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SHORT COURSE OF GENERAL PATHOLOGY

Part 1

Educational book

MINISTRY OF HEALTH OF UKRAINE
MINISTRY OF EDUCATION AND SCIENCE OF UKRAINE

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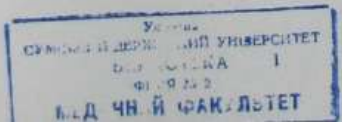

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Посібник містить короткий виклад теоретичного матеріалу основних тем загальної патоморфології, що відповідає програмі, затвердженій МОЗ України і ЦМК з вищої медичної освіти. У посібнику представлені цифрові мікро-та макро-фотознімки, викладений їх опис та наведені приклади тестових і ситуаційних завдань до кожного заняття.

Для англомовних студентів вищих медичних навчальних закладів III-IV рівнів акредитації.

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Introduction

This textbook was written in conformance with new training program in pathological morphology for higher educational establishments of Ukraine which was worked out based on European credit-transfer system principles.

The authors didn't set an object to develop comprehensive textbook. The aim of the book is clearly and easily assist student to acquire habits of synthetic generalization of pathologic processes demonstration and their interpretation in cause-effect correlations.

Textbook is structured by modules. Its first part covers one module– general pathologic processes and tumors growth. Notional modules include theoretical knowledge base, self-control system and artwork of pathologic processes macroscopic and microscopic manifestations, guiding student to reach specific objects in creative way.

Training plan description in "Pathological morphology" discipline during general pathologic processes and tumors growth morphology study

Training discipline structure	Hours, including				Year of training	Type of control
	Total	Auditorium		SSW		
		Lectures	Practical classes			
Module 1 "General pathologic processes and tumor growth morphology" *Notional modules 4*	90 hours / 3,0 ECTS credits	16	38	36		Current and summary (standardized)

Module 1

General pathologic processes and tumors growth

Notional module 1
Introduction. Morphology of cells and tissues injury

Lecturers – 4 hours
Practical classes – 8 hours
Student's self-work – 7 hours
Form of student's individual self-work – thesis or library-research papers

Specific objects:

- *To explain the place of pathologic anatomy as science, area of practical medicine and training subject.*
- *To learn methods of pathologic anatomy investigation.*
- *To analyze stages of pathologic morphology formation and national scientists' contribution into international development of pathologic morphology.*
- *To interpret the reasons and morphology of microbodies' stereotyped and specific injuries.*
- *To explain cell-matrix interactions*
- *To explain cellular and extracellular trophism mechanisms.*
- *To explain the reasons and mechanisms of trophic disturbances.*
- *To explain mechanisms of cells and tissues reversible and irreversible damages.*
- *To interpret morphology of intracellular, extracelluiar proteins, hydrocarbons, lipids accumulation and its consequences.*
- *To interpret morphology of endogenous and exogenous pigments accumulation and its consequences.*

- *To describe tissues, organs and systems macro- and microscopic changes under intracellular and extracellular proteins, hydrocarbons and lipids accumulation and under pigments metabolism disturbance.*
- *To interpret mineral metabolism disturbance morphology and this disturbance consequences.*
- *To interpret morphology and consequences of necrosis: macro and microscopic modifications of tissues, organs and systems under various clinical-morphological forms of necrosis.*
- *To interpret apoptosis (programmed cell death) morphology.*
- *To interpret organ insufficiency morphology.*
- *To explain fundamentals of tanatology.*
- *To interpret the concept of death and its signs.*

Theme 1. Subject and tasks of pathologic morphology. Methods of pathologic morphology investigations. Main stages of pathologic morphology development.

Basic matters for self-training:

Pathologic morphology is a science studying structural (material) fundamentals of diseases to comprehend material foundations of medical science as well as profound study of disease clinical picture with latter utilization of acquired knowledge in the practical work of physician.

Tasks of pathologic morphology:

- to study cell pathology;
- to study general pathologic processes, aggregation of which determine morphologic manifestation of these of those diseases;
- to study etiology, pathogenesis and morphology of diseases at different stages of their development

(morphogenesis) structural basis of recovery, complications and consequences;

- to study morphology and mechanisms of organism adaptation and compensation processes in response to pathogenic factors and environment conditions influence;

- to study pathomorphism of diseases, originating in connection with living conditions of the person, which are changing, as well as the result of various therapeutic actions (pathology of therapy);

- to study postmortem examination service organization.

Pathologic morphology as fundamental and clinical field of medicine. Clinical-anatomic orientation of national pathologic morphology. Principle structure and function unity.

Disease morphologic and clinical manifestation comparison at every stage of disease onset.

Clinical-anatomy analysis, synthetic generalization of diagnostic signs of diseases and their interpretation in cause-effect correlations.

Methods of pathologic morphology investigations are autopsy, biopsy, surgery material study, experimental modeling.

Modern methods of biopsy material study. Biopsy: types, meaning for diseases early recognition and treatment, benign and malignant tumors identification, surgery feasibility and scope determination, and patient's living prognosis.

Various studies of diseases' structural fundamentals: organism, system, tissue, cell, cubcellular, molecular.

Post mortem aim, specific matters of early and planned autopsy of died patient. Autopsy importance to clarify causes and mechanisms of patients' death, analysis of the quality of diseases diagnostic in patients' lifetime and quality of patients' treatment.

Characteristics of pathologic morphology development. Contribution of D.Morganyi, K.Rokytanskyy, R.Vyrkhov in international pathologic morphology development.

Stages of national pathologic morphology formation.

Accessory aids to student's self-work

Pathologic anatomy being fundamental medical-biology science is at the meeting point of medical theory and practice. Main assignment of pathology anatomy service is lifetime and posthumous diagnostic of diseases, study of etiology, pathogenesis and tanatogenesis of the most widespread diseases, control of clinical diagnostic quality and therapeutic process effectiveness as well as physicians' professional advanced training.

Basic methods of diseases posthumous and lifetime diagnostic

Basic methods of diseases posthumous diagnostic are macroscopic (autopsy) and microscopic (necropsy), lifetime diagnostic are microscopic (biopsy, cytology) and experiment. Accessory methods are as follows: biological (bacteriologic, virologic, serologic, hematological, tissue culture method), chemical (histochemical, immunohystochemical, atomic absorptiometry, quantitative analysis, qualitative analysis, biochemical), physical (hystoautoradiography, roentgenography, roentenostructural analysis, ultrasonic diagnostics).

Autopsy (from Greek – to see somebody, to see in own eyes). *Function :*

- scientific-cognitive process development. During autopsy not only last terminal stage of disease is fixed, but also morpho-fuctional changes dynamics is clarified.

For example, stages of cardiac (nutmeg, portal, small nodular) liver cirrhosis or secondary tuberculosis. Based on acquired knowledge new classifications of diseases are developed and old ones are updated;

- control of treatment-prophylactic facility work quality. It determines non-conformity or conformity of clinical and postmortem diagnosis, cause of death. Due to study of latter the efforts of medical personnel can be concentrated to eliminate them further on. For example, it was revealed that pulmonary edema is often registered in cardio section as direct cause of death. By the way of analysis the cause of incorrect diagnosis can be found. It could be poor qualification of physician, insufficient reanimation measures or ungrounded utilization of medicines, etc. Autopsy is used to analyze new diagnostic procedures, medicines, surgery methods of treatment effectiveness determination;

- contagious diseases detection and prophylaxis, especially those subject to quarantine;

- students and practicing physicians training. Not in vain on the gamble of Sorbonne (Paris) prosectorium in XIV century it was written: "Here is the place where mors trains to live". It's analysis of diagnostic, treatment faults should be mandatory for every physician. M. Pyrogov mentioned "Medical mis-actions is a science of special importance ". Definition of medical error was given by I.Davydovskyi "This is honest mistake of physician and, in case this mistake happened, there is no other way to improve except by own mistakes investigation". Besides above said, there is no better science than to see changes of organs and systems gross observed. That's owing to autopsy excellent anatomic atlases of Leonardo da Vinci, Rembrandt, M.Pyrogov appeared;

- finding new diseases, their aetiology and path morphogenesis, for example, presentation of familial hypertrophic cardiomyopthy, a number of hereditary and

congenital diseases, prion diseases, B type chronic gastritis, etc.

Necropsy (from Greek некроз - dead and опзіз - to look) are done to confirm or deny revealed gross manifestation of pathologic processes on cellular and subcellular levels.

Biopsy (from Greek біоз - life and опзіз – to look) is microscopic examination of alive human beings' tissues. Biopsy could be urgent (tissues examination during surgery), as well as planned to clarify diagnosis or under preventive examinations. To carry out urgent examination the method of frozen sections or replicas is used. Last one is used for cytological examinations. Main purpose of biopsies is to make out accurate intravital diagnosis. Material for biopsy is tissues extracted in surgical way and for cytology – secrets (urine, sputum, blenna, mammary secretions, etc.), replicas from tissues and swabs as well as cells acquired by aspiration from mammary glands, liver, lymph glands, lungs, pancreatic glans, etc. Utilizing auxiliary research methods pathomorphological changes on subcellular and molecular levels are determined. Thus, with electron microscopic methods histogenesis of a number of tumors is revealed, with immunehistochemical methods – hormones, receptors, immunoglobulins, antigenic proteins, ferments, karyogens and with histochemical methods – various classes of proteins, fats, carbohydrates, metals and ferments.

Experiment is quite rarely used in pathoanatomy. However it is known that some illnesses existence can be proved utilizing research model. En example could be guinea-pigs infection with urine of kidneys ill with tuberculosis.

Nowadays ***in situ hybridization*** is used more and more widely. The essence of hybridization technology is based on

the fact that nucleic acid bases are complementary to each other in one chain. Utilization of marked test makes it possible to find complementary nucleic acids in the cells. Latter could be a portion of native dezoxyribonucleic acid (DNA) cell, a portion of ribonucleic acid, bearing information from certain genes or a portion of virus genome. In such a way, it could be found morphologically in a cell where target is localized or if target is absent. Utilizing above named method it is possible to determine presence of papilloma virus, cytomegalovirus, virus of herpes.

Practical activity of pathologist on modern stage

On the modern stage of medicine development considerable changes in illnesses clinical pictures, morphology and consequences, namely pathomorphism, are seen caused by wide introduction of new hormonal medicines, antibiotics, drug-mediators into physicians' practice as well as by environment contamination with xenia-biotics. It is also caused by new reanimation measures, artificial blood circulation, mechanical ventilation and organs transplantation introduction into medical practice. More often doctor sees combination of several severe illnesses. He/she also is faced with "therapy pathology" problem, meaning disease states caused by medical interventions.

