis of amino acids. Selenocysteine. Conversion of amino acids in specialized products – serine (ethanolamine, choline, phospholipids), tryptophan (NAD^+, serotonin, melatonin), tyrosine (thyroid hormones, catecholamines, dopamine, melanin), arginine (creatine phosphate, citrulline, nitric oxide, polyamines). Glutathione as a reducing agent and antioxidant. Products of glutamine and glutamate metabolism. Special features of	40,41

	amino acids metabolism in different tissues. 41. Impairment of amino acids metabolism. Enzymopathies associated with metabolism of tyrosine (phenylketonuria, tyrosinosis, alkaptonuria, albinism), tryptophan (pellagra) and aliphatic amino acids (methylmalonic acidemia). Parkinson's disease and L-DOPA.	
8	42. Purine nucleotide biosynthesis and degradation. Enzyme defects in purine metabolism (immunodeficiencies). Tissue specificity. Regulatory enzymes of biosynthesis. Purine analogues as antiviral agents. Hyperuricemia due to enzyme defects (Gout, Lesch-Nyhan syndrome). Xanthine oxidase inhibition. 43. Pyrimidine nucleotide biosynthesis and degradation. Regulatory enzymes. Allosteric response and orotic aciduria.	42,43
9	44. Iron metabolism. Iron-binding proteins. Iron absorption mechanism in cells. Transferrin receptors. Impaired iron homeostasis – iron deficiency anemia and iron overload. Iron, oxidative stress and neurodegenerative diseases. 45. Porphyrine biosynthesis. Cellular localization and regulation of the biosynthesis pathway. Types of porphyrias. 46. Hemoglobin degradation. Bile pigments. Transportation of bile pigments in the body. Jaundice. Types of jaundice.	44,45,46
10	47. Integration of metabolism. Interconnection between the metabolism of carbohydrates, lipids, amino acids and nucleotides. Role of key metabolites and key enzymes. Tissue and organ specificity. Adaptation during starvation.	47
11	49. Molecular mechanisms of cell cycle regulation. Cyclins and cyclin-dependent kinases. Regulation of synthesis and degradation of cyclins. Control mechanisms in different stages of the cell cycle. Role of p53 and pRB for overcoming the restriction points of the cell cycle.	49
12	55. Principles of intercellular communication. Signal transduction. Organization and participants in signaling pathways. Types of extracellular signals. Membrane and intracellular receptors. Characteristics of signaling pathways – amplification, convergention and divergention. General principles of regulation – phosphorylation, adapter proteins and proteins with GTP-ase activity. 56a. Secondary mediators in signal transduction. Types of secondary mediators. Cyclic AMP (cAMP) and adenylate cyclase system. Nitric oxide and cyclic GMP (cGMP). Calcium and calmoduline.	55,56a
13	56b. Lipid mediators, products of phospholipid and sphingolipid degradation: inositol-3-phosphate, DAG, eicosanoids, ceramides and sphingosine-1-phosphate. 57. Role of protein kinases and protein phosphatases in signal transduction. Receptor and non-receptor protein tyrosine kinases.	56b,57

	Receptor and non-receptor protein serine/threonine kinases. Protein kinase A. Protein kinase C, PKG, PI3K, MAPK phosphorylation cascade. Receptor and soluble protein tyrosine phosphatases	
14	63. Molecular mechanisms of oncogenesis. Tumor cells features. Tumor markers. Factors causing cancers. Direct carcinogens and pro-carcinogens. Pro-carcinogen metabolic activation. Stages of chemical carcinogenesis. Oncogenes and proto-oncogenes. Mechanisms of transformation of oncogenes into proto-oncogenes. Oncogenes and growth factors. Oncogenic viruses. Oncogenes and signal transduction. Tumor-suppressor genes. Mechanisms of tumor cell progression and metastasis. Telomerase and cancer. Anticancer therapy drugs – mechanism of action. P-glycoproteins.	64
15	66. Extracellular matrix (connective tissue). Types and functions of structural proteins. Types and functions of proteoglycans and glycosaminoglycans. Diseases due to mutations in genes for structural proteins. Mucopolysaccharidoses. 68. Blood biochemistry. Characteristics of plasma proteins. Acute-phase protein – albumin. Acute-phase proteins: haptoglobin, ceruloplasmin, antiproteases – α_1-antitrypsin and α_2-macroglobulin, complement, C-reactive protein. Disorders in synthesis and metabolism of plasma proteins. Electropherogram and densitogram of serum proteins – clinical significance. |Blood coagulation system. Factors and regulation of blood coagulation	66,68

Program of the exercises in biochemistry for students in medicine

Winter term

week	***Topic of the exercise***
1.	Amino acids and peptides
2.	Protein molecules as polyelectrolyte. Nucleic acids
3.	Test – biopolymers
4.	Enzymes – biochemical features and mechanism of action
5.	Enzymes: Kinetics
6.	Test – Enzymes
7.	Bioenergetics and biologic oxidation
8.	Mechanisms and pathways by which cells obtain energy

9.	Test – Bioenergetics
10.	Pathways in glucose metabolism
11.	Other pathways of hexose metabolism
12.	Gluconeogenesis and the control of blood glucose
13.	Test – carbohydrates metabolism
14.	Lipids. Lipid transport and storage. Cholesterol metabolism
15.	Metabolism of acylglycerols and sphingolipids

Summer term

week	***Topic of the exercise***
1.	Metabolism of fatty acids
2.	Test – Lipid metabolism
3.	Metabolism of proteins and amino acids I
4.	Metabolism of proteins and amino acids II
5.	Nucleotides – Metabolism of purine and pyrimidine nucleotides
6.	Test – Proteins, amino acids and nucleotides metabolism
7.	Porphyrins and bile pigments
8.	Signal transduction I
9.	Signal transduction II
10.	Test – Signal Transduction
11.	Cancer, cancer genes and growth factors
12.	Diabetes mellitus
13.	Nutrition, digestion and absorption
14.	Hemostasis and trombosis
15.	Biochemistry of the liver

QUESTIONNAIRE IN BIOCHEMISTRY

1. Protein functions. Hetero-, iso- and aloproteins. Peptides, polypeptides and proteins. Amino acids as structural units of the proteins. Classification according to the chemical nature of the radical and the polarity at pH 7.0. Levels of organization of the protein molecule. Primary structure of the proteins.

2. Conformation. Properties of the peptide bond. Secondary structure. α-Helix, β-sheet and random coil characterization. Supersecondary structures – motifs and domains. Tertiary structure – types of chemical bonds involved in it. Fibrous and globular proteins.

3. Quaternary structure – role in the regulation of the biological activity of the proteins. Maintaining mechanisms in the conformation of the proteins – involved enzymes and chaperons. Importance of the relation between structure and function of the proteins in Medicine.

4. Isoelectric point and protein precipitation. Denaturation. Electrophoresis. Electrophoretic profiles of serum proteins, role in diagnosis.

5. Nucleic acids – types and biological role. Chemical composition, chemical bonds in and between nucleotides. Free nucleotides with important biological meaning. Features of polynucleotide chains. Watson and Crick model. Purine and pyrimidine analogues as anticancer and antiviral agents.

6. Primary structure of nucleic acids. Conformation of DNA and different types of RNA. Nucleosomes. Importance of histone and nonhistone proteins for maintenance of the DNA conformation. Denaturation and renaturation of DNA. Hyperchromic effect and melting point. Ribozymes – role in the process of RNA maturation and their potential uses as inhibitors of gene expression.

7. Characteristics of enzymes as biological catalysts. Coenzymes and prosthetic groups. Enzyme names and classification. Mechanisms of enzyme catalysis. Enzyme–substrate complex. Active site. Specificity of enzyme action.

8. Enzymatic reaction kinetics. Time-scale dependence of the enzyme reactions rates. Initial velocity. Dependence of the enzyme reaction rate on enzyme concentration. Enzyme units. Temperature and pH effects on enzyme reaction rates.

9. Enzyme reactions kinetics. Dependence of the enzyme reaction rate on substrate concentration. Michaelis – Menten equation about enzyme reaction velocity. Michaelis constant. Lineweaver – Burk plot (equation).

10. Reversible and irreversible inhibition. Competitive and noncompetitive inhibitors. Vmax and Km in the presence of competitive and uncompetitive inhibitor. Enzyme activators.

11. Enzyme activity regulation. Regulation of absolute enzyme amount – constitutive and inducible enzymes. Factors affecting the half-life of enzymes. Regulation of catalytic activity by compartmentalization and shuttle mechanisms, polyenzymatic complexes, phosphorylation – dephosphorylation and allosteric control. Retroinhibition.

12. Clinical significance of enzymes. Intracellular enzymes in serum (myocardial infarction, hepatitis). Changes of the typical functional serum enzymes. Diagnostic significance of isoenzymes (creatine phosphokinase and lactate dehydrogenase). Hereditary enzyme diseases (Gout, Lesch-Nyhan syndrome).

13. Water-soluble vitamins. Biological functions. Avitaminoses (diseases caused vitamin deficiencies)

14. Lipid-soluble vitamins. Biological functions. Avitaminoses and hypervitaminoses.

15. Bioenergetics. Features of organisms as open chemical systems. The first and the second laws of thermodynamics and their application in living organisms. Coupling of endergonic with exergonic processes using macroergic compounds. Types of macroergic bonds and compounds. Central role of the system ATP/ADP.

16. Characteristics of biological oxidation. Substrates of biological oxidation and final hydrogen acceptors. Oxidoreductases. Important redox systems: NAD^+/NADH, $NADP^+$/NADPH, FMN/FMN.H_2, FAD/$FADH_2$, CoQ/$CoQH_2$, hem groups in cytochromes, lipoate, ascorbate.

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

18. Respiratory chain – localization, function and molecular structure. Places for proton translocation. Oxidative phosphorylation coefficient (P/O). Respiratory control, phosphate potential. Inhibitors of electron transportation (barbiturates, antimicin A, KCN). Effect of barbiturates and alcohol combination. Mitochondrial diseases.

19. Chemiosmotic theory for the mechanism of oxidative phosphorylation in the respiratory chain. ATP synthase. Effect of uncoupling agents (2,4-dinitrophenol). Natural uncoupling agents. Oxidative phosphorylation inhibitors (oligomicin).

20. Free oxidation. Heat production. Role of thermogenin in mitochondria of brown adipose tissue. Electron transport in endoplasmic reticulum. Generation and neutralization of superoxide, hydrogen peroxide and hydroxyl free radical.

21. Citric acid cycle – importance in catabolism and anabolism. Chemical reactions, metabolic and energetic balance. Regulation mechanisms. Pyruvate dehydrogenase deficiency.

22. Glucose metabolism – absorption in the intestinal tract and glucose transport systems. Glycolysis – importance, chemical reactions, energy production under anaerobic and aerobic conditions. Tissue specificity of glycolysis. Metabolic fate of NADH, lactate and pyruvate. Relationship between glycolysis and respiratory chain – hydrogen transfer shuttle systems from cytoplasm to mitochondria (malate-aspartate and glycerophosphate shuttle). Pasteur effect. Connection between glycolysis and citrate cycle. Lactic acidosis. Hemolytic anemia caused by pyruvate kinase deficiency. Cancer and glycolysis.

23. Gluconeogenesis. Cellular compartmentalization and tissue localization. Importance. Overcoming the irreversible steps of glycolysis. Gluconeogenesis regulation. Gluconeogenesis substrates. Role of gluconeogenesis in the kidney. Fructose-1,6-bisphosphatase deficiency, hypoglycemia and premature babies, hypoglycemia and alcohol toxicity.

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

25. Galactose and fructose metabolism. Galactosemia. Essential fructosuria. Fructose intolerance.

26. Glycogen metabolism - degradation and synthesis. Muscles and liver peculiarities. Regulation. Glycogenoses.

27. Regulation of carbohydrate metabolism and blood sugar level. Involvement of the different tissues and organs. Cori cycle. Regulatory enzymes and hormones. Features of carbohydrate metabolism in various tissues.

28. Lipids – classification. Lipid digestion – enzymes. Lipid transport in the body. Composition, origin and functions of lipoprotein complexes. Lipoprotein complexes receptors. Familial hypercholesterolemia.