Above named changes in medical practice complicated anatomist to define various processes pathogenesis, especially – genesis. To solve these problems the practice of mutual with hospital physicians discussion found morphologic facts is widely introduced at the moment. Besides that subspecialty of pathologists are widely spread. Thus anatomists working in Oncology Dispensaries, Tuberculosis Dispensaries, Cardiac Dispensaries, Infection hospitals, etc. become narrowly focused specialists. Quite often their work in these establishments narrows down to small range of diseases

interpretation. This relates to scientific-research institutes and laboratories in which these specialists carry out ancillary work ordered, formally describe found morphological changes and give these descriptions to the others to analyze and interpret. It often occurs in laboratories where experiments are carried out, for example, to study new medicines effect. In these circumstances anatomist becomes morphologist, specialist with narrow range of cogitation, restricted by his/her methods data and clinical field of medical establishment he works at.

As practice shows the most part of his/her working hours anatomist spends for life-time diagnostics of diseases. However, utilizing such forms of biopsy as puncture, aspiration, trepanobiopsy, etc. as well as cytology, chemical and physical methods, anatomist controls the course of curative process and disease dynamics in general. In our days his/her services are asked by surgeons, oncologists, gastroenterologists, renal pathologists, cardiologists. It's just study of kidneys, liver, skin biopsy made it possible to extend imagination of glomerulopathies, viral hepatitis, rheumatic diseases pathogenesis, to define their clinicopathologic forms.

In our days anatomist is not limited with pathologic process affirmation only, more and more often he/she gives definition of its stages, prognosis. Whereas earlier it was enough to diagnose only presence of cancer or sarcoma, this diagnosis is not complete now. Anatomist is required to differentiate accurately histological accessory of tumor, tumor maturity stage as the character of medical intervention depends on that. It is this to cause wide introduction of histochemical, electron microscope, morphometric, immunological morphological investigation.

Clinical-laboratory data is more often used for biopsy interpretation as it would be incorrect to use widely ancillary methods but evaluate pathologic process only by morphology data. As it is known, sometimes biopsy is taken in non-

standard location, so morphologic diagnosis can differ from clinical one. In such a case the results are discussed by clinicians who are interested and have equal rights participants of diagnosis process.

Theme 2 Elements of cell ultrastructural pathology. Cell-matrix interactions. Cellular and extracellular mechanisms of trophism regulation. Alteration: intracellular pathology

Theme topicality: Alteration or injury is the most wide spread reaction of living tissues as an answer to pathogenic action. Its various levels morphologic manifestations exists under each disease, and degree of injury intensity determines functional ability of organs and tissues. Knowledge of alteration structural manifestations gives capability to evaluate properly the dynamics of diseases course and to foresee their consequences.

The aim is to study alteration reasons, morphologic characteristic at ultrasonic level and its significance in the diseases development, clinical course and consequences.

Specific aims: 1) To know reasons, morphology and consequences of intracellular pathology.

2) To learn to identify alteration manifestations on intracellular level.

3) To be able to compare alteration manifestations on electron-diffraction patterns under various intracellular structures injury.

Basic matters for self-work

Cell is elementary living system, able to exchange with environment.

Modern concept of cellular organelles structure and functions. Nucleus: structural-functional characteristics.

Plasmolemma: structure, features, injury consequences. Cytoskeleton and its components.

Cell pathology as integrative idea. Cell nucleus pathology. Mitosis pathology, chromosomal aberrations and chromosome diseases. Stereotyped injuries of ultructructures as an answer to various impacts. Cell membranes pathologic modifications and cells modifications under plasmolemma injury. Pathologic modifications of endoplasmic reticulum. Golgi complex pathologic modifications. Pathologic modifications of mitochondrion. Pathologic modifications of lysosomes. Pathologic modifications of peroxisomes. Pathologic modifications of cytoskeleton (microfilaments, microtubules). Cells movement and its role in pathology. Specific modifications of ultrastructures: receptors' "diseases", lysosomes, mitochondrial, peroxisomal " diseases".

Cell-matrix interactions. Cellular and extracellular regulation mechanisms.

Epithelial tissue, basal membrane, conjunctive tissue: morphologic characteristic, basic functions.

Cellular adhesion. Information process in the course of intercellular interaction (endocrine, paracrine and autocrine regulation). Cellular junctions pathology.

Mechanisms of signal transduction, signals transmission through intracellular receptors. Cytokines: classification, sources, functions.

I Accessory material for self-work

Pathologic process is natural organism response in reply to injury factor. Various in its origin the latter is able to act directly or indirectly (through humoral or reflex influence) on cells and tissues, they reply this influence with stereotyped reactions: alteration, blood supply disturbance, compensation and adaptation, inflammation, give tumors growth. In some

cases these are superficial and reversible changes and in the other cases they are deep and irreversible. Any of them could be a constituent of general pathologic process. It is established that in most cases organism reacts injury with adaptive, defense and compensatory reactions. In case of their insufficiency diseases is developed quite often. For example, inflammation as defense-adaptive reaction occurs as a reply to alteration, cause by mechanical trauma, temperature, chemical agents, infection agents and other injury factors. Simultaneously alteration and blood supply disturbance are constituent elements of inflammation, which often is main manifestation of disease and disease often develops in case of their insufficiency.

Alteration (from Lat. alteratio – change) or injury are modifications of cells structure, intercellular substances, tissues and organs expressed in their disfunctions. The causes of alteration are various. Factors can influence cellular and tissue structures directly (trauma mechanical, thermal, electrical, barometric, toxins of endogenous and exogenous origin) as well as indirectly through humoral (thyrotoxicosis, allergy), or reflex (vasospasms causing hypoxia) influences. Character and degree of alteration depends on pathogenic factor strength and nature as well as on functional features of the organ and tissue. Injury mostly occurs in functionally active parenchymatous structures (heart, cerebrum, liver, kidneys) or on histion level. In some cases superficial and reversible changes of intracellular ultrastructures occur and in the other cases they are deep and irreversible and can end with specific cells, whole organs dying off or even whole organism death. Alteration includes dystrophy and necrosis which as a rule are consequent stages of injury and can develop on ultrastructure and cell levels.

Ultrastructural pathology

Is manifested with injury of plasmolemma, nucleus, mitochondrio, granular and granular endoplasmic reticulum, Golgi apparatus, lysosomes, microfilaments, cytoplasm, etc.

Plasmolemma pathology causes active membrane transport disturbance, water-electrolytic metabolism imbalance, cells swelling and edema. In certain cases under plasma membrane injury some substances delve into cytoplasm and various types of cellular degenerations occurs. Complete injury of Plasmolemma causes cell necrosis.

Membrane injuries conditionally can be distributed into:
Transport, functional-metabolic, structural

Plasma membranes pathology variations:

- local lysis of Plasmolemma is often observed under ionizing radiation influence, chemical agents, antigens action;
- excessive generation of vesicles with further small vesicles merger into big blisters and cavities. Plasmolemma surface increase could be observed owing to micropinocytic vesicles which is a sign of tissue sharp swelling. Under substantial swelling membrane integrity is broken and cell ruins;
- microplasma outgrowths development- occurs under hypoxia;
- folds, cytoplasma outgrowths, invaginations, blisters forming by cell membranes occurs under various injury factors, hypoxia influence;
- membranes thickening is the result of ferments activity suppression and phospholipin number decrease.
- plasma membrane local injuries, its lysis, which is observed under ionizing radiation influence, antigens, chemical agents action, intoxication, hypoxia;

• olive-like structures creation occurs under intensive lipids peroxidation with radiation, chemical and other injuries influence.

Nucleus pathology variations:

• nucleus capsule external membrane protrusion occurs under influence of ionizing radiation, hypoxia, starvation, viral infections, tumor growth;

• nucleus shape change with deep invaginations development in nucleus capsule under toxic substances action, hypoxia, cell hyper function;

• perinuclear space enlargement occurs under hypoxia, ionizing radiation influence, starvation;

• internal membrane protrusion as well as distortion occurs under neoplastic (tumor) processes;

• pores size decrease in nucleus capsule is developed under ionizing radiation action, viral infections, etc.;

• nucleus pores number decrease is developed under ionizing radiation, cell ageing;

• nucleus pores number increase is observed under intoxications, tumor growth, regeneration disturbance;

• nucleus capsule to endoplasmic reticulum communication disturbance occurs under intoxications, protein insufficiency, neoplastic process;

• nucleoplasm clarification and its edema occurs in conditions of hypoxia, under ionizing radiation action;

• chromatin margination into small or big randomly situated aggregates under ionizing radiation influence, chemical regents action and various mutagens;

• lipid, viral, protein, glycogen inclusions occurence in nucleus due to infections, intoxications, diabetes mellitus, etc.;

• mitosis pathology is observed under the influence of ionizing radiation, chemical agents;

• nucleus pyknosis (nucleus corrugation into homogenous hyperchromic aggregation), karyorrhexis (nucleus disintegration into separate fragments), karyolysis (complete dilution of nucleus)

Mitochondrion pathology variations:

- swelling, vacuolization, matrix clarification occurs under ionization radiation, chemical agents influence;
- cristas shape change, their deformation and destruction, their fragmentation occurs under hypoxia, neoplastic (tumor) growth;
- mitochondrion matrix hardening under intoxications;
- shape change and scalloped mitochondrion formation due to hypoxia, at water-salt metabolism imbalance;
- local or complete injury of external membrane under hypoxia, intoxication, radiation;
- mitochondrion myelinic (mucoid) degeneration under ionization radiation, excessive peroxidation of lipids;
- calcium osmic granules accumulation in matrix under hypoxia, intoxications.

Granular and agranular endoplasmic reticulum pathology variations:

- fragmentation, swelling, partial or full loss of ribosomes under influence of hypoxia, hypovitaminosis or neoplasic growth;
- shape or size change under hypoxia, intoxications;
- tubular dilation with osmo structures appearance under intoxications, burns, acute functional cell overload;
- structure simplification;
- ribosomes and polysomes disaggregation;
- irregular ribosomal-lamellar vomplexes creation;

- endoplasmic reticulum atrophy under proteinic starvation, liver diseases,
- intoxications.

Golgi apparatus pathology variations:

- cisterns swelling under hypoxias;
- dictyosomes number increase at the cost of its membranes, secretory granules, vesicles and vacuoles hyperplasia under increased functional activity;
- apparatus size decrease or apparatus structural components collapse under viral infections.

Lysosomes pathology variations:

- primary lysosomes decrease under influence of hypoxia, chemical factors, ionization radiation influence;
- primary lysosomes increase under hypertrophic processes;
- cellular elements accumulation in secondary lysosomes under immune injuries, intoxications, hypoxia;
- lysosomes membrane penetrability increase under hypoxia, toxic substances action, radiation, infection diseases.

Microfilaments injury

Is manifested with their number increase under neoplastic growth, wounds incarnation, liver diseases, alcoholism, cholestasis, cardiomyopathies, etc..

Practical class 1-2

Theme 3 Morphology of cells and tissues reversible and irreversible injury. Intracellular and extracellular accumulation (uptake) of proteins, hydrocarbons and lipids. (Parenchimatous and mesenchimal dystrophies)

Theme topicality: cells and tissues reversible and irreversible injury attributes to general pathologic processes. This injury is often observed under tissue or cellular metabolism disturbance, under cell metabolism substances accumulation or accumulation of endogenous or exogenous pathologic products and is manifested with structural-morphologic changes. These injuries occurs in cells or tissues under various diseases, so knowledge of this theme is necessary for correct understanding and satisfactory learn of the other subsections of general and special anatomical pathology.

Aim: to learn etiology, mechanisms of development, morphologic phenomenon and consequences of cells and tissues reversible and irreversible changes.

Specific purposes:

1. To know varieties of intracellular uptakes, their development mechanisms.
2. To learn the causes, patho- and morphogenesis, morphologic phenomenon, consequences of proteins, glycogens, lipids accumulation in cells and tissues.
3. To know essence of extracellular uptakes, to be able to diagnose hyaline changes in the cells and tissues.

Basic matters for self-work:

Intracellular accumulations (uptakes): definitions, development mechanisms. Varieties: cell metabolism normal

products accumulation, accumulation of pathologic products (exogenous or endogenous).

Protein uptakes (proteinosis): causes, pathogenesis and morphogenesis, morphologic characteristics and methods of diagnosis, clinical symptoms and syndromes, consequences.

Glycogen uptakes (glycogenosis): causes, pathogenesis and morphogenesis, morphological characteristics and diagnosis methods, clinical manifestations, consequences. Acquired and congenital glycogen uptakes.

Lipids uptakes (lipidosis): causes, pathogenesis and morphogenesis, clinical-morphological characteristics, diagnosis methods, consequences. Steatosis. Fatty modifications of myocardium, liver, kidneys. Cholesterol and its esters. Acquired and congenital lipids metabolism disturbances, morphological characteristics.

Extracellular uptakes. Hyaline modifications (degenerations). Intracellular and extracellular hyaline: morphogenesis, morphological characteristics. Hyaline modifications under various pathologic conditions.

I Accessory material for selfwork

Cells and tissue reversible changes occurs in the result of tissue or cell metabolism disturbance and are accompanied with these substances (proteins, fats, hydrocarbons) which exists as norm intracellular or tissue uptakes and appearance of those pathological which do not exist in the norm. These changes are named metabolic products pathologic uptakes or *dystrophies* (from Lat. dys – disturbance, trophe – nutrition). Intracellular uptake of substances causes parenhymatous degenerations development. Parenhymatous degenerations occurs mostly in highly specialized cells of parenhymatous organs (kidneys, liver, heart, cerebrum, etc.). Acquired or congenital fermentopathies underlie parenhymatous degenerations development. These fermentopathies make a big

group of storage diseases or thesaurismoses. Latter contain a big group of storage diseases or thesaurismoses.

Causes of metabolism products abnormal uptake

1 *Cell pathology*. Cells are not able to utilize substances as energy or plastic material or release them. This is caused mostly by cells structure injury with various factors, sometimes by congenital or acquired ferments pathology, which participate in metabolism *(fermentopathies)*.

2 *Function disturbance of transport systems*, providing both substances supply to tissues and cells and metabolism products excretion. It is often observed under cardiovascular collapse and pulmonary insufficiency.

3 *Endocrine and nervous regulation of trophism disorders.*

Mechanisms of metabolism products abnormal uptake

Infiltration is excessive penetration of metabolism products from blood into cells and intercellular substance with their subsequent uptake due to ferment system, providing their metabolism, insufficiency. Substances metabolism products abnormal uptake by way of infiltration is observed in liver, kidneys, aorta wall.

Decomposition (phanerosis) occurs under cell and intercellular substance ultrastructures destruction due to intoxication, hypoxia or other reasons. Ultrastructures membranes are made of proteins, fats and hydrocarbons, so under their destruction these substances are accumulated and stored in cells.

Distored synthesis is synthesis of those substances in cells and tissues which are not observed in them as a norm. As an example, it's glycogen synthesis in nephron tubules epithelium under diabetes mellitus, alcohol hyaline synthesis in hepatocytes.

Transformation is the creation of one kind of metabolism products from intermediate disintegration products, which should be utilized for proteins, fats and hydrocarbons synthesis. For example, it's fats and hydrocarbons components transformation into proteins under starvation, fats and hydrocarbons components transformation into glycogen under diabetes mellitus.

Metabolism products abnormal uptake classification

Classification by the kind of metabolism disturbance prevail:
a) protein, b) fat, c) hydrocarbon, d) mineral

By pathologic process localization:
a) parenchymatous (modifications in the organs parenchymatous cells - cardiomyocytes, hepatocytes, ganglionic cells of cerebrum, etc.);
b) stromal-vascular (modifications in organs stroma);
c) mixed (changes in parenchyma and stroma).

Depending on genetic factors influence:
a) congenital, b) acquired.

By process spread:
a) general, b) local.

Morphology of proteins abnormal uptake (proteinosis)

Occurs under proteins metabolism disturbance. Tissues proteins form cells as plastic materials (capsule, nucleus, cytoplasm, intracellular organelles) as well as intercellular stroma – collagen, elastic, reticulin fibers, basic intercellular substance, vessels, nerves. By proteins metabolism disturbance development location proteinosises are divided into parenchymatous, stromal-vascular and mixed. .

Under parenchymatous proteinosis physical-chemical features of intracellular proteins are violated. At the beginning grain effect occurs in cytoplasm at the cost of protein inclusions, which is manifestation of cell ultrastructures overstrain (hyper function). This process is reversible. Quite often proteins disbolism is combined with Na-K-pump operation faults, which is accompanied with natrium ions uptake and cells hydration. In case intoxication, hypoxia, inflammation or other reasons of proteinosis increase this cause cells destructive changes intensification. The following kinds of parenchymatous proteinaceous degenerations (proteinosis) are recognized: hyaline-drop, hydropic (vacuolar), keratinization.

At hyaline-drop proteinosis proteins compacts and become similar to hyaline cartilage. Big hyalinoid drops of protein occur in cells cytoplasm. Sometimes coagulation necrosis develops and cells die, organ function decreases, but macroscopic changes are not found. This kind dystrophy is often observed in hepatocytes under alcoholic hepatitis (Mellori bodies), in renal tubules epithelium under nephrotic syndrome, etc.

Hydropic or dropsy proteinosis is characterized by intracellular fluid increase, in which cytoplasm proteins are dissolved due to hydrolytic pigments action. Vacuoles full of cytoplasm fluid occur in cells. Further on cells cytoplasm transforms into blisters full with fluid, intracellular organelles

destroy, cell dies off and coliquation necrosis develops. Organs also didn't change macroscopically. Hydropic proteinosis often develops in liver under viral hepatitis, in kidneys under glomerulonephritis, etc.

Keratinization proteinosis is characterized with excessive keratin generation on the surface of plane keratinized epithelium – hyperkeratosis, ichthyosis. The causes of keratinization development is chronic inflammation, avitaminosis, skin development abnormalities. Leukoplakia which is mucous tunics epithelium pathologic keratinization, also belongs to this process and can become a source of malignant growth.

Extracellular uptakes

Extracellular uptakes occur in the result of metabolism disturbance in organs stroma or in vessels walls, so they are named stromal-vascular or mesenchymal proteinosis. Important attention is paid to proteinosis developing in the result of proteins metabolism in conjunctive tissue and are found in stroma and vessels walls. Primary pathologic changes are developed on histion level, consisting of microcirculation channel: basic substance, fibers (collagen, reticulum, elastic), cells (fibroblasts, fibrocytes, lymphocytes, labrocytes, histiocytes), nerves. Basic substance is connecting, cementing, fiber and cells are situated in it. By chemical composition it is polymer of composite protein-hydrocarbon molecules – mucopolysaccharides (glycosamineglycanes). The following relates to stromal-vascular proteinosis: mucoid swelling, fibrinoid swelling (fibrinoid), hyalinosis, which are considered to be consequent stages of conjunctive tissue destruction.

Mucoid swelling – is primary disorganization of conjunctive tissue. *Causes*: hypoxia, allergy, endocrine pathologies. It often occurs under rheumatic and infection diseases, atherosclerosis, it is found in artery walls, cardiac valves, endocardium, heart. Basic substance depolymerization

underlies its development. As a consequence it becomes hydrophilic, attracts liquid, vessel wall penetrability increases. Basic substance hydration, collagen fibers swelling occurs. With vascular-tissue penetrability growth conjunctive tissue saturates with blood plasm proteins, in first turn with albumines and globulins. *Macroscopically* organ or tissue mostly doesn't change. *Microscopically* phenomenon of metachromasia is observed: glycosamineglycanes are painted with toluidine blue in red color. Described changes in conjunctive tissue provided that the reason was eliminated are reversible and tissue structure is rehabilitated.

Fibrinoid swelling is following stage of conjunctive tissue disorganization. Under substantial growth of vascular-tissue penetrability fibrinogen sweats in stroma from vessels clearance, which rather quickly precipitates in strings of fibrin, collagen fibers are destroyed (broken, fragment), conjunctive tissue basic substance chemical composition is changed. Under fibrinoid swelling deep and irreversible disorganization of conjunctive tissue is observed, which is accompanied with basic substance and fibers destruction against the background of considerable increase of balls vascular permeability. *Macroscopically* organ doesn't change, *microscopically* collagen fibers become homogenous, eosinophilic, becomes yelow when painted with picrofuchsin, pyroninophil and argyrophil. *Consequence* Fibrinoid necrosis is developed in the final of the process. *Significance* – organ function disturbance under heart disease formation, joints immobility, luminal narrowing and vessel wall elasticity decrease, organ function termination under renal insufficiency at malignant hypertension, when fibrinoid changes as well as arterioles and cappilars necrosis develops.

Hyalinosis is the final stage of tissue disorganization and is characterized with uptake of collagen destruction products, plasm proteins, polysaccharides, which merge into homogenous

mass which consolidates as time passes, becomes semi-transparent similar to hyaline cartilage, so it is called hyaline. This is complex fibrillar protein. Hyalinosis occurs as a consequence of fibrinoid swelling, plasmorrhagia, sclerosis, necrosis. It develops as the result of peculiar completion of sclerosis in scarring, cardiac valves under rheumatism (local conjunctive tissue hyalinosis). *Macroscopically* fibrous conjunctive tissue becomes dense, cartilaginous, whitish, semi-transparent. *Microscopically* collagen fibers loss fibrillarity and merge into homogenous dense cartilaginous mass, cells squeeze and atrophy.