29. Cholesterol synthesis. Regulation. Removal from the body.

30. Cholesterol derivatives (steroid hormones, vitamin D, bile acids) – structure and biological role.

31. Triacylglycerol metabolism - degradation and biosynthesis. Hormone-sensitive adipocyte lipase. Glycerol metabolism.

32. Oxidation of fatty acids with even and odd number of carbon atoms. Energetic balance. Enzyme defects of the oxidation.

33. Ketogenesis. Utilization and oxidation of ketone bodies in extrahepatic tissues. Ketonemia and ketonuria. Ketoacidosis during fasting and diabetes.

34. Fatty acids biosynthesis. Citrate shuttle. Role of acetyl-CoA carboxylase. Acylsintase – multifunctional enzyme. Desaturation of fatty acids. Essential fatty acids deficiency.

35. Metabolism (synthesis and degradation) of glycerophosphatides. Biological role of phospholipases A_1, A_2, C and D. Eicosanoid synthesis and biological activity. Cyclic and linear pathways of formation. COX-1 and COX-2 inhibitors. Sphingolipids – types, structure and importance. Sphingolipidoses.

36. Lipid metabolism disorders. Atherosclerosis, tissue ischemia and myocardial infarction. Obesity. Role of leptin in obesity. Fatty liver

37. General reactions of amino acids degradation: oxidative deamination, transamination, transdeamination, decarboxylation, biogenic amines. Clinical significance of aminotransferases.

38. Ammonia detoxification by glutamate dehydrogenase reaction, glutamine synthesis, urea cycle and ammoniagenesis. Role of the liver, muscles and kidneys in the detoxification of ammonia.

39. General pathways for degradation of amino acid C-skeletons. Glucogenic and ketogenic amino acids. One-carbon-atom residues – types, sources, importance. Role of the S-adenosyl methionine derivatives and folic acid derivatives. Therapeutic application of folate analogues. Phenylalanine and tyrosine catabolism – phenylketonuria, tyrosinosis, albinism, alkaptonuria. Tryptophan catabolism – pellagra.

40. Amino acids synthesis. Nonessential and essential amino acids. Common reactions in the synthesis of amino acids. Selenocysteine. Conversion of amino acids in specialized products – serine (ethanolamine, choline, phospholipids), tryptophan (NAD^+, serotonin, melatonin), tyrosine (thyroid hormones, catecholamines, dopamine, melanin), arginine (creatine phosphate, citrulline, nitric oxide, polyamines). Glutathione as a reducing agent and antioxidant. Products of glutamine and glutamate metabolism. Special features of amino acids metabolism in different tissues.

41. Impairment of amino acids metabolism. Enzymopathies associated with metabolism of tyrosine (phenylketonuria, tyrosinosis, alkaptonuria, albinism), tryptophan (pellagra) and aliphatic amino acids (methylmalonic acidemia). Parkinson's disease and L-DOPA. .

42. Purine nucleotide biosynthesis and degradation. Enzyme defects in purine metabolism (immunodeficiencies). Tissue specificity. Regulatory enzymes of biosynthesis. Purine analogues as antiviral agents. Hyperuricemia due to enzyme defects (Gout, Lesch-Nyhan syndrome). Xanthine oxidase inhibition.

43. Pyrimidine nucleotide biosynthesis and degradation. Regulatory enzymes. Allosteric response and orotic aciduria.

44. Iron metabolism. Iron-binding proteins. Iron absorption mechanism in cells. Transferrin receptors. Impaired iron homeostasis – iron deficiency anemia and iron overload. Iron, oxidative stress and neurodegenerative diseases. Post-translational control of iron metabolism.

45. Porphyrine biosynthesis. Cellular localization and regulation of the biosynthesis pathway. Types of porphyrias.

46. Hemoglobin degradation. Bile pigments. Transportation of bile pigments in the body. Jaundice. Types of jaundice.

47. Integration of metabolism. Interconnection between the metabolism of carbohydrates, lipids, amino acids and nucleotides. Role of key metabolites and key enzymes. Tissue and organ specificity. Adaptation during starvation.

48. DNA biosynthesis – enzymes. Replication mechanisms. Repair, reparation systems. Drugs affecting replication. Tumor suppressor genes and DNA repair.

49. Molecular mechanisms of cell cycle regulation. Cyclins and cyclin-dependent kinases. Regulation of synthesis and degradation of cyclins. Control mechanisms in different stages of the cell cycle. Role of p53 and pRB for overcoming the restriction points of the cell cycle.

50. Recombinant DNA technologies. DNA recombination. Role of restrictases, reverse transcriptase and chemical methods. DNA sequences identification – electrophoresis, Southern blotting. Sanger didesoxinucleotid method for DNA sequencing. DNA amplification: cloning, polymerase chain reaction (PCR).

51. Application of recombinant DNA technology in medicine. DNA polymorphisms. Identification of mutations by allele-specific analysis and PCR. Identification of variable number tandem repeats (VNTR). Production of human therapeutic proteins. Gene therapy. Transgenic animals.

52. Biosynthesis of different types RNA – enzymes. Inhibitors of RNA synthesis. Maturation of RNA molecules. Impairment of the maturation.

53. Prokaryotic and eukaryotic genes structure. Gene code. Protein biosynthesis – stages and enzymes. Inhibitors of protein biosynthesis

54. Regulation of gene expression in eukaryotes: at the DNA level, at the transcription level and at the translation level. Molecular diseases.

55. Principles of intercellular communication. Signal transduction. Organization and participants in signaling pathways. Types of extracellular signals. Membrane and intracellular receptors. Characteristics of signaling pathways – amplification, convergention and divergention. General principles of regulation – phosphorylation, adapter proteins and proteins with GTP-ase activity.

56. Secondary mediators in signal transduction. Types of secondary mediators. Cyclic AMP (cAMP) and adenylate cyclase system. Nitric oxide and cyclic GMP (cGMP). Calcium and calmoduline. Lipid mediators, products of phospholipid and sphingolipid degradation: inositol-3-phosphate, DAG, eicosanoids, ceramides and sphingosine-1-phosphate.

57. Role of protein kinases and protein phosphatases in signal transduction. Receptor and non-receptor protein tyrosine kinases. Receptor and non-receptor protein serine/threonine kinases. Protein kinase A. Protein kinase C, PKG, PI3K, MAPK phosphorylation cascade. Receptor and soluble protein tyrosine phosphatases.

58. Extracellular ligands interacting with plasma membrane receptors. Peptide hormones and catecholamines – hypothalamus-pituitary system, hormones of the adenohypophysis (anterior pituitary) and neurohypophysis (posterior pituitary), natriuretic hormone, renin-angiotensin system, calcitonin and parathyroid hormone, pancreatic hormones – insulin, glucagon and somatostatin; catecholamines.

59. Extracellular signals interacting with the plasma membrane receptors. Growth factors – epidermal growth factor (EGF), platelet-derived growth factor (PDGF), fibroblast growth factors (FGFs), insulin-like growth factors (IGFs), transforming growth factors (TGFs). Cytokines – interleukins (ILs), interferons (INFs), erythropoietin, tumor necrosis factors (TNFs).

60. Types of plasma membrane receptors. Receptors associated with ion channels. Receptors linked to G-proteins. Receptors with tyrosine kinase activity. Receptors associated with functions of other tyrosine kinases. Receptors with tyrosine phosphatase activity. Receptors with serine kinase activity. Receptor guanylate cyclases.

61. Extracellular signals interacting with intracellular receptors. Steroid hormones. Types and biological activity. Synthesis of steroid hormones in adrenal cortex and gonads. Thyroid hormones – synthesis and biological activity. Vitamin D3 – synthesis and biological activity. Retinoic acid – biological activity. Types of intracellular receptors. Type I receptors – glucocorticoid, mineralocorticoid, androgen and progesterone receptors. Type II receptors – for thyroid hormones, vitamin D3 and retinoids. Anti-inflammatory effects of glucocorticoids by inhibiting NF-kB-dependent signaling pathway. Antiestrogens.

62. Apoptosis – molecular mechanisms and biological role. Internal and external pathways of apoptosis. Signals of death-receptors. Role of caspases in apoptosis. Anti-apoptotic signals for cell survival – role of PI3K and PKB/Akt. Regulation and clinical significance of programmed cell death.

63. Molecular mechanisms of oncogenesis. Tumor cells features. Tumor markers. Factors causing cancers. Direct carcinogens and pro-carcinogens. Pro-carcinogen metabolic activation. Stages of chemical carcinogenesis. Oncogenes and proto-oncogenes. Mechanisms of transformation of

oncogenes into proto-oncogenes. Oncogenes and growth factors. Oncogenic viruses. Oncogenes and signal transduction. Tumor-suppressor genes. Mechanisms of tumor cell progression and metastasis. Telomerase and cancer. Anticancer therapy drugs – mechanism of action. P-glycoproteins.

64. Pathobiochemical mechanisms of *Diabetes mellitus*. Classification. Type I diabetes (T1D)and Type II diabetes (T2D) and impaired glucose tolerance. Metabolic disorders and complications of T1D and T2D. Insulin resistance. Diabetes and obesity. Biochemical indicators in the diagnosis of diabetes.

65. Mechanisms of cellular adhesion. Types of adhesion molecules. Biological role of adhesion molecules involved in leukocyte transendothelial migration in inflammation. Participation of integrins in cell signals of angiogenesis and cell proliferation. Integrin receptors and cell proliferation. Cytoskeleton and cell adhesion. Types of cell contacts. Actin and actin filaments – assembly regulation of actin filaments. Clinical significance.

66. Extracellular matrix (connective tissue). Types and functions of structural proteins. Types and functions of proteoglycans and glycosaminoglycans. Diseases due to mutations in genes for structural proteins. Mucopolysaccharidosises.

67. Bones as a mineralized connective tissue. Chemical composition of bones. Osteoblasts, osteocytes and osteoclasts – role in the formation and remodeling of bones. Biochemistry of ossification and bone resorption. Regulation of bone metabolism. Metabolic and genetic disorders affecting the bones. Biochemistry of cartilage. Calcium metabolism and factors influencing the calcium homeostasis.

68. Blood biochemistry. Characteristics of plasma proteins. Acute-phase protein – albumin. Acute-phase proteins: haptoglobin, ceruloplasmin, antiproteases – α_1-antitrypsin and α_2-macroglobulin, complement, C-reactive protein. Disorders in synthesis and metabolism of plasma proteins. Electropherogram and densitogram of serum proteins – clinical significance. |Blood coagulation system. Factors and regulation of blood coagulation.

69. Biochemistry of digestion. Food types and their biological value. Some clinical aspects of feeding. Digestion and absorption of carbohydrates. Digestion and absorption of lipids. Digestion and absorption of proteins. Processes in the colon. Secretor activity of the gastrointestinal tract. Disorders of digestion and absorption.

70. Biochemistry of the liver. Metabolic functions. Synthesis of specific products. Metabolism of xenobiotics.

M E D I C A L E T H I C S

Course of training: 2nd year
Semesters of training: IV semester
Examination: current assessment at the end of the IV semester
Classes: 30 hours
Lecturer: Associate Professor Maria Stoykova, DDM

ACADEMIC CURRICULUM

Forms of the classes	***Classes***				***Credits***
	weekly	***III sem.***	***IV sem.***	***Total***	
Lectures	1	-	15	15	***1,9***
Classes	1	-	15	15	
Total	***2 hours***	***-***	***30 hours***	***30 hours***	

ANNOTATION*:* Origin and nature of medical ethics. The physician's behavior with incurable and terminally ill patients. The problem of the death. Euthanasia. Medical mistakes. Ethical aspects of palliative care for terminally ill patients. Quality of life from and its value from the standpoint of bioethics. Experiments in medicine. Genetics and human reproduction.

AIM OF THE DISCIPLINE*:* Acquisition of the professional competence and attitudes of ethical and deontological problems in the work of the physician.

OBJECTIVES OF THE COURSE:

✓ Principles of medical ethics.

✓ Ethical guidelines in the practice of various medical specialties in the daily activities of the various categories of medical staff.

✓ Theoretical and practical formulation of concepts and values in medical ethics - informed consent, the structure of coping for personality, confidentiality, the truth and hope, iatrogeny, etc.