Heart in such cases is enlarged, ventricular cavities are dilated, mitral valve flappers are dense, whitish color, conjoint in between each other, considerably deformed. This kind of hyalinosis is peculiarly expressed in rough vicious cicatrix after burns (keloid). *Consequences* are unfavorable because of considerable deterioration of organ or injured tissue function.

Systemic hyalinosis develops in vessels walls under hypertension disease, diabetes mellitus (vascular hyalinosis) and is mostly expressed in kidneys, cerebrum, eye retina, pancreas. Considering occurrence pathogenesis three kinds of vascular hyaline are recognized: simple is observed under hypertension disease, atherosclerosis; lipohyaline is developed under diabetes mellitus; complex hyaline occurs in the result of immunopathologic disturbances and vessel wall fibrinoid disorganization at collagenosis.

Morphology of lipids pathological uptake (lipidosis)

Occurs as the result of fats metabolism disturbance.

Lipidosis are divided into parenchymatous and stromal-vascular (mesenchymal) fatty (adipose) degenerations. To reveal fats frozen sections are colored with sudan III or IV.

Parenchymatous lipidosis are manifested with neutral lipids (triglycerides) drops uptake in cells cytoplasm and are the

results of cytoplasm fats metabolism disturbance. Mostly they are found in myocardium, lever, kidneys.

Myocardium lipidosis is characterized with lipoproteids drops uptake in cardiac hystiocytes. As a rule it is observed under intoxications (diphtherial, alcohol, with phosphoric compounds, arsenic, diseases of liver, kidneys, thyrotoxicosis, etc.), long time general hypoxia (anemia, chronic pulmonary and cardiovascular insufficiency), Under oxygen deficiency process of oxidative phosphorylation and ATP synthesis in cardiomyocytes decreases, fatty acids beta-oxidation violates. So fats coming into cell are not completely utilized as plastic and power material and they accumulate in cytoplasm. Besides that under hypoxia membrane lipoprotein complexes destruction is observed (decomposition or phanerosis). *Macroscopically* heart at this process enlarges in size, its chambers stretch, myocardium becomes flaccis, of clay-yellow color, retraction ability of cardial muscle decreases. From myocardium side especially on papillary muscles surface, trabeculas, it is observed yellow-grey striation– " tiger heart", which is caused by dystrophy. *Microscopically* fat uptakes in muscular cells groups, situated downstream cappilars venous elbow and small veins where hypoxia factor is mostly expressed.

Liver lipidosis is characterized with fat content increase in hepatocytes. Quite often it is the result of imbalance between increased fats supply under hyper lipidemia (alcoholism, diabetes mellitus, general obesity), their decreased assimilation (fatty acids oxidation in mitochondrions under hypoxia or toxic influences) and lipids excretion decrease by liver cells under apoprotein production decrease which transports fats in the form of lipoproteins. This is observed in case protein insufficiency in food or under gastrointestinal disturbances, poisoning with ethanol, phosphor, etc., congenital defects of ferments metabolizing fats. *Microscopically* first

occurs saw type, then small drop and large drop degeneration. Three stages of liver lipidosis are distinguished:
1- fat uptake in hepatocytes, 2- fat uptake with mesenchymal reaction development, 3- fat uptake with liver fibrosis and cirrhosis development. Fat fills all cytoplasm and gradually pushes nucleus aside to periphery and modified hepatocytes becomes similar to adipocytes. Fatty degeneration prevalence in peripheral portions of liver part confirms infiltration mechanism of its development, which is observed under hyperlipidemia. Fatty degeneration development prevalence in central portions of liver part is connected with decompensation mechanism and is observed under hypoxia or intoxication. *Macroscopically* liver is enlarged, loose (of pastry consistency), yellow or clay color.

Kidneys lipidosis is often observed under nephrotic syndrome, chronic renal insufficiency when hyperlipidemia and lipiduria occur. Fat excess is excreted from organism with kidneys and constipates them. *Microscopically* fat occurs in proximal, distal or convoluted renal tubules epithelium in cells basal portions. Nephrocytes lipidosis often joins hyaline-drop degeneration and hydropic proteinosis. *Macroscopically* kidney is enlarged, flaccid, cortical layer is dilated with signs of swelling, of grey color with yellow specks.

Congenital lipid metabolism disturbances are manifested with systemic lipidosis and pertain to fermentopathies (diseases of storage or uptake). The following diseases are marked out: cerebrosine lipidosis (Gaucher's disease), sphingomyelin lipidosis (Niemann-Pick disease), generalized gangliosidosis (Tay-Sachs disease), generalized gangliosidosis (Norman-Landig disease), which are accompanied with liver, spleen, marrow, nervous system and other organs and tissues damage.

Stromal-vascular lipidosis include neutral fat metabolism disturbance in adipose tissue and adipose depot as

well as cholesterol and its ethers in arteries walls under atherosclerosis.

General disturbance of neutral fats metabolism is manifested with neutral fat stocks increase or decrease in hypodermic fat tissue, mesentery, pericardium, marrow, etc. General uptake of neutral fat in fat depots is called obesity. The following is recognized: primary or idiopathic obesity the cause of which is unknown and secondary obesity which occurs under endocrine, cerebral and hereditary diseases. By external signs obesity kinds are as follows: upper, mid, lower and universal symmetric. By morphologic signs hyper plastic type is marked out characterized with fat cells (adipocytes) quantity increase in organism as well as hypertrophic (malignant) type the basis of which is adipose cells size increase several times and triglycerides content increase in cytoplasm several times.

Under general obesity the important clinical attention is paid to heart injury. In this case adipose tissue grows under pericardium, surrounding organ like case. Lipocytes uptake in myocardium stroma between cardiac hystiocytes, squeezing the latter ones which causes their atrophy. Right portion of the heart is the most injured one. Sometimes the whole thickness of right ventricle myocardium is changed with adipose tissue, that can cause cardiac rupture or accelerate decompensation process.

Neutral fat local uptake is observed under Madelung's syndrome, Dercum's disease and Weber-Krischen's desease, as well as vacant obesity when organ atrophied portion is substituted. The essence of Dercum's disease is in painful lipomas occurrence in subcutaneous adipose tissue of extremities and trunk. Weber-Krischen's disease is characterized with recurrent nonpurulent cellulites with productive granulomatous inflammation development around sphacelous adipose tissue.

General decrease of adipose tissue occurs under emaciation (cachexia). Tissue becomes loose, flabby, is saturated with liquid, sliming.

Cholesterol and its ethers' metabolism imbalance is a basis of atherosclerosis development. Uptake of cholesterol fractions, lipoproteins of various density, proteins in arteries' walls causes formation of fat detritus (atheroma) and conjunctive tissue enlargement (sclerosis). Hereditary cholesterol metabolism disturbance is observed under family hypercholesterolemic xanthomatosis, manifested with xanthalasms formation (cholesterol deposition in skin, big vessels' walls, heart valves and other organs).

Carbohydrates pathologic uptake (glycogenosis) morphology

The most valuable in carbohydrates metabolism disturbance is glycogen, glycosamineglycanes and glycoproteins. The most important in this pathology is glycogen metabolism disturbance occurring under diabetes mellitus. In case insulin deficiency in blood the tissues utilize sugar insufficiently causing sugar level increase in blood (hyperglycemia), and glycogen quantity in tissues decreases. Kidneys remove sugar excess with urine (glucosuria). In the result of glucose polymerization under its resorption from plasma ultrafiltrate glycogen is accumulated in tubules epithelium, mesangium and membranes of glomerule vessels. The most of it is in epithelial cells and in Henle's loop lumens (narrow segment). Epithelium in these sections of nephron becomes high, with light and foamy cytoplasm. Changes in kidneys under diabetes mellitus are finalized with sclerosis development called diabetic glomerulosclerosis.

Hereditary (glycogenosis) occurs under deficiency of ferment which splits glycogen and the latter accumulates in cells. These includes hepatorenal glygenosis, Pompe disease, MacArdles and Gerce's under which glycogen structure is not damaged, as well as Forbes-Cori (type 3 glycogenosis) and Anderson's disease (type 4 glycogenosis) under which this structure is changed.

Under glycoproteins metabolism disturbance (mucins and mucoids which are the base of mucus) mucus degeneration develops. The typical manifestation of it is mucoviscidosis which is systemic disease, charactristic of which is high viscosity of mucus, causing development of retention cysts and sclerosis in pancreas, bronchi, digestive and other glands. Besides that this degeneration is often observed under catarrhal inflammation of nose mucous tunic (rhinitis), mucous tunic of larynx (laryngitis), bronchi (bronchitis), stomach (gastritis), etc. *Macroscopically* excess of mucus is seen on mucous tunic, and this mucous trickles down from the surface. *Microscopically* wine glass like cells appear in mucous tunic and release mucus. Also desquamation or cells necrosis is observed, glands' excretory ducts are clogged with mucus which is accompanied with cysts formation.

Glycoproteins and glycosamineglycanes uptake in organs' stroma is accompanied with collagen fiber as well as cartilage and adipose tissue substitute with mucus-like mass. Damaged tissues cells have star-like shape. This process is called tissue sliming and it is observed under cachexias and myxedema. Carbohydrates uptake *consequence* can be reversible and under process progress they become semi-transparent, looks like mucus, colliquative necrosis develops.

II Algorithm of the practical part of classes

To learn and be able to describe orally macropreparations

1 *Dim swelling of the kidney*. Organ is quite enlarged, flabby consistence, on cut parenchyma and also capsule of the kidney lost their usual lustre, they have dim appearance. Such changes in kidneys develop at the infectional, infectional-allergic, toxical injury, in disorders of blood circulation in organ as a result of chronic cardiac insufficiency.

2 *Fatty dystrophy (degeneration) of the liver ("goose liver")*. Liver is enlarged, flabby consistence, yellowish-ochre colour. In cutting of the organ, thin coating of fat is seen. Name possible mechanisms of development and in which diseases such pathological process can develop.

3 *Fatty dystrophy (degeneration) of myocardium ("tiger heart")*. Heart is enlarged, flabby, with dilatated chambers. On a cut myocardium is dim, yellowish-brown colour. On the side of endocardium the yellow- white striation is seen, especially in the area of trabecular muscles of the right ventricle. Name causes and mechanism of development of the indicated changes.

4 *«Glazed» spleen*. Organ's capsule is hyalined, it is thicked and reminds glaze (cooled, saturated solution of sugar beated up with egg-white, with which confectionery is decorated). Explain mechanism of development and diseases in which this pathological process arises.