✓ Physician - Patient Relationship. Models of the physician – patient and other medical staff and prevention/resolve the conflicts between them.

✓ Patient rights.

✓ Ethical aspects in the implementation of palliative care for terminally ill patients and the process of dying.

✓ Euthanasia problems from the standpoint of bioethics.

✓ Deontological and legal responsibility of the physician in admission of medical errors.

✓ Discussion of documents from Helsinki and Tokyo, concerning experimental medicine and transplantation of vital organs. Bulgarian legislation on the issue.

✓ Ethical aspects of human reproduction and the new reproductive techniques; ethical issues of cloning.

TRAINING METHODS AND APPROACHES: Lecture presentations, discussions, case studies, role plays, small group works and individual works.

TECHNICAL FACILITIES AND EQUIPMENT FOR THE PURPOSE IN TEACHING: Multimedia, educational films, training programs.

CONTROL AND ASSESSMENT:

✓ Current assessment – test, case/ written or oral examination.

METHODS FOR CONTROL OF KNOWLEDGE: Test control, written classes, analyses and solution of problem situations and cases.

MANDATORY COMPETENCIES: Learning approaches for analyses, evaluation and management of the more important expressions of ethical issues in medical practice, contemporary interpretation of the concepts of quality and cost of living in order to implement strategies to manage style and way of life, overcoming of the risk factors; skills making for adequate medical and ethical decisions in difficult situations at clinical practice.

PROGRAMME OF THE LECTURES

1-st Lecture - ***Bioethics Introduction. Bioethics Topics: Advance Care Planning. Advance Directives.***

Medical Ethics or Bioethics***;*** History; Greek Hippocratic Oath; Several of the most prominent issues in medical ethics*:* research ethics, defining death, reproductive medicine; economic Issues; the Business of Medicine; The Science of Medicine; the art of Medicine;

How is advance care planning different from advance directive; What are the goals and expected outcomes of advance care planning; Who should I approach for advance care planning; When and where should I initiate advance care planning?

2-nd Lecture - ***Informed Consent. Confidentiality. Physician-Patient Relationship – models***

The elements of full informed consent. How much information is considered "adequate"; What sorts of interventions require informed consent. Informed Consent in the Operating Room Parental Decision Making: Maternal fetal conflict.

Where does the duty of confidentiality come from; What does the duty of confidentiality require; What kinds of disclosure are inappropriate; When can confidentiality be breached; What if a family member asks how the patient is doing. Cross-cultural Issues and Diverse Beliefs with an Emphasis in Pediatrics:; Do not Resuscitate Orders:

What is a fiduciary relationship; How has the physician - patient relationship evolved; Four models of the physician – patient relationship; Will the patient trust me if I am a student; Managed care: What is "managed care"; What do "capitation" and other managed care systems involve; What ethical concerns does managed care raise;

3-rd Lecture –***Medical principles of bioethics***. ***Mistakes***

The commonly accepted principles of health care ethics include: respect for autonomy; nonmaleficence; the principle of beneficence; justice.

How do mistakes occur; Do physicians have an ethical duty to disclose information about medical mistakes to their patients; How do I decide whether to tell a patient about an error; Won't disclosing mistakes to patients undermine their trust in physicians and the medical system; By disclosing a mistake to my patient, do I risk having a malpractice suit filed against me? What if I see someone else make a mistake

4-th Lecture – *Patients right. Law and Medical Ethics. The Relationships between Law and Medical Ethics. Professionalism.*

Declaration on the Rights of the Patient; Declaration of Physician Independence and Professional Freedom. Law and Medical Ethics: Definitions - Sources of Authority; Roles of Medical Ethics and the Law ; How can I find out what the law says on a particular subject; The Relationships Between Law and Medical Ethics. Professionalism*:* What does it mean to be a member of a profession; What is the difference between a profession and a business; What are the recognized obligations and values of a professional physician; Is professionalism compatible with the restrictions sometimes placed on physician's judgments in managed care;

5-th Lecture - *End of Life Issue. Breaking Bad News Euthanasia*

What is a "good death"? What goals should I have in mind when working towards a decent death for my patient; How do you know when someone is dying; Palliative care. What should I know about the hospice approach; What you need to understand to care for the dying; How do physicians who care for the dying deal with their own feelings; Robert Buckman's Six Step Protocol for Breaking Bad News; Spirituality and Medicine. Termination of Life - Sustaining Treatment. Truth-telling and Withholding Information.

6-th Lecture – *Moral aspects of the human reproduction.*

Moral problems in conection with reproduction – contraception; abortion. Infertility – artificial insemination. In –vitro fertilization. Genetics and human reproduction.

7-th Lecture - *Cloning*.

Sheep cloning. Social debate about Dolly's cloning. What type of cloning has future? Benefit of human cloning.

PROGRMME OF THE CLASSES

1rst exercise - *Informed Consent.*

- What is informed consent?
- The goals and elements of the full informed consent.
- Parental Decision Making.
- Who has the authority to make decisions for children?
- What if parents are unavailable and a child needs medical treatment?
- Maternal - fetal conflict.

2nd exercise – *Confidentiality*.

- Objectives of four levels of medical secret.

- Cross-cultural Issues and Diverse Beliefs with an Emphasis in Pediatrics - cases.
- What kinds of treatment can parents choose not to provide to their children?
- Can a patient demand that I provide them with a form of treatment that I am uncomfortable providing?
- Can parents refuse to immunize their children?

3rd exercise - ***Medical mistakes. Professionalism.***

- Two types of medical mistakes
- Should you tell the parents about your mistake?
- The relationship between Low and Medical Ethics - cases.
- Professionalism - cases.
- Public Health Ethics - cases.

4th exercise - ***End of Life Issues***.

- Robert Buckman's Six Step Protocol for Breaking Bad News;
- Palliative care – cases
- Euthanasia – definition, types, legislation and cases.
- Physician-Assisted Suicide-cases.
- Termination of Life-Sustaining Treatment - cases.
- Truth-telling and Withholding Information.

5th exercise - ***Physician-Patient Relationship.***

- Models of the physician-patients relationship - cases.
- Spirituality and Medicine – cases.
- Managed care - cases.

6th exercise - ***Patient rights.Ethics Committees and Ethics consultation.***.

- Patient rights - declarations
- The goals of ethics committees
- What does an ethics committee does;
- Who becomes a member of an ethics committee;
- What is the difference between an ethics committee and an ethics consultant;
- Futility - cases.

7th exercise - ***Moral aspects of the human reproduction. Cloning.***

- Moral problems in connection with contraception and abortion – cases
- Moral problems in connection with infertility - cases
- Moral problems in connection with cloning.

CONSPECTUS OF BIOETHICS

1. Bioethics Introduction - Definition; History; Principles.
2. Bioethics Topics: Advance Care Planning. Advance Directives.
3. Informed Consent.
4. Parental Decision Making. Maternal fetal conflict.
5. Physician - Patient Relationship - models. Professionalism.
6. Managed care. Public Health Ethics.
7. Medical principles of bioethics.
8. Confidentiality.
9. Cross-cultural Issues and Diverse Beliefs with an Emphasis in Pediatrics.
10. Do not Resuscitate Orders. Termination of Life-Sustaining Treatment
11. Mistakes. Law and Medical Ethics.
12. The Relationships between Law and Medical Ethics.
13. Truth-telling and Withholding Information. End of Life Issues. Breaking Bad News.
14. Euthanasia.
15. Spirituality and Medicine.
16. Patient rights.
17. Ethics Committees and Ethics consultation. Futility.
18. Moral aspects of the human reproduction.
19. Cloning.

References:

1. Bioethics topics – University of Washington School of Medicine, 2010.
2. Doyle D, Hanks GWC, MacDonald N. et al. Oxford Textbook of Palliative Medicine- *2nd edition*. Oxford University Press, New York, 1997.
3. Jivkova Chr. Biomedical ethics. Publishing house „East – West", Sofia, 2008.
4. Lecture course in bioethics. Lecturer: Associate Professor dr. M. Stoikova, 2012.
5. Reich WT et al. Encyclopedia of Bioethics (Revised Edition). Simon Schuster and MacMillan, New York , 1995.

MEDICAL UNIVERSITY - PLOVDIV

FACULTY OF MEDICINE

PROGRAMME

IN

BIOSTATISTICS

Prepared by Prof. R. Stefanov, MD, PhD on 14 June, 2012

Approved by the Departmental Council on 15 June, 2012

Confirmed by the Faculty Council on…...……., 2012

MEDICAL UNIVERSITY – PLOVDIV

FACULTY OF MEDICINE

COURSE NAME
BIOSTATISTICS

TYPE OF COURSE ACCORDING TO THE UNIFORM STATE REQUIREMENTS
Mandatory

LEVEL OF EDUCATION:
Master degree /MSc/

FORM OF EDUCATION:
Lecture courses, practical courses, self-training.

SEMESTERS OF EDUCATION:
4th semester

AUDITORIUM CLASSES:
15 hours of lecture courses, 15 hours of practical courses

TECHNICAL EQUIPMENT APPLIED IN THE TRAINING:
PC, Multimedia and statistical software

TRAINING METHODS: lecture courses, practical courses, additional tutorial hours

CONTROL AND EVALUATION:

- ✓ *Ongoing evaluation* – weekly tests, oral examinations
- ✓ *Final evaluation* – combined: written part – solving a biostatistics problem and oral examination

Score assessment
Weekly tests
Semester exam:
Yes /written and oral examination/
State Exam
No
Lecturer
Prof. Rumen Stefanov, MD, PhD – Full Professor at the Department of Social Medicine and Public Health
Department:
Social Medicine and Public Health

ANNOTATION

Conceptual overview of statistical methods with emphasis on applications commonly used in medical research. Basic Biostatistical concepts. Key stages and general requirements for conducting a scientific study. Application of essential statistical analyses in the processing of medical data.

COURSE OBJECTIVES: The objective of the Biostatistics course is to develop:

1. Basic knowledge of the medical statistics' general theory.
2. The ability to apply the statistical methods in medicine.
3. Skills for right interpretation of the studies that are reported in scientific journals, as well as the capacity to perform such analyses.
4. Practical skills and to be trained in essential PC techniques by using statistical software products with medical application.

COURSE TASKS:

Proficiency in the most important properties of the Biostatistics' nature, functions, scopes and purposes in particular:

- providing a better understanding and exact description of medical phenomena;
- proper and efficient planning of a statistical inquiry in the field of medical science;
- collecting an medical data;
- presenting complex data in a suitable tabular and graphic form for an easy and clear comprehension of data;
- understanding the nature and pattern of variability of a phenomenon through scientific observations;
- drawing valid inference, along with a measure of their reliability about the population parameters from the sample data

OBLIGATORY COMPETENCIES:

1. *Theoretical knowledge* – mastering:

- the basic Biostatistics analyses;
- the comparison between past and present results with a view to ascertain the reasons for changes in the future;
- formulation and hypothesis testing; development of scientific theories.

2. *Practical skills:*

- real-life data manipulation;
- applying suitable methods of comparison;
- testing various hypothesis by appropriate/ statistical tools;
- have experience in using statistical software;
- understanding and interpreting the scientific study's results.

CURRICULUM

Type of courses	*Course hours*				*Credits*
	Every second week	*III semester*	*VI semester*	*All*	
Lecture courses	2	-	15	15	***1,8***
Practical courses	2	-	15	15	
All	***4 hours***		***30 hours***	***30 hours***	

PROGRAMME IN BIOSTATIOSTICS

FOURTH SEMESTER

№	LECTURE COURSES	HOURS	DATE
1.	Methodology of medical investigations	2	
2.	Biostatistics – definition, nature, functions, scopes, aim and purposes	2	
3.	Inferential statistics – sample size, types and sources of data, hypothesis, power	2	
4.	Basic statistical concepts – error, significance. Types of variables and their graphic presentation	2	
5.	Descriptive Statistics – mean, median, mode, standard deviation, standard error of the mean, confidence interval	3	
6.	Crosstabulation – percentage distribution, standard error of proportion, confidence interval. Cross tabulation – chi square, Fisher's exact test	2	
7.	Correlation analysis	2	

TOTAL 15 – hours

PROGRAMME IN BIOSTATISTICS

FOURTH SEMESTER

№	PRACTICAL COURSES	HOURS	DATE
1.	Methodology of medical investigations. Biostatistics – definition, nature, functions, scopes, aim and purposes	2	
2.	Inferential statistics – sample size, types and sources of data, hypothesis, power	2	
3.	Basic statistical concepts – error, significance. Types of variables and their graphic presentation	2	
4.	Descriptive Statistics – mean, median, mode, standard deviation, standard error of the mean, confidence interval	3	
5.	Crosstabulation – percentage distribution, standard error of proportion, confidence interval. Cross tabulation – chi square, Fisher's exact test	2	
6.	Correlation analysis	2	
7.	Time series analysis of medical events	2	

TOTAL – 15 hours

LECTURE COURSE SYLLABUS

LECTURE №1 – 2 hours. Methodology of medical investigations.

Planning and organization – main phases. Conduction of the investigation – objects and units of observation; indices, place, time, type, plan, team, administration of the study. Data processing and analysis of results - statistical analyses, information managing, statistical tables.

LECTURE №2 – 2 hours. Biostatistics – definition, nature, functions, scopes, aim and purposes.

Why Biostatistics? The role and relevance of statistics. What exactly is statistics? Reasons for Understanding Statistics. How can a statistician help medical science?

LECTURE №3 – 2 hours. Inferential statistics – sample size, types and sources of data, hypothesis, power.

Population and sample. Sample size calculations. Paired and unpaired data. Sources of information. Probability. Null Hypothesis and Alternative Hypothesis. Statistical power.

LECTURE №4 – 2 hours. Basic statistical concepts – error, significance. Types of variables and their graphic presentation.

Type I and Type II Errors. Statistical significance. Variable types – nominal, ordinal, interval and ratio variables. Graphic Presentation – histogram, scatterplot, dot plot, box plot, line chart and pie chart. Normal distribution, skewness, kurtosis. Logarithms.

LECTURE №5 – 3 hours. Descriptive Statistics – mean, median, mode, standard deviation, standard error of the mean, confidence interval.

Why Do We Need Descriptive Statistics? Averages. Standard deviation. Mean and SD. The Empirical Rule – Three Sigma rule. Standard Error of Mean. Central Limit Theorem. T-test.

LECTURE №6 – 2 hours. Crosstabulation – percentage distribution, standard error of proportion, confidence interval. Cross tabulation – chi square, Fisher's exact test.

Tables of frequency distribution. Crosstabulation. 2x2 tables. Statistics in Crosstabulation Tables - Pearson Chi-square and Yates Correction of Chi-square. Fisher Exact Test.

LECTURE №7 - 2 hours. Correlation analysis AND REGRESSON ANALYS. ANOVA.

The notion of response and predictor variables. Negative and positive correlation. Simple Linear Correlation (Pearson r). Nonparametric Correlation (Spearman r). Linear Regression. Multiple Regression. Interpolation and Extrapolation. ANOVA.

PRACTICAL COURSE SYLLABUS

PRACTICAL №1 – 2 hours. Methodology of medical investigations. Biostatistics – definition, nature, functions, scopes, aim and purposes.

Main stages of statistical survey. Planning and execution.. Compilation of statistical material and registration. What are the two kinds of statistical observation? Partial statistical observation and material selection patterns.

PRACTICAL №2 – 2 hours. Inferential statistics – sample size, types and sources of data.

Traits of monitoring and units of observation. General population and representativeness of the data. Sample size. Data management and classification. Statistical tables. Statistical analysis.

PRACTICAL №3 - 2 hours. Basic statistical concepts – error, significance. Types of variables and their graphic presentation.

Examples from Bulgarian and foreign literature (real-life medical studies) – Type I and Type II Errors; statistical significance; variable types – nominal, ordinal, interval and ratio variables; graphic presentation – histogram, scatterplot, dot plot, box plot, line chart and pie chart; and data distribution – normal, skewness, kurtosis.

PRACTICAL №4 - 3 hours. Descriptive Statistics –;. Confidence interval. Hypothesis and power.

Variation Analysis – how to calculate mean, median, mod, standard deviation, standard error of the mean and Alternative analysis – how to calculate percentage distribution, standard error of proportion. Algorithm for Confidence interval calculation and test of working (Null) Hypothesis for both analyses.

PRACTICAL №5 – 2 hours. Crosstabulation– chi square.

Nonparametric Hypothesis Test. Limitations and advantages in comparison with parametric methods. Pearson's Chi-square Test – contingency tables.

PRACTICAL № 6 – 2 hours. Correlation analysis.

Association and correlation. Correlation coefficient calculation methods. Correlation coefficient rank evaluation. Application of Z-transformation for determining the range of the

confidence interval of the mean for the population. Test of working hypothesis – comparison between two correlation coefficients. Required number of cases – representative sample.

PRACTICAL №7 – 2 hours. Time series analyses of medical events.

Time series analyses – key elements and basic requirements. Trends in phenomena changes. Curve fitting - the line of best fit or trend line. Method of the least squares. Main characteristics of seasonal fluctuations. Simple Average Method and Adjusted Mean for calculating the seasonal index.

SYLLABUS IN BIOSTATISTICS

1. Biostatistics – definition, aim, tasks, Plan and organization of a statistical investigation
2. Inferential statistics and sampling, Basic statistical concepts – hypothesis, power
3. Basic statistical concepts – error, significance. Type of variables and their graphical presentation
4. Descriptive statistics – mean, median, mode. Descriptive statistics – standard deviation, standard error of the mean, confidence interval
5. Cross tabulation – percentage distribution, standard error of proportion, confidence interval. Cross tabulation – chi square, Fisher exact test
6. Correlation analysis
7. Analysis of Time Series.

Recommended literature:

1. Introductory Biostatistics. Chap T. Le. 2003. John Wiley and Sons, Inc., Publication.
2. Biostatistics A Methodology for the Health Sciences. Gerald Van Belle, Lloyd D. Fisher, Patrick J. Heagerty, Thomas Lumley. 2004. John Wiley and Sons, Inc., Publication.
3. New Developments in Biostatistics and Bioinformatics. Jianqing Fan, Xihong Lin, Jun S. Liu. 2009. Higher Education Press.
4. Basic Biostatistics. Robert C. Elston, William D. Johnson. 2008. John Wiley and Sons, Ltd., Publication.
5. Lecture course
6. Manual in Biostatistics
7. Internet sources:
    a. http://www.statsoft.com/textbook/time-series-analysis/
    b. http://www.animatedsoftware.com/statglos/statglos.htm#random_sample
    c. http://onlinestatbook.com/stat_sim/

M I C R O B I O L O G Y

Course of education: 2nd and 3th course
Semester of education: IVnd and Vth term
Exam: After Vth semester
Total: 135 hours
Lecturer and Examinator: Prof. Marianna Murdjeva, MD, PhD

Plan of education

Type of studies	***Horarium***				***Credits***
	Weekly	***IV sem.***	***V sem.***	***Total***	
Lectures	2/2	30	30	60	
Practical exercises	3/2	45	30	75	***9,6***
Total	***5/4 hours***	***75 hours***	***60 hours***	***135 hours***	

ANNOTATION: Microbiology is a study discipline that acquainted the students with morphological and biological characteristics of microorganisms, particuliarity in the development of infectious process, specific and non-specific immune defense mechanisms, prophylaxis and control of infections.

AIM OF DISCIPLINE: The aim of education of microbiology is:

1. To acquaint the medical students with the characteristics of the most important for humans microorganisms and with the methods for microbiological diagnosis.
2. To build knowledge and skills for correct clinical interpretation of microbiological results.
3. Mastering of principles of antimicrobial chemotherapy.
4. Mastering of methods of immunoprophylaxis and immunotherapy of infectious diseases.

TASKS OF THE DISCIPLINE:

- ✓ Introduction to morphology, physiology and pathogenic factors of microorganisms with medical importance for human pathology;
- ✓ Study of route of origin and course of infectious disease;
- ✓ Study of defense mechanisms – innate immunity and adopted immunity and principles of immunoprophylaxis and immunotherapy of infectious diseases;
- ✓ Antimicrobial chemotherapy – study of mechanisms of action of the main groups and representatives of antimicrobial agents as well as the mechanisms for development of bacterial resistance;
- ✓ Study of microbiological diagnosis of infectious diseases; structure and the role of microbiological laboratory in etiological diagnosis of infectious diseases; skills for correct clinical interpretation of laboratory results;

- ✓ Study of the role of environment for spreading out of infectious agents and microbiological control of environment – principles of disinfection and sterilization.

METHODS OF EDUCATION: lectures, practical classes, seminars, circle groups

TECHNICAL EQUIPMENT APPLIED IN EDUCATION: multimedia, microscopes, slide show.

CONTROL AND EVALUATION:

- ✓ *Continuous control* – oral examination, tests, seminars
- ✓ *Final control* – entrance test, written exam, conversation

METHODS FOR CONTROL OF KNOWLEDGE: tests, oral examination

OBLIGATORY COMPETENCES:

- ✓ *Theoretical knowledge* of students – to know:
  - morphology, physiology and genetics of the main groups of microorganisms;
  - methods and means for disinfection and sterilization;
  - action of antibiotics and mechanisms of bacterial resistance;
  - theoretical base of immunity, immunoprophylaxis and immunotherapy;
  - characteristics of medically important pathogenic and indigenous flora and their diseases;
- ✓ *Practical skills* of the students:
  - elaboration of stained microscope preparations;
  - ability to work with immersion microscope;
  - reading and interpretation of antibiograms;
  - interpretation of results from microbiological examination;
  - reading and interpretation of some immunological reactions

LECTURE PROGRAM

LECTURE №1 – 2 hours: Subject, tasks and historical development of microbiology. Introduction in general microbiology.

Introduction. Subject, aims, historical development and achievements of microbiology. Taxonomy of microorganisms. Characteristics of different groups of microorganisms: Eukaryotes and Prokaryotes.

LECTURE №2 – 2 hours: Morphology and structure of microorganisms.

Morphology of microorganisms: size and shape of microorganisms; structure of bacterial cell. Methods for examining of morphology and structure of bacteria, fungi, mycoplasmae and viruses.

LECTURE №3 – 2 hours: Bacterial physiology

Chemical composition of bacteria: water, minerals, proteins, carbohydrates, lipids, nucleic acids.Their role for biology and for diagnosis, pathogenesis and therapy of infectious diseases. Bacterial enzymes. Bacterial metabolism: catabolic processes. Different bacteria according to their mechanism of biological oxygenation. Anabolic processes (assimilation). Assimilation products and their role in pathogenesis, diagnosis and therapy of infectious diseases. Bacterial

growth and bacterial propagation. Principles of cultivation (in vitro) and nutrition requirements of bacteria. Prototrophs and auxotrophs.

LECTURE №4 – 2 hours: Bacterial genetics.

Genotype and phenotype of viruses, phages and bacteria. Bacterial genome – chemical composition, structure and functions. Plasmids (extrachromosomal elements). Types of plasmids and their role. Bacteriophages – structure, temperate phage, lytic phage, importance. Heredity and mutability in microorganisms – definition of the concepts. Importance of recombination and mutations in bacteria for biology and medical practice. Gene engineering-role in theory and medical practice.

LECTURE №5 – 2 hours: Sterilization and disinfection. Role of the environmental factors on microorganisms.

Sterilization. Methods of sterilization. Influence of chemical factors on microorganisms. Mechanisms of action. Olygodynamics. Disinfection. Disinfection agents. Influence of biological factors on microorganisms. Influence of physical factors on microorganisms: heat, drying, light, atmospheric pressure, osmotic pressure, radiation.

LECTURE №6 – 2 hours: Antimicrobial agents and antimicrobial therapy of infectious diseases.

Antimicrobial agents. Main groups and mechanisms of action. Mechanisms of resistance to antimicrobial agents. Antibiotic susceptibility tests.

LECTURE №7 – 2 hours: The Doctrine of infection. Characteristics and forms of the infectious process. The role of microorganisms in the infectious process. Pathogenic factors.

Correlation between macro- and microorganisms - mutualism, commensalisms, parasitism, saprophytism. Infection, infectious process, infectious disease - definition. The role of microorganism in infectious disease: pathogenicity, virulence-infectious doses, contagiousity, invasiveness, toxigenity. Pathogenic factors: factors of invasion-types, mechanisms of action; factors of aggression - endo- and exotoxins. Mechanisms of action.