5 *Hyalinosis of heart valves* – valves of heart are thicked deformated, glassy (hyaline). Name possible cause of pathological changes origin.

6 *Superfluous development of subcutaneous adipose cellular tissue* of the front abdominal wall in total obesity. It is necessary to mark sharp increase of thickness of adipose layer, colour soft consistence. What are the causes of development of such changes?

7 *Obesity of heart.* Heart is enlarged, there is thick layer of adipose cellular tissue under epicardium, which whaps round the heart, like a case. What are the causes of indicated changes? What is the pathological prognosis of this pathology?
8 *Atherosclerosis of aorta.* Aorta's intima is covered by plenty of yellowish spots, there are places of ulceration. Explain in which disease such pathology arises?
9 *Artheriosclerotical nephrosclerosis.* Kidney is diminished in size, its surface is small-hilly owing to presence of numeral areas of sticking. Atrophy of nephrons and substitution by connective tissue as a result of violation of blood supply took place in these areas. That is connected with hyalinosis of arterioles and collapse of capillary loops in glomerula. In neighboring areas of kidney hypertrophy of uninjured nephrons took place, that stipulated their insignificant thrusting above a surface as grey-red granules. Kidney is a bit deformed, the width of cortical layer is diminished. Such kidney, that appeared as a result of hyalinosis of kidney arteries, is named primary-wrinkled.

To learn micropreparations from a theme and be able to draw the essence of pathological process with proper designations
1 *Hyaline drops in cytoplasm of epithelium of kidney ducts.* Preparation is stained by hematoxilin-eosin. There are pink corn of proteins in the epithelium of curled tubules of the proximal part of nephron, they have different size. Sizes of epithelial cells are enlarged, cytoplasm has changed transparency, clearance of tubules is narrowed. Designate 1. hyaline corns in the tubules epithelium; 2. narrowed clear space of ducts.
2 *Fatty dystrophy (steatosis of liver).* Preparations are stained by hematoxilin-eosin and also by sudan III for the exposure of the fatty inclusions which are located mainly on periphery of hepatic lobule. In majority fatty drops fully substitute the

cytoplasm, ousting nuclei on periphery of hepatocyte. Same causes of development of such changes. What is the mechanism of appearance of the fatty inclusions in hepatic cells? Designate 1)drops of fat in hepatocytes, 2)not damaged hepatocytes. 3)glycogenous infiltration of tubules epithelium of kidney.

3 *Glycogen in the epithelium of kidney.* Preparation is stained by Best's carmine for the exposure of glycogen in the epithelium of tubules of kidney, which accumulates mainly in the narrow part of nephron. Thus the granules of reddish-violet color appear in the epithelium of duets. Cytoplasm is foamy, transparent. The height of nephrothelium is increased. Specify what illness such changes in kidneys develop? What changes will develop in kidneys at that? Designate: 1- glycogen in the epithelium of duets 2- uninjured tubules.

4 *Hyalinosis of arteries of spleen.* Preparation is painted by hematoxilin-eosin. Considerable thickening of arterial walls which are homogeneous, rose colour, is seen. Clear space of arteries is sharply narrowed. What type of hyalinosis takes place in this preparation? Designate: 1)deposition of hyaline in walls of arterioles, 2)pulp of spleen.

5 *Obesity of heart.* Preparation is stained by hematoxilin-eosin. Accumulation of adipose cells between cardiomyocytes is marked: atrophy of muscular fibers. At what decease this process is found? Designate: 1- atrophied cardiomyocytes, 2- drops of fat between cardiomyocytes

6 *Arteriosclerotic nephrosclerosis.* Preparation is stained by hematoxilin-eosin. Considerable thickening of walls of arteries in kidney glomerules which are homogenous, rose colour is seen. Clearance of arteries is considerably narrowed. Glomerules are atrophied, substituted by connective tissue. In neighboring areas there are glomerules with signs of hypertrophy, plethora of vessels. Designate: 1- accumulation of hyaline in the wall of arterioles, 2- atrophied glomerules.

7 *Squamous cell carcinoma of skin with keratinization.* Preparation is stained by hematoxilin-eosin. Considerable thickening of epidermis in which atypical polymorphic squamous epithelium growth is seen. Between mass of atypical cells there are numerous homogenous, rose colour , horny (substance) forms. Designate: 1- accumulation of horny substance, 2- epidermis.

Situation tasks

1 Patient ill with lacunar tonsillitis shows high temperature (up to 40 °C); apparent tachycardia, traces of protein are found at urine analysis. After recovery cardiac performance became normal, laboratory test of urine indices are without deviations. Name possible changes in myocardium and kidneys and mechanism of their development.

2 Considerable protein content (up to 15g a day) is observed for a long time in urine of patient with kidneys pathology. What kind of kidneys degeneration it testifies?

3 Patient ill with chronic leukemia shows apparent anemia developed (40 g/l hemoglobin for 8 months). Heart sounds are impaired, subdued, heart boundary is extended. Death occurred from cardiac decompensation. What kind of degeneration developed in myocardium? Name mechanism of its development. What macroscopic changes will be found under postmortem examination (autopsy)?

4 Woman, 45 years old, cook, was taken for treatment with obesity developed because of reduced motion activity and excessive amount of food using rich with fats and hydrocarbons, complains of appression in right hypochondrium, sometimes nausea. Enlarged liver is palpated. What changes occurred in liver? Describe their morphogenesis,

5 Woman, 39 years old, portions of grey-pale color were found on neck of uterus mucous tunic. Leukoplakia was found under

biopsy material investigation. What kind of degeneration is it? What is the clinical meaning of it?

6 Patient suffered from aortic valve rheumatic failure. Death came from chronic cardiovascular collapse. Autopsy showed crescent valves in aorta mouth are thickened and webbed, opaque, dense, of milk-white color. What pathologic process developed in aorta valves?

7 Patient suffered from hypertension disease and died from kidney insufficiency. Under microscopic investigation the following changes of arterioles were found in kidneys: their walls are thickened, luminal narrowing is observed, intima is in the form of homogenous mass of red color. Autopsy shows kidneys' size reduction, small-grained surface. What degeneration developed in arterials' walls?

8 Autospy of patient died from infarction showed changes in aorta intima, it's uneven, dense limens narrowing it are seen, as well as whitish-yellow plaques and spots. What pathologic process developed in aorta intima?

Answers on situational tasks

1 Reversible injury of parenchymatous structures developed in myocardium and kidneys in the form of proteinosis (muddy swelling) and lipidosis. Mechanism of their development is phanerosis in the heart and infiltration in kidneys.

2 Testifies irreversible injury proteinosis – hyaline-drop and hydropic degeneration.

3 Lipidosis, decomposition, infiltration, transformation, adipopexia under epicardium, cardiac muscle wall flabbiness, heart cavities enlargement.

4 Lipidosis, adipose drops sedimentation in hepatocytes, later on associated with mesenchymal reaction, structural changes in the organ.

5 Keratinization, precancerous process.

6 Valves' hyalinosis (hyaline degeneration).

7 Vascular wall hyalinosis.
8 Atherosclerosis of aorta.

Test tasks

1 Hemorrhage developed from esophagus's varicose veins of S. patient suffered with chronic alcoholism and cardiac cirrhosis, this hemorrhage caused his death. Autopsy: liver is fine gibbous, reduced in size, solid, of yellow color. Under liver histological research (coloring with hematoxylin-eosin) big optically empty vacuoles are found in hepatocytes, which contain substance which is colored black with osmium acid. Optically empty vacuoles in hepatocytes are:
A. Large-drop (globular) adipose degeneration. **B.** Hyaline inclusion. **C.** Pseudovacuoles of hyaloplasm. **D.** Vacuolar or hydropic degeneration. **E.** Alcoholic hyaline (Mellori corpuscles).

2 Autopsy of patient died of lung-cardiac insufficiency showed significantly enlarged anemic liver of doughy consistence, of yellow color. Under hematoxylin-eosin coloration vacuoles of various sizes were found in hepatocytes' cytoplasm. What degeneration is it?
A. Mesenchymal. **B.** Hydropic. **C.** Hyaline-drop.
D. Carbohydrate parenchymatous. **E.** Parenchymatous adipose.

3 Girl, 18 years old, suffered from sharp pain in swallowing, neck lymphadenopathy, temperature increased up to 39^0C. There are whitish-yellow spots on tonsils mucus tunica which are hard to separate creating defect. State degraded progressively. Patient died on 8^{th} day of disease under growing effects of cardiac insufficiency. What histologic changes in cardiomyocytes are the most likely to be found ?

A. Mucus degeneration. **B.** Adipose degeneration. **C.** Hyaline-drop degeneration. **D.** Bladder degeneration. **E.** Hydropic degeneration.

4 Autopsy of patient died of malignant neoplasm shows that kidneys are enlarged, dark, with edema, their capsule is tense, easy to take off, surface with grayish tint, cerebral layer is cyanotic. Describe microscopic changes of tubules epithelium.
A. Adipose stromal-vascular degeneration. **B.** Hyaline-drop degeneration. **C.** Cloudy degeneration. **D.** Carbohydrate-parenchymatous degeneration. **E.** Adipose parenchymatous degeneration.

5 Autopsy of patent died of chronic cardio-vascular insufficiency revealed "tiger heart". From endocardioum side yellowish-white strips are seen, myocardium is dark, clay-yellow. What process caused this pathology?
A. Adipose degeneration of cardiomyocytes. **B.** Carbohydrate degeneration of cardiomyocytes. **C.** Hyaline-drop degeneration of cardiomyocytes. **D.** Simple adiposis cardiaca. **E.** Cardiac muscles amyloidosis.

6 Patient M., 46 years old, died on the third day after unknown mushrooms eating. Diagnosis: acute hepatic failure. Autopsy shows that liver is insignificantly enlarged, flaccid, clay like. What kind of degeneration is observed in hepatocytes in this period?
A. Lipofuscinosis. **B.** Hyaline-drop. **C.** Carbohydrate. **D.** Adipose. **E.** Hydropic.

7 The child was diagnosed with faucial diphtheria in the hospital. Child died of cardiac insufficiency. Autopsy showed that cardiac cavity is transversally enlarged. Cardiac muscle is dark, flaccid, striped in section, with yellowish portions. Small

vacuoles are found in cytoplasm of some cardiomyocytes with cytoplasm conserved. Vacuoles are colored black by osmium acid in frozen sections. What kind of degeneration is found in cardiomyocytes?

A. Bladder. **B.** Carbohydrate. **C.** Adipose. **D.** Hyaline-drop. **E.** Hydropic.

8 Patient ill with hypertension disease was diagnosed with prolonged hypertension stroke. What postmortem changes will be observed in arterioles wall?

A. Calcinosis. **B.** Hyalinosis. **C.** Amyloidosis. **D.** Fibrinoid necrosis. **E.** Sclerosis.

Test tasks answers

1. A; 2. E; 3. B; 4. C; 5. A; 6. D; 7. C; 8.D;

Illustrations to theme

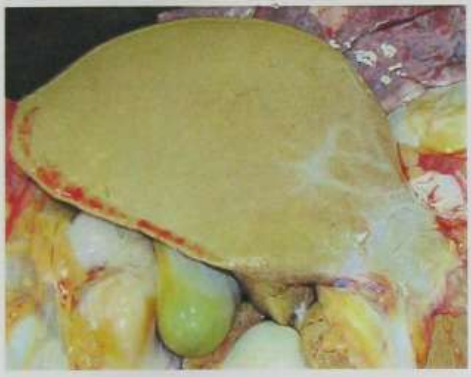


Figure 1 – Liver lipidosis ("goose liver"). Liver is enlarged, of flaccid consistency, of ochre-yellow color. Name possible mechanisms of development and the diseases during which this pathological process occurs.

Figure 2 – "Glazed" spleen. Organ capsule is hyalinized. It is thickened, resembles glaze. Name mechanism of development and diseases causing this process.

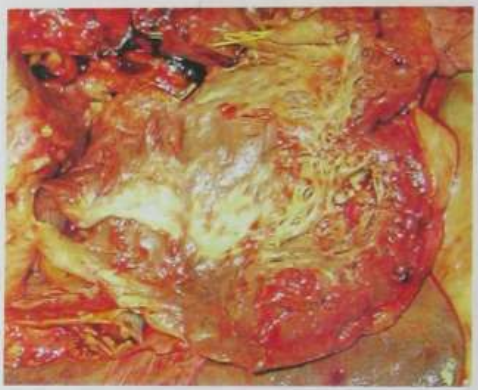


Figure 3 – Cardiac valves hyalinosis – mitral valves are thickened, deformed, glassy. Name the causes of pathologic changes.

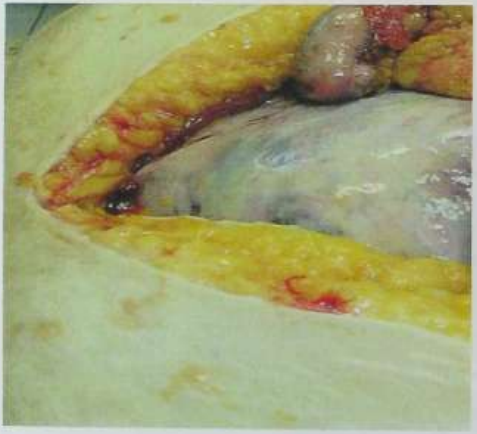


Figure 4 – Excessive growth of subcutaneous fatty tissue of ventral abdominal wall under general obesity. Name possible causes.

Figure 5 – Atherosclerosis of aorta. Aorta's intima is covered with big amount of yellowish spots, in some places ulcers are seen. Name diseases causing this pathology,

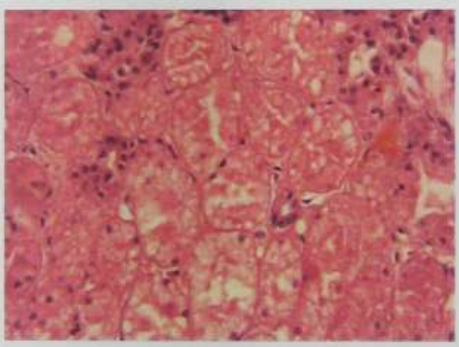


Figure 6 – Hydropic degeneration of nephrothelium. Specimen is colored with hematoxylin and eosin. What is uptake mechanism of marked by vacuole in crimped nephron tubulas epithelium cytoplasm?

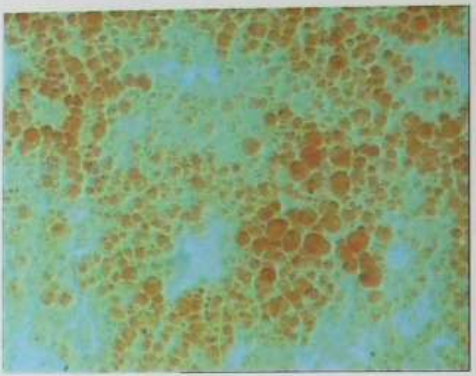


Figure 7 – Liver lipidosis. Specimen is colored with sudan III. In the majority of hepatocytes adipose drops replace cytoplasm in full. Name the cause of such changes development. What is the mechanism of adipose inclusions appearance in hepatic cells?

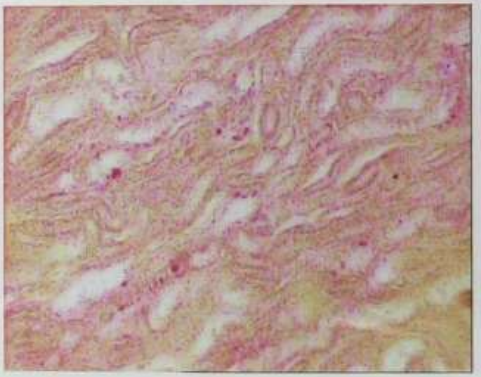


Figure 8 – Kidney tubules epithelium glycogene infiltration. Specimen is colored with Besta carmine. Granules of reddish-violet color are found in tubules epithelium. Name disease under which such changes in kidneys develop. What changes will occur in glomerules at that?

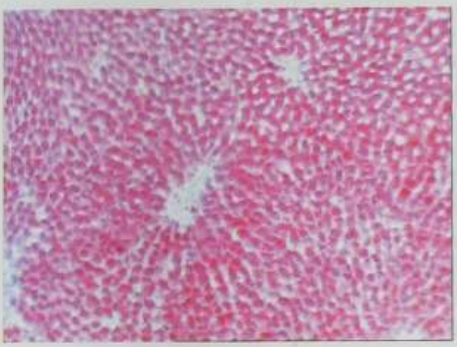


Figure 9 – Glycogen uptake in hepatocytes cytoplasm. Specimen is colored with periodic acid. There is big quantity of red color granules in hepatocytes. Name the diseases at which hepatic glycogenome is possible.

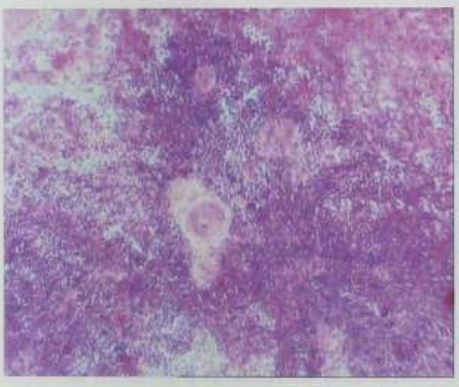


Figure 10 – Spleen arteries hyalinosis.. Specimen is colored with hematoxylin and eosin. It is seen that arterial walls are sharp thickened, they are homogenous, of red color, arteries lumen is sharply narrowed. What kind of hyalinosis exists in this specimen?

Practical class 3

Metabolic disease. Morphology of pathologic accumulation of endogenous and exogenous pigments. Morphology of mineral metabolism disease

Importance of the topic: metabolic disease rather often occurs in practice of clinicians and should be considered as a manifestation of general pathologic processes. Often it occurs at endocrine diseases, as well as at pathology of gastrointestinal tract and hepatobiliary system and it reveals through structural morphologic changes. Knowledge of issues of this topic enlarges the minds of would-be clinicians concerning the kind of changes that underlie various pathologic processes at one or another disease.

Purpose: to study causes, development mechanism, morphologic manifestations and consequences of accumulation of endogenous and exogenous pigments, as well as mineral metabolism disease.

Specific goals: 1 To learn varieties of metabolic diseases and their development mechanisms.

2 To study causes, development mechanism, pathogenesis and morphogenesis, morphologic presentations and consequences of accumulation of endogenous and exogenous pigments, as well as mineral metabolism disease.

3 To learn to differentiate various kinds of pigment metabolic diseases and mineral metabolism diseases according to morphologic signs.

4 To evaluate functional importance and consequences of accumulation of endogenous and exogenous pigments, as well as mineral metabolism diseases, to know how to diagnose their morphologic manifestations in cells and tissues.

Basic matters for self-training

Iron metabolic disease and metabolic disorder of hematogenous pigments. Metabolism and pathogenic action of iron, formation of anabolic and catabolic ferritin. Classification of hematogenous pigments. Toxic forms of ferritin: causes and consequences of their formation.

Hemosiderosis (topical and extensive): causes, pathogenesis, morphologic characteristics and consequences. Acquired and congenital hemochromatosis: morphologic characteristics and consequences.

Hematoidin, hematin, porphyrin: features and area of formation, morphologic characteristics and consequences of their accumulation.

Bilirubin metabolic disease: causes, pathogenesis and anatomical pathology of hemolytic jaundice, hepatic jaundice, obstructive jaundice. Pathogenic effect of increased bilirubin, complications and causes of death at jaundice.

Melanin formation disorder. Causes, pathogenesis, morphologic characteristics of hypopigmentation (leukoderma, vitiligo, albinism) and hyperpigmentation (common melanoderma, local melanosis, pigmented nevus).

Nucleoprotein metabolic disease. Podagra and gouty arthritis: classification, aetiology, pathogenesis, stage of disease and morphologic characteristics of joints' changes, clinical presentations, complications and consequences. Podagric nephropathy. Clinicopathologic characteristics.

Copper metabolic disease. Hepatolenticular degeneration (Wilson's disease).

Potassium metabolic disease. Periodic paralysis.

Calcium metabolic disease. Acute hypocalcemia and hypercalcemia: definition, pathogenesis, consequences and their role in thanatogenesis. Calcinosis (calcification): definition, classification, morphogenesis of metastatic

calcification, dystrophic calcification and metabolic calcinosis; consequences, the role of calcification of organs in thanatogenesis.

Stone formation: localization, causes, pathogenesis, types of stones, consequences and complications of stone formation.

1 Auxiliary materials for self-training to practical lesson

Pathologic accumulation of endogenous pigments rather often is represented in metabolic disease of complex proteins – chromoproteins, nucleoproteins, glucoproteins and lipoproteins. Chromoproteins, or colored proteins, are endogenous pigments, to which hematogenous, proteinogenous and lipidogenous pigments are referred. Metabolic disease of complex proteins is observed in parenchyma, as well as in stroma of tissues and organs.

Iron metabolic disease and metabolic disorder of hematogenous pigments

Ferritin, hemosiderin, bilirubin are referred to hematogenous pigments. There are pigments which may be accumulated in organism at physiological conditions and at some diseases; hematoidin, hematin, porphyrin are pigments which are formed only at pathologic processes. They are generated from hemoglobin at destruction (hemolysis) of erythrocytes.