LECTURE №8 – 2 hours: The role of environment for emerging of the infectious process. Epidemiological process. Factors and mechanisms of transmission of the infectious agents in the epidemic process.

Pathogenesis of the infectious process - entry, spread, localization of infectious agents. Defense of the host. Forms of infectious disease: exogenous and endogenous. Primary, reinfection, secondary: superinfection, coinfection; local and generalized infection; focal infection; septicemia, bacteriaemia, viraemia, toxemia, pyaemia. Types of septicemia - transient, obligatory, sepsis- SIRS (Systemic inflammatory reaction syndrome). The role of the microorganism in the infectious process. The role of the environment for emerging and cours of the infectious process. Epidemic process - factors and mechanisms. Characteristics of epidemic process: source of infection, mechanism of transmission and susceptible individuals.

LECTURE №9 – 2 hours: Innate immunity. The protective role of skin, mucous membranes, organs and normal microbial flora. Humoral and cellular factors of innate immunity. Phagocytosis, inflammation.

Defense mechanisms of the host - innate immunity and adopted immunity. The protective role of skin, mucous membranes, secretions, resident microbial flora. Cellular factors of

innate immunity. Phagocytosis. Inflammation. Humoral factors of innate immunity - lysozyme, complement system, interferons and cytokines, acute phase proteins.

LECTURE №10 – 2 hours: Immunity (host defense against foreign aggression). Antigens and antibodies.

Antigens: characteristics of antigens; antigen determinants (epitopes), valency of antigens; different antigens of microorganisms. Structure of antibodies. Immunoglobulin classes and their function.

LECTURE №11 – 2 hours: Adoptive immunity. Specific humoral and cellular immunity. Immunological tolerance.

The anatomy and structure of immune system. Central and peripheral organs. Cells of immune system - T and B lymphocytes. CD markers - subpopulations, origin, role in immune reaction. Cell immunity - forms. Humoral immunity. Beginning and development of immune response; cell cooperation. Primary and secondary immune response. Genetic control and regulation of immune response. HLA-system. Immunological tolerance - mechanisms.

LECTURE №12 – 2 hours: Immune pathology; immunodeficiency and autoimmune diseases.

Immunopathology. Immunological reactions and diseases. Immunological tolerance. Autoimmune diseases. Immune deficiencies - disorders and diseases. Infectious diseases of the immune system.

LECTURE №13 – 2 hours: Allergy - definition and forms.

Allergy - definition and forms. Immediate allergic reactions - anaphylaxis, atopy, clinical significance. Cytotoxic allergic reactions. Allergic phenomena due to immune complexes - serum sickness, Arthus phenomenon, clinical significance. Delayed type hypersensitivity - Koch phenomenon, contact dermatitis. Clinical significance.

LECTURE №14 – 2 hours: Immune prophylaxis and immune therapy.

Immune prophylaxis and immune therapy. Vaccines and sera. Immunomodulation.

LECTURE №15 – 2 hours: Antigen-antibody reactions: agglutination, precipitation, neutralization, complement fixation test. Labelled immune reactions – immunofluorescence, radioimmune, enzyme-immune test, Western blot. Mechanism and practical application of the reactions in microbiological diagnosis.

Antigen-antibody reactions: agglutination, precipitation, neutralization-toxin, antitoxin, ASO, virus-neutralization test. Complement fixation test. Labeled immune reactions - immunofluorescence, radioimmune and immunoenzyme tests, Western blot. Hybridoma biotechnology. Monoclonal antibodies. Their significance in the diagnosis of infectious diseases.

LECTURE №16 – 2 hours: Microbiological diagnosis of infectious diseases. Staphylococci. Streptococci.

Microbiological diagnosis of infectious diseases-collection, transport and examination of specimens, interpretation of results. Family Micrococcaceae. Genus Staphylococcus: S. aureus. Genus Streptococcus: S. pyogenes.

LECTURE №17 – 2 hours: Streptococcus pneumoniae. Mycobacterium tuberculosis. Mycobacterium leprae. Causative agents of atypical mycobacteriosis.

Genus Streptococcus: S. pneumoniae. Family Mycobacteriaceae. Genus Mycobacterium: M.tuberculosis, M. leprae.

LECTURE №18 – 2 hours: Corynebacterium spp., Bordetella spp., Haemophillus spp., Neisseria spp.
Genus Corynebacterium: C. diphtheriae. Genus Haemophillus: H. influenzae. Genus Neisseria: N. meningitidis, N. gonorrhoeae.

LECTURE №19 – 2 hours: Anaerobes - Clostridium tetani, gasgangrene species, Clostridium botulinum. Non-spore forming anaerobes.
Family Bacillaceae. Genus Clostridium: C. tetani, C. perfringens, C. novyi, C. difficile, C. septicum, C. histolyticum, C. botulinum.

LECTURE №20 – 2 hours: Infections with high biological risk - Yersinia pestis, Vibrio cholerae, Bacillus anthracis, Francisella tularensis, Legionella spp., Brucella spp.
Genus Yersinia: Y. pestis, Y. enterocolitica, Family Vibrionaceae, Genus Vibrio: V. cholerae biotype cholerae, V. cholerae biotype eltor, Genus Bacillus: B. anthracis, Genus Francisella: F. tularensis, Genus Legionella: L. pneumophila, Genus Brucella.

LECTURE №21 – 2 hours: Facultative pathogenic enteric bacteria – E. coli, Klebsiella spp., Proteus spp., etc.
Family Enterobacteriaceae - general characteristics. Escherichia coli, Klebsiella spp, Enterobacter spp., Serratia spp., Proteus spp., Providentia spp., Morganella spp. – morphology, biology, biochemical production, pathogenic factors, diseases, microbiological diagnosis.

LECTURE №22 – 2 hours: Pathogenic enteric bacteria – Shigella spp., Salmonella spp., Salmonella typhi, Salmonella paratyphi A and B, causative agents of food poisoning.
Causative agents of bacterial dysentry-classification. Morphology, biology, biochemical production. Antigenic composition. Pathogenesis and immunity. Microbiological diagnosis. Salmonella spp. General characteristics – morphology, biology, biochemical production. Antigenic composition and Kauffmann-White classification. Pathogenic factors. Diseases – typhoid and paratyphoid fevers, food poisoning by non-typhoid salmonella spp. Pathogenesis and immunity. Microbiological diagnosis. Specific prophylaxis and therapy in salmonella infections. Salmonellae as causative agents of food poisoning.

LECTURE №23 – 2 hours: Spirochetes. The causative agents of syphilis. The causative agent of relapsing fever. The causative agent of Lyme disease. Leptospira spp.
Order Spirochetales. Genus Treponema. Etiologic agents of human diseases - syphilis, Yaws, pinta. Epidemiology, laboratory diagnosis, treatment, prevention and control. Genus Borrelia - human diseases, morphology, laboratory diagnosis, epidemiology, treatment, prevention and control. Genus Leptospira: species, morphology, physiology, laboratory diagnosis.

LECTURE №24 – 2 hours: Mycoplasma spp., Chlamydia spp., Rickettsia spp., Coxiella spp., Erlichia spp., Bartonella spp.
Family Mycoplasmataceae. Genus Mycoplasma: M. pneumoniae, M. hominis. Family Chlamydiaceae. Genus Chlamydia: C. trachomatis, C. pneumoniae, C. psittaci. Family Rickettsiaceae. R. prowazekii. Coxiella burnetii, Genus Erlichia and Genus Bartonella.

LECTURE №25– 2 hours: Pathogenic fungi - Candida spp., Cryptococcus spp., Aspergillus spp., Actinomycetes.

Fungi-differences between fingi and bacteria. Classes of fungi - yeasts, moulds, dimorphic. Medical problems, caused by fungi. Classification of human mycoses. Genus Candida - albicans and non-albicans species. Clinical syndromes of candidiasis. Microbiological diagnosis, treatment. Cryptococcus neoformans - morphology, serotypes, clinical syndromes, microbiological diagnosis, treatment. Genus Aspergillus-species, morphology, clinical presentation of the disease, microbiology diagnosis, treatment. Genus Actynomycetes - morphology of the species. A. israeli, A. naelsundii, A. bovis. Clinical forms of actinomycosis. Microbiological diagnosis. Antifungal agents.

LECTURE № 26 - 2 hours: Viruses - structure, characteristics, diagnosis. Picornaviruses
Viral structure. Taxonomy of viruses. Replication of viruses. Effect of viruses on host cell. Laboratory diagnosis and threatment of viral infections. Family Picornaviridae – classification. Genus Enterovirus - properties. Poliomyelitis and other enteroviral diseases – epidemiology; pathogenesis, clinical symptoms, laboratory diagnosis, treatment and prevention. Genus Rhinovirus.

LECTURE № 27 - 2 hours: Orthomyxoviridae, Paramyxoviridae.
Orthomyxoviridae. The causative agent of grippe. Paramyxoviridae. The causative agents of paragrippe, epidemic parotitis, measles. Respiratory syncitial virus.

LECTURE № 28 - 2 hours: Adenoviridae, Herpesviridae, Poxviridae.
Family Adenoviridae: Genus Mastadenovirus and Genus Aviadenovirus - structure and replication. Disease mechanisms and illness, associated with adenoviruses. Laboratory diagnosis. Epidemiology, prevention and treatment. Family Herpesviridae, Subfamily Alphaherpesvirinae: HSV-Hepres simplex type 1 and type 2 Genus Varicellovirus - Varicella zoster – (type 3). Subfamily Bethaherpesvirinae: Genus Cytomegalovirus - HHV-5 (CMV) and Genus Roseolovirus - Human herpes virus type 6 and type 7 viruses. Subfamily Gammaherpesvirinae: Genus Lymphocryptovirus - HHV - Epstein Barr virus (EBV) and Genus Rhadinovirus - HHV-8. Unique features of herpes viruses, disease mechanisms, clinical manifestation of infection. Laboratory diagnosis. Epidemiology and modes of control. Family Poxviridae: Genus Orthovirus - Variola virus and Genus Molluscipoxvirus - Molluscum contagiosum virus. Structure and disease, associated with poxviruses. Laboratory diagnosis. Vaccinia as a form of cowpox, used for the smallpox vaccination.

LECTURE № 29 - 2 hours: Togaviridae, Flaviviridae, Buniamviridae, Rhabdoviridae.
Family Togaviridae: Genus Alfavirus – structure, hosts, vectors, distribution, diseases, clinical prevention; Genus Rubivirus – Rubella virus - disease, congenital defects, epidemiology; Genus Arterivirus (not human pathogens). Family Flaviviridae: Genus Flavivirus - structure, replication, diseases, vectors, hosts, distribution, clinical presentation. Genus Pestivirus; Genus Planitvirus; Genus Hepacivirus – Hepatitis C and G viruses (HCV, HGV). Laboratory diagnosis, modes of control. Family Bunyaviridae. Members, vectors, hosts, clinical presentation, laboratory diagnosis and modes of control. Family Rhabdoviridae - Lyssa virus: structure, disease mechanisms, laboratory diagnosis, treatment and prophylaxis.

Lecture № 30 - ***2 hours. Hepatitis viruses. Human immunodeficiency virus (HIV) – the causative agent of AIDS (acquired immuno-deficiency syndrome)***

Hepatitis viruses transmitted via oral-fecal route (HAV, HEV) and parenteral route (HBV, HDV, HCV) – properties; pathogenesis of acute and chronic viral hepatitis; laboratory diagnosis; threatment and prevention. HIV- classification, structure, life cycle. AIDS – epidemiology; pathogenesis; clinical picture; laboratory diagnosis; treatment and prevention.

PROGRAM FOR PRACTICALS

EXERCISE №1 – 3 hours: Microscopy. Types of microscopes. Immersion-oil microscopic system. Wet-mount and Hanging-drop preparation.

AIM: To take a first-hand look at the microbiological laboratory. To learn rules of immersion-oil microscopy, wet-mount and hanging-drop preparation techniques.

DEMONSTRATION OF: Structure, equipment and working rules in microbiological laboratory. Preparation of wet-mount and hanging-drop slide.