Ferritin is generated from hemoglobin at intensive intravascular hemolysis of erythrocytes – catabolic form. Anabolic form is generated from iron absorbed in bowels . At conditions of hypoxia ferritin is restored into an active form (SH-ferritin) which is an adrenalin antagonist, that's why it acts vasoparesically, i.e. as vasodilator. An active ferritin is

accumulated at incompatible blood transfusion and collapse of vessels is observed, then a syncope takes place.

Hemosiderin is generated from hemoglobin only in macrophages (intracellularily). It appears outside the cell only after cell destruction. It looks like small brown seeds; tissue acquires brown coloration at evident hemosiderosis. One can distinguish common and topical hemosiderosis. Common hemosiderosis is developed at intensive intravascular hemolysis of erythrocytes (incompatible blood transfusion, hemolytic poisoning). Unconjugated hemoglobin is captured by macrophages of unitary mononuclear phagocyte system of liver, spleen, lymph nodes, bone marrow, thymus gland in which hemoglobin turns into hemosiderin. Listed organs acquire brown coloring.

Topical hemosiderosis arises at areas of extravasation. Erythrocytes are absorbed outside the vessels by macrophages, in which hemoglobin turns into hemosiderin. An example of topical hemosiderosis is pulmonary hemosiderosis which is developed at venous plethora of lungs accompanied by diapedetic extravasations.

Hemochromatosis is a peculiar disease closely related to common hemosiderosis. There could be primary and secondary one. Primary (hereditary) hemochromatosis is referred to storage diseases, caused by a hereditary defect of small intestine ferments. A secondary one is conditioned by acquired enzymatic deficiency of systems providing food iron metabolism.

Bilirubin is a bile pigment generated at destruction of hemoglobin and detachment of haem in reticulum- endothelial (mononuclear) system. Increased bilirubin (bilirubinhemia) is evidence of jaundice. One can distinguish hemolytic jaundice, hepatocellular jaundice and obstructive (mechanical) jaundice.

Hemolytic jaundice arises at infectious diseases, intoxications, isoimmune and autoimmune conflicts, massive hemorrhage, as well as erythrocytopathy and hemoglobinopathy.

Hepatocellular jaundice arises at liver diseases of various aetiology, in case defective hepatocytes are not able to capture bilirubin, its conjugation to glucuronic acid and excretion are disturbed. Obstructive (mechanical) jaundice arises at retention of bile outflow from liver.

Hematoidin is a pigment which doesn't contain iron. It is accumulated in central areas of hemorrhage in the distance of living tissues.

Hematin – is an oxidized form of haem. The following pigments are referred to: malarial pigment which is generated from hemoglobin under influence of malarial plasmodia, muriatic hematin which is generated at hemoglobin interaction with intestinal juice ferments and hydrochloric acid (it colours erosions and bottom of bleeding ulcer into black and brown), as well as formalin pigment which occurs in histologic specimen fixed by acid formalin.

Hematoporphyrin is a pigment which is melanin antagonist. Its small quantity is contained in blood, urine and stool, it heightens light sensibility of skin. Excess accumulation of this pigment is called porphyria. It could be caused by congenital defect of porphyrin metabolism or acquired one: lead or barbiturate poisoning, avitaminosis PP, etc. Such patients are UV hypersensitive which causes burns, ulcers, skin atrophy and depigmentation. Bones and teeth are coloured into brown.

Metabolic disorder of proteinogenous pigments. Melanin chromogenesis disorder.

Melanin, as well as adrenochrome and pigment of enterochromaffin cell granules are referred to proteinogenous (tyrosinogenous) pigments which are tyrosine and tryptophan metabolic derivatives.

Melanin is a brown-black pigment which determines color of skin, hair and eyes. Melanin chromogenesis disorder could appear in increase or decrease of this pigment in skin. There could be local or extensive process. There could be congenital or acquired pathology. Extensive hypopigmentation or hypomelanosis (albinism) appears as a result of hereditary deficiency of tyrosinase. Local hypomelanosis (vitiligo, leukoderma) appears as a result of disorder of neuroendocrine control of melanogenesis at leprosy, diabetes mellitus, hyperparathyroidism, Hashimoto's thyroiditis, syphilitic skin affection. Extensive acquired hypermelanosis declares itself in excessive accumulation of melanin in skin (melanoderma) and is observed at emaciation, Addison's disease, endocrine disorders, pellagra, scurvy. Extensive congenital hypermelanosis declares itself in spotted skin pigmentation, hyperkeratosis and edema – pigmentary xeroderma. Local congenital hypermelanosis is represented by birthmarks or nevus, acquired one is observed at pregnancy, pituitary adenoma, lentigo, melanosis coli at constipation.

Adrenochrome is an adrenalin oxidation product. It occurs in the form of granules in cells of medullary substance of adrenal glands.

Pigment of enterochromaffin cell granules occurs in cells of diffuse endocrine system: enterochromaffin cells of stomach, bowels, B and C cells of thyroid gland, cells of juxtaglomerular apparatus of kidney, cells of Langans's islands of pancreas. It is considered to be a serotonin analog. Carcinoids or tumors made of above mentioned cells possess a significant serotonin activity. In such cases patients get carcinoid syndrome.

Metabolic disorder of lipidogenous pigments

Lipofuscin and lipochromes are referred to lipidogenous pigments.

Lipofuscin is a pigment of goldish colour. Its perinuclear location is an evidence of active metabolic processes. Its accumulation (lipofuscinosis) at the periphery of a cell is an evidence of activity decrease of respiratory ferments in a cell. Lipofuscinosis is occurred at aging, cachexy. The organs are colored into brown – brown atrophy of myocardium, liver.

Lipochrome colours lipocytes, adrenal gland cortex, blood serum, yellow body of ovary into yellow. At pathologic conditions the quantity of lipochromes is increased in fatty tissue at diabetes mellitus, lipidic-vitaminous metabolic disorder, drastic emaciation.

Metabolic disorder of nucleoproteids

It could be often observed at excessive formation of uric acid and its salts which determines development of podagra, urolithiasis, uric acid infarct. At most cases pathology is determined by congenital purine metabolic disorder. Over-use of animal proteins, kidney diseases are of a significant importance for disease pathogenesis. Uric acid sodium deposits in joints (synovial membrane, articular cartilages of hands and feet), synovial membranes of tendon with necrosis

areas developed, granulomatosis giant-cell reaction, painful arthroliths, deformation of joints are typical for podagra and gouty arthritis. Podagric nephropathy – uric acid salt deposits in ducts and gathering tubes with obstruction of their lumens and inflammatory, sclerotic and atrophic changes – arises as complication.

Copper metabolic disorder

It could be most often observed at hereditary hepatolenticular degeneration or Wilson's disease. Copper accumulation is observed in liver, brain, kidneys, pancreas,

Potassium metabolic disorder cornea – typical green-brown Kaiser- Fleischer ring at the periphery of cornea. Dystrophic and sclerotic changes are the result of copper accumulation in organs.

It could declare itself in increase of potassium in blood and tissues which is observed at Addison's disease as result of affection of adrenal glands. Decrease of potassium causes periodic paralysis – fit of weakness and motor paralysis development.

Calcium metabolic disorder

It could declare itself in increase or decrease of calcium concentration in blood (hypocalcemia and hypercalcemia). Calcium metabolic disorder results in development of calcifications (calcinosis) – calcium salts deposits in intercellular substance or cells, that's why calcifications are divided into intercellular and extracellular ones. According to development mechanism there are metastatic, dystrophic, metabolic calcifications. Calcifications also could be systemic or local.

Metastatic calcifications are more often systemic and appear at hypercalcemia caused by the following:

- disorder of endocrine control of calcium metabolism (hyperproduction of parathyroid hormone, calcitonin deficiency), excessive vitamin D content;
- intensive calcium excretion from bones (multiple fractures, myelomatosis, tumor deposits of bones, osteomalacia, hyperparathyroidic osteodystrophy);
- disorder of calcium excretion from organism (colonic involvement, chronic dysentery, mercuric chloride poisoning, kidney diseases: polycystic renal disease, chronic nephritis).

Most often there are calcium salts deposits in lungs, mucous coat of stomach, kidneys, miocard, walls of arteries.

Dystrophic calcifications or petrifications are of local character and result in calcium salts deposits formation in necrosis areas or areas of severe dystrophic changes of tissues (tuberculosis, gumma, infarction, atherosclerosis of vessel wall, mitral valve at endocarditis, dead parasites).
Change of physicochemical composition of tissues and local increase in phosphatase activity determine their development, there is no hypercalcemia observed at the same time.

Metabolic calcinosis appears at instability of buffer systems of organism (calcium gout, interstitial calcinosis). *Consequences* of calcifications are unfavorable in most cases.

Stone formation is appearance of solid concrements in caval organs or excretory ducts of glands. Stones appear in biliary and urinary tracts, excretory ducts of pancreas and salivary glands, bronchi and bronchiectasis, as well as in vessels and bowels. Stone formation is caused by acquired or hereditary metabolic diseases (metabolic disorders of carbohydrates, fats, nucleoproteins, minerals). Among local factors there are secretion disorder, secretion congestion, inflammation.

Depending on localization and form of organ in which stones appear there are solitary, multiple, round, oval stones, stones with processes, cylindrical, smooth and shaggy stones. Cholelithic disease and urolithiasis, pressure bedsore, perforation of organs, fistulas, inflammation of walls of caval organs, jaundice, hydronephrosis are the consequences of stone formation.

II Algorithm of practical part of the lesson

Learn and describe orally macropreparations

1) *Brown induration of the lungs.* It is an example of local haemosiderosis. Haemosiderosis is always an evidence of haemoglobin destruction. In that case haemosiderin forms in alveolar and tissue macrophages of the stroma. Insufficiency of the lymphatic system of the lung stipulates accumulation of this pigment in stroma, that gives rusty tinge to the lung. Lymphostasis, presence of unnecessary protein, hypoxia stipulates activation of fibroblasts and development of pneumosclerosis. Accordingly to that organ becomes dense (induration). Lung is enlarged, densed, brown colour with numerous rusty disseminations owing to accumulation of haemosiderin. In venous plethora, conditioned by that that right ventricle of heart force blood to the basin of pulmonary artery (small circle of bloodcirculation) and left ventricle is not able to pump blood from lungs into aorta. Owing to defect of valves or affection of myocardium, blood congests in small circle of blood circulation. Vessels widen, permeability of their walls increase so, that not only fluid part of blood exudates into alveoli (oedema of lungs), but also erythrocytes the last are exogenous that's why they are absorbed by macrophages in which haemoglobin turns into brown colour haemosiderin. Intensity of colouring depends on duration of venous plethora of lungs.