PRACTICAL TASKS: Microscope examination by immersion-oil system of stained preparations of staphylococci, streptococci, enteric rods, yeasts (Candida spp.), vibrio and clostridia. Observing spiral microorganisms under dark-field microscope.

EXERCISE №2 – 3 hours: Simple staining methods Loeffler and Pfeiffer .

AIM: To learn techniques of preparation and staining of smears by methods of Loeffler and Pfeiffer.

DEMONSTRATION OF: Neisseria gonorrhoeae from urethral discharge, stained with methylene blue solution (Loeffler), Helicobacter pylori from gastral biopsy specimen, stained by Pfeiffer and Vibrio cholerae, stained also by Pfeiffer.

PRACTICAL TASKS: Preparation of a smear from a solid culture and staining it by Loeffler method and another smear from culture, grown in a liquid nutrient medium (broth), staining it by Pfeiffer method.

EXERCISE №3 – 3 hours: Differential staining methods – Gram and Neisser .

AIM: To learn the differential bacterial staining methods – Gram and Neisser.

DEMONSTRATION OF: A mixed microbial culture of staphylococci (Gram +) and enteric bacteria (Gram –), stained by Gram method. Examination of C. diphtheriae, stained by Neisser method.

PRACTICAL TASKS: Preparation and staining of a smear with a mixed culture of Gram (+) and Gram (–) bacteria by Gram. Staining by Neisser method a preparation of C. pseudodiphtheriticum.

EXERCISE №4 – 3 hours: Differential staining methods. Ziehl-Neelsen (acid-fast bacteria), Möller (spores) and Klett (capsules).

AIM: To learn differential bacterial staining methods – Ziehl-Neelsen, Möller and Klett.

DEMONSTRATION OF: M. tuberculosis from sputum, stained by Ziehl-Neelsen. Spores of B. anthracis, stained by Möller. Capsule of S. pneumoniae from blood, stained by Klett. Capsule of B. anthracis, stained by Klett.

PRACTICAL TASKS: Staining a preparation from sputum by Ziehl-Neelsen. Preparation of a smear from spore-forming bacteria (Bacillus spp.) and staining it by Möller.

EXERCISE №5 – 3 hours: Sterilization and Disinfection.

AIM: To learn methods for sterilization and disinfection of materials and areas.

DEMONSTRATION OF: Rooms for sterilization. Appliances: Koch steamer, hot air oven, autoclave and sterilization control rules, UV lamps. Devices and material for sterilization. The way of packing up devices for sterilization (swabs, tubes, petri dishes, pipettes, filters etc.). Different disinfectants – surface active agents, phenols, halogens, aldehydes, alcohols, metalic salts, dyes. Methods for control of disinfection.

EXERCISE №6 – 3 hours: Seminar. Subjects: Morphology, physiology of microorganisms and microbial genetics.

AIM: To confirm theoretical knowledge in reading material.

Test and questions on the material.

EXERCISE №7 – 3 hours: Bacterial growth. Nutrient media. Isolation of pure culture.

AIM: To learn the constituents of the bacteriological culture media; various artificial media in common use in the diagnostic laboratory, techniques of inoculation of agar plates (streak plate), tubed media, liquid media (broths) and semisolid media; aerobic and anaerobic cultures and methods for isolation of pure culture.

DEMONSTRATION OF: Different culture media and inoculation methods. Isolation of pure culture. Cultural characteristics of colonies – smooth (S) and rough (R) colonies. Examples. Ability of microorganisms to lyse red blood cells – α and β hemolysis on blood agar. Golden colonies of S. aureus. Streak plates, slants and broths, as well as EMB, Deoxycholate citrate agars and common agar with Gram (+) and Gram (–) bacteria. Pure and mixed cultures. Jars, pouches, incubators for cultivation of fastidious microorganisms.

PRACTICAL TASKS: Inoculation of streak plate, tubed media, broth and semisolid media with S. epidermidis and specimen from pus. Distinguishing smooth from rough colonies. Interpretation of α and β hemolysis on blood agar streak plate inoculation colonies. Exercise on flaming the loop and drowing the streak plate manipulation.

EXERCISE №8 – 3 hours: Biochemical activity of Bacteria.

AIM: To learn the methods for biochemical characterization and identification of bacteria.

DEMONSTRATION OF: Nutrient media for detection of biochemical activity of microorganisms: EMB, Deoxycholate citrate agar, Kligler. Tests for saccharolytic activity (detecting carbohydrate splitting enzymes): gas production in sugar containing media, methyl-red reaction (MR), Voges-Proskauer reaction. Tests for proteolytic activity: detection of indole in broth media, H_2S production, detection of urease activity, gelatin liquefaction, milk peptonization. Tests for decarboxylation and deamination of aminoacids (arginine, lysine,

ornitine). Tests for oxidase and catalase activity. Inoculated Kligler media with E. coli, Klebsiella spp., Salmonella spp., S. typhi, Shigella spp., Proteus spp., Vitek 2 system for identification of Gram (+) and Gram (–) bacteria. Variations of Api system for identification of microorganisms.

PRACTICAL TASKS: Reading lactose (+) and lactose (–) colonies, streaked on selective and differential media. Detection of indol reaction with Ehlich solution. Drawing indole (+) and indol (–) reactions. Detection of methyl-red reaction. Drawing of MR(+) and MR(–) results. Inoculation of pure cultures into Kligler medium.

EXERCISE №9 – 3 hours: Detection of bacterial pathogenic factors. Susceptibility test for detection of bacterial resistance to antimicrobial agents.

AIM: To learn methods of detecting the pathogenic bacterial factors and the technique for performing and reading an antibiogram.

DEMONSTRATION OF: Plasma – agglutination slide test (clumping test). Plasma-coagulase test. α and β haemolysis on 5% sheep blood agar. Inoculation of tetanus exotoxin in a mouse. S. pneumoniae and B. anthracis capsules in Klett stained preparations. Different panels with antibiotic disks, used in antibiograms, according to the causative agent and the site of isolation. Interpretation of zone inhibition according to CLSI criteria, considering the nature of infectious agent. E test interpretation and MIC results from Vitek 2 System panels.

PRACTICAL TASKS: Performing a plasma – agglutination test and drawing the result. Identifying and drawing the encapsulated bacteria in preparations, stained by Klett method. Performing antibiotic sensitivity disk diffusion test (Bauer-Kirby) and interpreting the results as S, I or R.

EXERCISE №10 – 3 hours: Basic Immunology. Antigens and antibodies and their interactions. Agglutination and precipitation.

AIM: To observe the morphology of cells, involved in the immune response. To learn mechanisms and performance of agglutination and precipitation tests.

DEMONSTRATION OF: Phagocytic cells-blood monocytes and polymorphonuclear neutrophils – blood smear, Giemsa stain. Lymphocytes and plasma cells, Giemsa stain. The NBT test for phagocytic activity of polymorphonuclear leucocytes. Phagocytic number and phagocytic index – Giemsa stain. Different agglutination and precipitation reactions – slide agglutination, tube agglutination, latex agglutination, Ascoli test, single radial immunodiffusion, Ouchterlony double diffusion, two dimensional immunoelectrophoresis, countercurrent immunoelectrophoresis.

PRACTICAL TASKS: Performance and reading of: slide and tube agglutination tests, co-agglutination test, ring precipitation test, direct and indirect haemagglutination tests, single radial and double immunodiffusion tests and immunoelectrophoresis. Drawing some of the cells, involved in the immune response.

EXERCISE №11 – 3 hours: Antigen-antibody reactions (continuation). Lysis. Complement fixation test (CFT). Neutralization (anti-streptolysin O test – ASO test).

AIM: To discuss and learn the scheme and principles of performing CFT, lysis and phenomenon of blocking and neutralizing effect of the antibodies.

DEMONSTRATION OF: The ingredients for CFT. The haemolytic system and its titration. Titration of complement. Wassermann reaction as the best known example for the use of CFT. The ASO test.

PRACTICAL TASKS: Reading CFT and ASO tests. Interpreting the results.

EXERCISE №12 – 3 hours: Immunological reactions with the use of labels – IFA, ELISA, RIA. Molecular biological methods in Microbiology and Immunology – DNA probes, Blotting techniques, PCR.

AIM: To learn principles, procedures and application of IFA, FACS, ELISA, RIA, DNA probes and PCR.

DEMONSTRATION OF: Direct IFA for detection of chlamydial elementary bodies in urogenital specimen – reading by fluorescent microscope. Indirect IFA for screening IgG antinuclear antibodies in serum by means of rat liver sections – reading by fluorescent microscope. Types of fluorescence. FACSorter dot-plot and histograms of T and B subpopulations. ELISA equipment – washing machine reader, ELISA plates, multichannel pipettes. ELISA for detection of antichlamydial antibodies in patient serum – reading optical density of positive and negative samples. Bands of amplified PCR product after agarose gel electrophoresis. Southern blot bands.

PRACTICAL TASKS: Drawing the elementary chlamydial bodies as seen under the fluorescent microscope in direct IFA from urethral specimen and the different patterns of immunofluorescence in rat liver cells. Reading of positive and negative ELISA tests.

EXERCISE №13 – 3 hours: Hypersensitivity reactions. Bioproducts – vaccines and sera.

AIM: To learn tests for diagnosis of hypersensitivity state. To get acquainted with the bio-products, used for specific prophylaxis and treatment of infectious diseases – vaccines and sera.

DEMONSTRATION OF: Anaphylaxic shock, performed on a guinea pig. Different bioproducts – vaccines and sera for prevention and treatment of infectious diseases. Doses and administration. Products for serological typing of microorganisms. A set for testing of hypersensitivity state.

PRACTICAL TASKS: Performing intracutaneous injections of diluted PPD (purified protein derivative) by means of a syringe and a needle into rabbits or guinea pigs (Mantoux test). Performing scarification procedure for testing hypersensitivity state before applying bioproducts.

EXERCISE №14 – 3 hours: Chlamidiae, Rickettsiae and Viruses – Nature, structure and methods of laboratory diagnosis.

AIM: To learn morphology, growth characteristics and methods of laboratory diagnosis of viruses, chlamydiae and rickettsiae.

DEMONSTRATION OF: McCoy tissue culture line – normal monolayer and with a cytopathic effect (CPE). Microscope preparations, stained with FITC labelled monoclonal antibodies (direct immunofluorescent test – IFA) for elementary bodies of chlamydiae. ELISA method for detection of virus particles and antibodies. Haemagglutination and haemagglutination inhibition tests in viral infectious, Weil-Felix reaction (antibody titre to Proteus OX-19 and OX-2) as a presumptive evidence of a rickettsial infection.

PRACTICAL TASKS: Drawing normal and with CPE tissue culture. Describing and drawing a scheme of a chicken embryo (allantoic and amniotic cavity, chorio-allantoic membrane, yolk sac) and inoculation places for rickettsiae, chlamydiae and viruses, according to their nature.

EXERCISE №15 – 3 hours: Recapitulation of practical skill and knowledge from the practical exercises 1 to 14.

EXERCISE №16 - 2 hours: Microbiological techniques for diagnosis of infection. General principles and specimen quality.

AIM: Students have to apply knowledge in one consequent scheme for microbiological diagnosis of infectious diseases.

DEMONSTRATION AND PRACTICAL TASKS: Learning of the common rules for specimens collection, labeling and transport. Microscopy of clinical specimen. The Gram technique. Distinguishing pure microbial cultures on different nutrition media. Identification tests: cultural, biochemical, detection of pathogenic factors, serotyping via agglutination reaction type Gruber. Reading of antibiograms. Microscopy of ready – made microscope preparations.

EXERCISE №17 – 2 hours: Microbiological diagnosis of pus. Diagnosis of staphylococcal and streptococcal infections.

AIM: To known the commonest causative agents of pus infections in human body. Methods for microbiological diagnosis.

DEMONSTRATION OF: Ready – made preparations of staphylococci and streptococci, stained by Gram technique. Demonstration of cultural characteristics of staphylococci and streptococci on different nutrition media and tests for their identification.

PRACTICAL TASKS: Detection of staphylococcal and streptococcal cultures on blood agar. Reading alfa- and beta-haemolysis. Reading Bacitracin-test and Optochin-test. Elaboration of staphyslide test and reading tube coagulase test. Reading antibiograms of staphylococci, beta- and alfa-haemolytic streptococci. Reading ASO (ant streptolysin O) reaction. Differential diagnosis between S. viridans and S. pneumoniae. MRSA screen agar – interpretation.

EXERCISE №18 – 2 hours: Microbiological diagnosis of tuberculosis and leprosy. Laboratory diagnosis of S. pneumoniae infections. The lower respiratory tract infections..

AIM: To learn the rules for specimen collection and microbiological examination of sputum, especially features in cases of inflammation process. To obtain knowledge for microbiological diagnosis in tuberculosis, leprosy and pneumococcal diseases. Bioproducts for specific prophylaxis and therapy.

DEMONSTRATION OF: Ready – made microscope preparations: of Mycobacterium tuberculosis in sputum, stained by Ziehl-Neelsen technique; Pneumococci, stained by Klett technique for capsule detection. Inoculation of M. tuberculosis on Lowenstein-Jensen medium. Cultural characteristics of pneumococci on blood agar and glucose broth. The Optochin and Inulin tests.

PRACTICAL TASKS: Elaboration of microscope preparation from sputum and staining via Ziehl-Neelsen technique for detection of M. tuberculosis. Reading positive and negative Optochin tests. Reading antibiograms of pneumococci on blood agar. Bioproducts for specific prophylaxis (BCG - vaccine) and for detection of allergy (PPD) caused in tuberculosis.

EXERCISE №19 – 2 hours: Microbiological diagnosis of diphtheria and whooping cough. Throat culture procedures. The upper respiratory tract infections.

AIM: To present students with microbiological diagnosis of diphthery and whooping cough and bioproducts for specific prophylaxis and therapy.

DEMONSTRATION OF: Ready – made microscope preparation of Corynebacterium diphtheriae stained by Neisser technique. Cultural characteristics of C. diphtheriae on Loeffler and Klauberg agars. The growth of Bordetella pertussis on Bordet-Gengou blood agar.

PRACTICAL TASKS: Microscope observation of ready – made preparation of Bordetella pertussis, stained by Gram. Elaboration a preparation of pseudodiphtherial bacteria, stained by Neisser technique. Bioproducts for specific prophylaxis (vaccines DTP and DT) and specific therapy for diphtheria (antidiphtherial serum).

EXERCISE №20 – 2 hours: Microbiological diagnosis of gas gangrene and tetanus. Isolation and identification of bacteria from infected wounds and abscesses. Detection of anaerobic bacteria.

AIM: To present students with microbiological diagnosis of gas gangrene and tetanus, specimen collecting and transport and bioproducts for specific prophylaxis and therapy.

DEMONSTRATION OF: Ready – made microscope preparation of C. perfringens and C. tetani, stained by Gram technique. Nutrition media for anaerobic cultivation – chopped-meat glucose broth; enriched thioglycolate medium; Schaedler blood agar and Wilson-Blair agar; cultural characteristics of causative agent of gas gangrene and tetanus. Toxin test in mice (blood from patient).

PRACTICAL TASKS: Staining by Gram a preparation from wound specimen with clostridia. Bioproducts for specific prophylaxis and therapy of gas gangrene and tetanus.

EXERCISE №21 – 2 hours: Microbiological diagnosis of bacterial meningitis. Microbioloigical diagnosis of CSF and punctates.

AIM: Learning differential microscope diagnosis of bacterial meningitis.

DEMONSTRATION OF: Ready – made microscope preparations from cerebro-spinal fluid (CSF) with Neisseria meningitidis, stained by Loeffler (methilene blue) and Gram techniques. H. influenzae, stained by Gram and other microorganisms as causative agents of bacterial meningitis as well. Cultural characteristics of H. influenzae on chocolate agar, Levinthal agar, and blood agar - the satellite phenomenon. Methods for microaerobically cultivation and demonstration of cultures of Neisseria meningitidis on Levinthal agar and blood agar. Cultural characteristics of pneumococci, staphylococci, and M. tuberculosis. Latex agglutination tests for detection of microbial antigens in CSF of patients.

PRACTICAL TASKS: Gram staining of preparations from CSF. Observation of ready – made microscope preparations with Neisseria meningitidis and H. influenzae. Reading of satellite phenomenon (H. Influenzae).

EXERCISE №22 – 2 hours: Microbiological diagnosis of particular dangerous infectious diseases – anthrax, cholera and plague.

AIM: To introduce to students microbiological diagnosis of plague, anthrax and cholera and relevant bioproducts for specific prophylaxis and therapy.

DEMONSTRATION OF: Ready – made microscope preparations – blood smear with Bacillus anthracis, stained by Klett for capsule detection; Vibrio cholerae, stained by Gram and Yersinia pestis, stained by Gram. Nutrition media, bacterial cultures, and biochemical tests for identification of cholera vibrion. The Ascoli precipitation reaction for detection of Bacillus anthracis.

PRACTICAL TASKS: Microscopy and staining of preparation with Bacillus anthracis. Elaboration of Ascoli precipitation reaction. Immunofluorescent microscopy of Bacillus anthracis.

EXERCISE №23 – 2 hours: SEMINAR. TEST.

Staphylococci. Streptococci. Streptococcus pneumoniae. Mycobacterium tuberculosis and other mycobacteria. Mycobacteruim leprae. Neisseria meningitides. Corynebacterium diphtheriae. Bordetella pertussis. Haemophillus influenzae. Causative agents of gas gangrene. Clostridium tetani. Bacillus anthracis. Vibrio cholerae. Yersinia pestis.

EXERCISE №24 – 2 hours: Microbiological diagnosis of dysentry, salmonellosis, and colienteritis. Microbiological examination of faeces.

AIM: To introduce to students the scheme of bacteriological examination of faeces in cases of infections, caused by members of family Enterobactericeae (pathogenic E. coli, Shigella, Salmonella).

DEMONSTRATION OF: Microscope preparation of Gram-negative rods. Selective and differential nutrition media for enteric bacteria – EMB agar, deoxycholate-citrate agar with colonies of lactose-positive and lactose-negative bacteria. Biochemical tests for identification. Serotyping via Gruber agglutination.

PRACTICAL TASKS: Elaboration of microscopic preparations of E. coli culture and stained by Gram technique. Dropping of biochemical tests for detection of indole-formation,

grade of acidity (MR), a Voges-Proskauer test (VP) etc. Elaboration of agglutination reaction type Gruber. Inoculation of faeces on differential medium.

EXERCISE №25 – 2 hours: Microbiological diagnosis of food poisoning.

AIM: To introduce to students microbiological diagnosis of food poisoning, caused by Staphylococcus aureus, Salmonella spp., Clostridium botulinum, Bacillus cereus, Campylobacter jejuni and methods for detection of Helicobacter pylori from biopsy material.

DEMONSTRATION OF: Blood agar and milk-salt agar, MRSA screen agar, salt broth for S. aureus. Media for clostridia: Schaedler and Zeisler agars, Perfringens agar, thioglycolate broth, Columbia agar for C. jejuni. Anaerobic jar or alternatives. Milk peptonisation of C. perfringens. Tube coagulase test and mannitol fermentation of S. aureus, Deoxycholate-citrate agar and EMB agar and selenite broth for enteric bacteria.

PRACTICAL TASKS: Microscopy of ready – made preparations of clostridia, gram-negative rods and staphylococci, stained by Gram; Helicobacter pylori, stained by Pfeiffer's technique and preparations, stained by Moller`s technique for detection of spores.

EXERCISE №26 – 2 hours: Microbiological diagnosis of typhoid fever, undulant fever and relapsing fever. Microbiological examination of blood culture.

AIM: To introduce to students the causative agents of bacteriemia and sepsis, as well as the methods for microbiological examination of blood.

DEMONSTRATION OF: Media for hemocultivating – soy-casein broth, thioglycolate broth, etc. Demonstration of growth of Salmonella spp. and Proteus spp. on EMB agar and desoxycholate-citrate agar, and selenite broth. Biochemical identification of Salmonella typhi and Proteus mirabilis. Nutritient media for brucellae. Preparations of Brucella spp. and Salmonella spp. stained by Gram. Colonies of staphylococci and streptococci on blood agar and tests for their identifications. Widal agglutination reaction for typhoid fever and Wright agglutination for brucellosis.

PRACTICAL TASKS: Differentiation of colonies of Salmonella spp. and Proteus spp. on differential media. Reading biochemical activity of S. typhi and P. mirabilis. Reading agglutination titers of Wright and Widal reactions.

EXERCISE №27 – 2 hours: Microbiological diagnosis of bacteriuria and fungiuria. Enumeration and identification of microorganisms in urinary tract infections.

AIM: To introduce to student the rules for specimen collection and transport of urine for microbiological examination and with methods for isolation and detection of most common urinary pathogens.

DEMONSTRATION OF: Cultural and biochemical features of E. coli, Klebsiella spp., Proteus spp., Pseudomonas spp., Candida spp. Cultivating urine via quantitative method with a calibrated loop. Demonstartion of Leptospira spp. under dark-field microscopy.

PRACTICAL TASKS: Cultivating urine on blood agar with calibrated loop. Reading urocultures with different grades of bacteriuria. Drawing Leptospira spp. under dark-field microscopy. Reading antibiograms of microbes, isolated from urine.

EXERCISE №28 – 2 hours: Microbiological diagnosis of gonorrhoea and syphilis. Microbiological examination of genital tract infections.

AIM: To introduce to students morphology and biology of the commonest, isolated from genital tract microorganisms.

DEMONSTRATION OF: Ready – made microscope preparation from urethra with N. gonorrhoeae; ready – made preparation with Candida albicans. Immunofluorescent preparation with elementary bodies of Chlamydia, isolated from cervix. Bacterial cultures of Candida albicans on Sabouroaud agar and Chromagar Candida; chlamydospores of Candida albicans on rice agar; test for filamentation. ELISA. Positive Wassermann test for syphilis.

PRACTICAL TASKS: Demonstration of N. gonorrhoeae in male urethra. Reading positive and negative Wassermann reactions.

EXERCISE №29 – 2 hours: Microbiological examination of materials with sanitary importance. Sanitary indicative microorganisms.

AIM: To introduce to students the way of specimen collecting, transport and a scheme for sanitary examination of water.

DEMONSTRATION OF: Nutrition media and materials for detection of colony-count and coli-titer in drinking water. Biochemical tests for detection of E. coli and Klebsiella spp. – IMVUC. Methods for qualitative detection of microorganisms in air. Nutrition media for enterococci. A Scherman test for identification of enterococci.

PRACTICAL TASKS: Taking a washing-down from hands for sanitary-microbiological examination and cultivating in a broth. Identification of E. coli, Klebsiella spp., Enterococcus spp.

EXERCISE №30 – 2 hours: Microbiological examination of viruses and rickettsiae.

AIM: To introduce to students the characteristics of viral and rickettsial diagnosis.

DEMONSTRATION OF: Inoculation of viruses in eggs. Cell cultures – normal and with cytopathic effect. Hurst phenomenon and Hurst reaction. ELISA readers. ELISA samples for diagnosis of viral markers (HBsAg, anti-HIV-1,2 antibodies, anti-HCV antibodies etc.).

PRACTICAL TASKS: Demonstration and drawing of viral infected eggs (embryos). Demonstration and drawing of cell culture –normal and with cytopatic effect. Reading ELISA tests.

SYNOPSIS

General microbiology

1. Subject and tasks of microbiology. The role of Pasteur and Koch for development of medical microbiology. Taxonomy of microorganisms – nomenclature and classification. General characteristics of different groups of microorganisms.
2. Morphology of bacteria – shape, size, arrangement. Methods for styding bacterial morphology. Bacterial structure – essential and nonessential components: cell envelope, cytoplasm and cytoplasmic inclusions, capsules, flagella, fimbriae, spores.
3. Bacterial genetics. Genotype and phenotype of bacteria. Genetic apparatus in bacteria. Bacterial chromosome as a genetic system. Extrachromosomal genetic elements. Bacteriophages – main types, structure, interactions with the microbial cell – lytic cycle, moderate phage, prophage, phage conversion. Phage typing. Mutations. Mutagenic factors – chemical and physical, mechanism of action, practical use. Genetic transfer – transformation, conjugation, transduction – mechanisms. The importance of bacterial and phage genetics. Genetic engineering. Contemporary genetic methods in clinical microbiology. DNA probes. PCR – polymerase chain reaction.
4. Bacterial physiology. Chemical composition of bacterial cell. Bacterial enzymes. Bacterial metabolism – catabolic and anabolic processes. Bacterial respiration. Bacterial nutrition. Transport of nutrients.
5. Bacterial growth and reproduction. Growth phases and growth curves. Bacterial culture – basic principles, culture media. Bacterial growth factors.
6. Influence of physical factors on microorganisms: heat, drying, light, atmospheric pressure, osmotic pressure, radiation. Sterilization. Methods of sterilization. Influence of chemical factors on microorganism. Disinfection types of disinfectants. Mechanism of action of chemicals upon bacteria. Oligodynamics. Influence of biological factors upon microorganisms: symbiosis, antagonisms, antibiosis.
7. Antimicrobial agents. Main groups and mechanism of action. Mechanisms of resistance to antimicrobial agents. Antibiotic susceptibility tests.
8. Viruses. Nature and properties. Methods for cultivation. Classification. Rickettsia. Nature and properties. Methods for cultivation. Classification.
9. The surrounding environment as a factor for spreading causative agents of infectious diseases. Microbial flora in water, soil, air. Microorganisms in foodstuff, hospital services, etc. Microorganisms of sanitary importance.

Infection and Immunity

10. Infection and infectious process. The role of microorganism in the infectious process. Pathogenecity. Virulence. Invasiveness. Toxigenecity. Pathogenic factors. Pathogenesis of the infectious process. Characteristics of infectious disease. Forms of the infectious process. The role of macroorganism in the infectious process. The role of environment for development and course of the infectious process. Epidemic process. Factors and mechanisms of transmission of the infectious agents in the epidemic process.
11. Innate immunity. The protective role of skin, mucous membranes, organs and normal microbial flora. Humoral factors of innate immunity – lysozyme, complement system, interferons and cytokines. Cellular factors of innate immunity. Phagocytosis. Inflammation.

12. Immunity. Definition. Types of immunity. The anatomy and structure of the immune system. Central and peripheral organs. Cells of the immune system.
13. Antigens. Types of antigens. Antigenic characteristics of microorganisms.
14. Humoral immunity. Mediators. Characteristics of antibodies (immunoglobulins). Structure and function of different immunoglobulin classes. Mechanism of action of antibodies. Local immunity.
15. Cellular immunity. Cells and mechanism of action. Forms of cellular immunity. Cellular cooperation in the immune response.
16. Development of the immune response. Recognition of antigens. The role of APC and MHC molecules. Dynamics of the immune response – primary and secondary immune response. Genetic control of the immune response. Humoral regulation of the immune response.
17. Allergy – definition and forms. Immediate allergic reactions – anaphylaxis, atopy, clinical significance. Cytotoxic allergic reactions. Allergic phenomena due to immune complexes – serum sickness, Arthus, clinical significance. Delayed type hypersensitivity – Koch phenomenon, contact dermatitis. Clinical significance.
18. Immunopathology. Immunopathological reactions and diseases. Immunological tollerance. Autoimmune diseases. Immunodeficiencies – disorders and diseases. Infectious diseases of the immune system.
19. Antigen-antibody reactions. Types: agglutination, precipitation, neutralization – toxin, antitoxin, ASO, virus-neutralization test. Complement fixation test. Mechanism and practical application of the reactions in microbiological diagnosis.
20. Labelled immune reactions – immunofluorescence, radioimmune and immunoenzyme tests. Hybridoma biotechnology. Monoclonal antibodies.
21. Immunoprophylaxis and immunotherapy. Vaccines and sera. Immunomodulation.

Special microbiology

22. Microbiological diagnosis of infectious diseases. Collection, transport and examination of specimens. Interpretation of results.
23. Staphylococcus spp. Classification. Morphology, biology, biochemical and toxin production. Pathogenic factors. Pathogenecity and Immunity. Microbiological diagnosis. Antibiotic treatment. MRSA – clinical importance and diagnosis.
24. Streptococcus spp. Classification. Morphology, biology, antigenic structure, biochemical and toxin production. Pathogenic factors. Pathogenecity of streptococcal infections. Disease and immunity. Microbiological diagnosis. Antibiotic treatment. Streptococcus pneumoniae. Morphology, biology, biochemical production and antigenic structure. Pathogenesis, diseases and immunity. Microbiological diagnosis. Specific prophylaxis and therapy.
25. Neisseria meningitidis. Morphology, biology, biochemical production, antigenic structure. Pathogenic factors. Pathogenesis, clinical forms of disease and immunity. Microbiological diagnosis. Specific prophylaxis and therapy. Neisseria gonorrhoeae. Morphology, biology, biochemical production. Pathogenic factors. Pathogenesis, clinical forms of disease and immunity. Microbiological diagnosis. Prophylaxis and therapy.
26. Enterobacteriaceae. Main groups enteric bacteria. General characteristics – morphology, biology, biohemical production, antigenic structure. Pathogenic factors. Escherichia coli. Morphology, biology, biochemical production, antigens, pathogenic factors,

diseases. The role of coli bacteria in human pathology. Immunity. Microbiological diagnosis.

27. Proteus spp. Providencia spp. Morganella. General characteristics – morphology, biology, biohemical production. Diseases. Their role as causative agents of infections. Microbiological diagnosis. Therapy. Klebsiella spp. Morphology, biology, biochemical production, pathogenic factors. Diseases. Microbiological diagnosis. Therapy. Pseudomonas spp. Morphology, biology, biochemical production. Pathogenic factors. Diseases. Immunity. Microbiological diagnosis. Therapeutic problems.
28. Salmonella spp. General chracateristics – morphology, biology, biochemical production. Antigenic composition and Kauffmann-White classification. Pathogenic factors. Diseases – typhoid and paratyphoid fevers, food poisoning. Pathogenesis and immunity. Microbiological diagnosis. Specific prophylaxis and therapy in salmonella infections.
29. The causative agents of dysentery (Shigella spp.). Classification. Morphology, biology, biochemical production. Antigenic composition. Pathogenesis and immunity. Microbiological diagnosis. Helicobacter pylori. Morphology, biology, biochemical production. Disease. Microbiological diagnosis. Therapy. Clostridium difficile. General characteristics.
30. Yersinia spp. The causative agent of plague (Yersinia pestis). Morphology, biology, pathogenic factors. Pathogenesis and immunity. Microbiological diagnosis. Specific prophylaxis and therapy. Yersinia enterocolitica. General characteristics.
31. Vibrio cholerae. Morphology, biology, biochemical production. Antigenic composition. Sero- and biotypes. Pathogenecity and immunity. Microbiological diagnosis. Specific prophylaxis and therapy.
32. Bordetella (Bordetella pertussis, Bordetelal parapertussis). Morphology, biology, pathogenic factors. Pathogenesis and immunity of whooping cough and other diseases. Microbiological diagnosis. Specific prophylaxis and therapy. Haemophilus spp. Morphology, biology, antigenic structure. Pathogenic factors. Disease and immunity. Microbiological diagnosis. Specific prophylaxis and therapy. Listeria monocytogenes. General characteristics.
33. Brucella. Species. Morphology, biology, biochemical production and pathogenic factors. Pathogenesis and immunity Microbiological diagnosis. Specific prophylaxis. Francisella tularensis. General characteristics. Legionella pneumophila. General characteristics.
34. Corynebacterium spp. Corynebacterium diphtheriae. Morphology, biology, biochemical production and pathogenic factors. Pathogenecity and immunity. Microbiological diagnosis of diphtheria Specific prophylaxis and therapy. Coryneforms (C. jeikeum, C. urealyticum, C. amycolatum, C. pseudodiphtheriticum). Clinical importance.
35. Mycobacteria. Mycobacterium tuberculosis. Morphology, biology. Pathogenic factors. Pathogenecity and immunity. Microbiological diagnosis. Specific prophylaxis. Atypical mycobacteria. Mycobacterium leprae. Morphology, biology, clinical forms. Microbiological diagnosis. Prophylaxis.
36. Genus Bacillus. Bacillus anthracis. Morphology, biology, pathogenic factors. Pathogenecity, disease and immunity. Microbiological diagnosis. Specific prophylaxis and therapy. Bacillus cereus. General characteristics and disease.
37. Anaerobic spore-forming bacteria – genus Clostridium. General characteristics. Clostridium tetani. Morphology, biology and toxin production. Pathogenecity and immunity. Microbiological diagnosis. Specific prophylaxis and therapy. The causative agents of gas gangrene. Morphology, biology and toxin production. Pathogenecity,

disease and immunity. Microbiological diagnosis. Prophylaxis and therapy. Clostridium botulinum. Morphology, biology and toxin production. Pathogenesis and immunity. Microbiological diagnosis. Prophylaxis and therapy.

38. Spirochetes (Spirochaetaceae). General characteristics. The causative agent of syphilis (Treponema pallidum). Morphology and biology. Pathogenesis and immunity. Microbiological diagnosis. Leptospira spp. Morphology and biology. Pathogenesis and immunity. Antigenic composition and serological types. Microbiological diagnosis. The causative agent of relapsing fever (Borrelia recurrentis). Morphology and biology. Pathogenesis and immunity. Microbiological diagnosis. The causative agent of Lyme Disease (Borrelia burgdorferi). Pathogenesis, immunity, microbiological diagnosis.
39. Mycoplasma spp. Classification. Morphology, biology, diseases. Microbiological diagnosis. L-forms of bacteria. Chlamydia. General characteristics. The causative agent of psittacosis and trachoma. Morphology and biology. Pathogenesis and disease. Microbiological diagnosis. Chlamydia as causative agents of sexually transmitted diseases. Therapy.
40. Pathogenic fungi. Candida spp. Morphology, biology. Pathogenesis and clinical forms. Immunity. Microbiological diagnosis. Therapy. Aspergillus, Cryptococcus, Actinomycetaceae. Morphology, biology, disease and microbiological diagnosis.
41. The causative agent of louse-borne typhus (Rickettsia prowazeki). Morphology and biology. Pathogenesis and immunity. Microbiological diagnosis. Specific prophylaxis. The causative agent of Mediterranean fever (Rickettsia conorii). Morphology and biology. Microbiological diagnosis. The causative agent of Q fever (Coxiella burnetii). Morphology and biology. Microbiological diagnosis. The causative agents of human ehrlichiosis (Ehrlichia). The causative agent of cat-scratching disease (Bartonella henselae). Morphology and biology. Immunity. Microbiological diagnosis.
42. Picornaviridae. Genus Enterovirus – the causative agent of polyomyelitis, coxackie infections and ECHO infections. Genus Rhinovirus – the causative agents of infectious rhinitis. Genus Aphtovirus – the causative agent of foot-and-mouth disease.
43. Orthomyxoviridae. The causative agents of grippe.
44. Paramyxoviridae. The causative agents of paragrippe, epidemic parotitis, measles. Respiratory syncytialvirus.
45. Arboviruses and rubella. Togaviridae – Genus Alphavirus and Genus Rubivirus. Flaviviridae – the causative agents of yellow fever, dengue, Sandfly fever, tick-borne encephalitis. Bunyaviridae – the causative agent of Crimean-Congo haemorrhagic fever. Hantaan virus.
46. Poxviridae – the causative agent of smallpox. Adenoviridae. Rhabdoviridae – the causative agent of rabies. Rotaviridae.
47. Herpesviridae. The causative agent of herpes simplex, the causative agent of varicella and herpes zoster. Human cytomegalovirus. The causative agent of infectious mononucleosis. Other herpesviruses.
48. The causative agents of viral hepatitis (HAV, HBV, HCV, HDV, HEV, HGV). Characteristics. Pathogenesis and immunity. Specific prophylaxis.
49. Retroviridae – the causative agent of AIDS (HIV).

LITERATURE:

1. Lecture course, Prof. Marianna Murdjeva, MD, PhD

2. Todar's Online Textbook of Bacteriology
   site: textbookofbacteriology.net
3. Medical Microbiology
   Edited by Samuel Baron
   http://www.ncbi.nlm.nih.gov/books/NBK7627/
4. Microbiology and Immunology On-line
   http://www.microbiologybook.org

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