2) *Haemorrhage in brain.* On the surface of the brain cut there is an area of tissue softening with blood infiltration, brown colour. Brown colouring is conditioned by accumulation of haemosiderin and haematoidin.

3) *Hydrochloric acid haematin on the bottom of ulcer of stomach wall.* There is deep defect of mucous, submucous and muscular layers of the stomach wall. Mucosa is hypertrophied, folds are protuberant around the ulcer. There is an ulcerated vessel and deposition of dark-brown colour pigment-hydrochloric acid haematin on the bottom of ulcer.

4) *Billiar cirrhosis of liver.* Liver is dense with small-granulated surface. On cut parenchyma is greenish-brown colour with connective tissue net, which is well discerned. Bile ducts are widened, filled with stones. What is the mechanism of stones formation? Name morphogenesis of icterus

5) *Brown atrophy of heart.* Heart is diminished in size, deposition of fat under epicardium is diminished, fat tinctures in brown colour. Such colour is conditioned by deposition of lipofuscin.

6) *Gallstones.* Gallbladder is enlarged, filled with stones of different sizes

7) *Stone of the kidney pelvis and hydronephrosis.* Big stone with branches, which form reminds mould of the pelvis, is situated in kidney pelvis. Atrophy of kidney parenchyma is marked

8) *Liming of heart valves.* Deformed, sclerotic heart valves with grey colour deposition of lime salts are seen in the preparation.

Study micropreparations from a theme and be able to draw the essence of pathological process with proper designations

1) Liver at the mechanical icterus. Preparation is stained with hematoxilin-eosin. In bile capillaries and ducts there are yellow colour concrements. Bile capillaries are widened, hepatocytes

are in condition of fatty dystrophy. Around the portal canal growing of connection tissue is marked. Determine type of icterus. Designate: 1- Bile fields in clearance of vessels; 2- Fatty dystrophy of hepatocytes; 3- Connective tissue growing.

2)Brown induration of lung. Preparation is stained with hematoxilin-eosin and also according to Perls. Haemosiderin deposits in interalveolar septa, alveoli. Organ's stroma is sclerotic. By what brown colouring and density of the organis conditioned? What is the origin of blue inclusions in staining of preparations according to Perls? Designate: 1- haemosiderin, 2 -sclerosis of interalveolar septa.

3) Haemosiderosis of liver. Preparation is stained according to Perls. By what hystochemical method is ferrum indicated in tissues? Indicate character of its deposition. In what pathology are such changes in liver possible? Designate: 1 - hepatocytes, 2 - haemosiderin, 3 - widen vessels.

4)Liming in fibromyoma. Preparation is stained with hematoxin-eosin. In fibromathous nodes deposition of calcium salts which are stained in dark-blue colour are seen. Designate: 1-calcium salt, 2- muscle fiber.

5) Melanoma of skin. Preparation is stained with hematoxilin – eosin. In areas of growing of atypical epithelial cells deposition of dark-brown pigment melanin is marked. To what pathology do such pathological changes in skin belong?

Designate: 1-atypical melanocyte, 2-deposition of melanin.

Situation tasks

1 At blood transfusion the patient has got low back pain and an arterial pressure decrease. Explain the mechanism of mentioned symptoms.

2 Calculous cholecystitic patient has got jaundice, low back pain, protein in urine. Define possible stone localization. What is the mechanism of jaundice and what changes are observed in kidneys?

3 Nidus of cerebral hemorrhage was discovered at the autopsy. The question has been raised concerning time of its appearance. How are you going to accomplish this task?

4 Skin hyper pigmentation, hypotonia, hypodynamia, hypoglucosemia are detected at consumptive patient. Define the mechanism of presentation of mentioned symptoms and give the name of the disease.

Answers to situational tasks

1 Low back pain is explained by development of hemoglobinuric nephrosis. The mechanism of presentation of mentioned symptoms is as follows: hemolysis of erythrocytes (its cause is unknown) has appeared at blood transfusion, the accumulation of unconjugated hemoglobin has caused toxic affection of kidney. An arterial pressure decrease could be explained by appearance of significant quantity of active reduced ferritin which is an adrenalin antagonist.

2 The stone has obstructed a biliary tract. The obstructive jaundice appeared. Bilirubin concentration in blood increased and its extraction from kidneys started. As a result toxic affection of kidney parenchyma was developed, that's why low back pain and protein in urine appeared.

3 Time of appearance of cerebral hemorrhage should be defined according to coloring of hemorrhage nidus. At hemorrhage area the hemolysis of erythrocytes occurs and hemoglobinuric pigments (ferritin, hemosiderin, bilirubin, hematoidin) are accumulated which provide corresponding coloring.

4 The affection of adrenal glands with necrotic changes of gland parenchyma is often observed at tuberculosis. As a result the synthesis of corresponding hormones, catecholamines, is distorted. That's why intermediate products of their synthesis (tyrosine, tryptophan acid) are used for excess synthesis of

melanin, it explains skin hyperpigmentation. The name of the disease is Addison's disease.

Test tasks

1 Brown-black pigment was detected at the bottom of stomach ulcer during gastroscopy. What is the name of this pigment?

A. Bilirubin; **B** Ferritin; **C.** Porphyrin; **D.** Hemosiderin; **E.** Muriatic hematin.

2 The patient with stomach cancer vomited coffee-like mass. Which pigment provided such color of gastric contents?

A. Hemosiderin; **B.** Bilirubin; **C.** Ferritin; **D.** Muriatic hematin; **E.** Porphyrin.

3 Deformation of aortal valve, its ulceration, petrified induration are discovered at necropsy of the 38 years old patient who died of acute cardiac insufficiency, there is a crunch defined at incision. Which pathologic process determined petrified induration of valves?

A. Hyalinosis; **B.** Amyloidosis; **C.** Metabolic calcification; **D.** Metastatic calcification; **E.** Dystrophic calcification.

4 The patient who has been ailing for a long time from rheumatism with development of mitral valvular disease got cough, rusty sputum. Which pigment provided such colour of sputum?

A. Melanin; **B.** Hemoglobin; **C.** Hemosiderin; **D.** Malarial pigment; **E.** ferrous sulfate.

5 Induration and calcium salts deposits are developed at area of incarnation after tuberculosis inflammation. What is the name of this process?

A. Calcification metastases; **B.** Dystrophic calcification; **C.** Morphology of hypercalcemia; **D.** Metabolic calcification; **E.** Restricted calcinosis.

6 The patient is complaining of pain in articulations of toes. The patient likes beer. There is a suspicion of podagra. Increase of which substance in his blood should be discovered in order to confirm diagnosis?

A. Bilirubin; **B.** Urea; **C.** Uric acid; **D.** Ketone bodies; **E.** Lactate.

7 As it is known from anamnesis the patient has tuberculosis of adrenal glands. An arterial pressure decrease, adynamy, decrease of 17-oxycorticosteroids in urine and plasma are defined. Skin has brown coloring. Metabolic disorder of which pigment does the patient have?

A. Lipochrome; **B.** Bilirubin; **C.** Lipofuscin; **D.** Melanin; **E.** Hemosiderin.

Answers to test tasks

1. E; 2. D; 3. E; 4. C; 5. B; 6. C; 7. D.

Illustrations to theme.

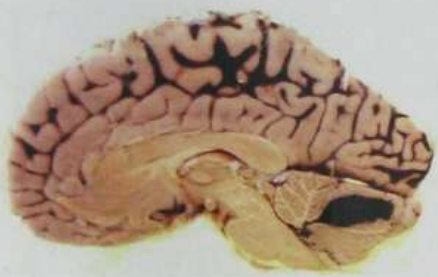


Figure 1 – *Cerebral hemorrhage*. On cerebellum slice surface hemorrhage region is observed. Brown coloration is absent on periphery. Say if it is fresh or old hemorrhage.

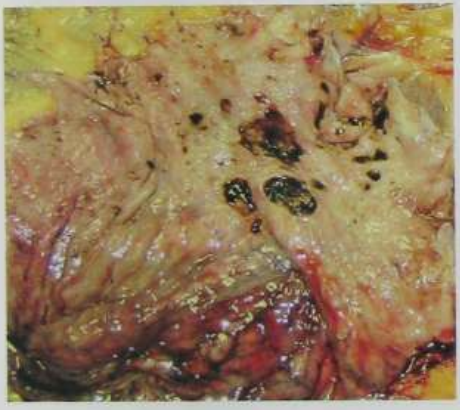


Figure 2 – *Muriatic hematin on the bottom is stomach wall ulcer*. There are deep defects of mucus tunic in stomach wall. On ulcers bottom there are dark brown pigment – muriatic hematin deposits.

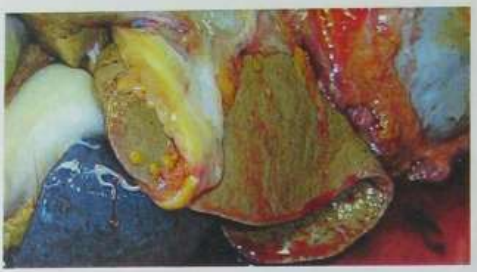


Figure 3 – *Biliary cirrhosis*. Liver is of green-brown color on section. Bile ducts are dilated, filled with stones. What is the mechanism of stones formation? Name jaundice morphogenesis

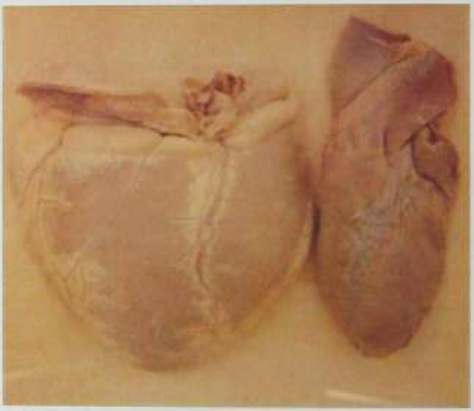


Figure 4 – *Brown atrophy of heart*. Heart size is decreased, fat is diminished under epicardium,
Fat is colored in brown. This color is caused by lipofuscin deposit.

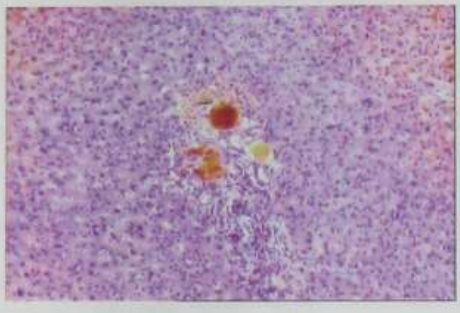


Figure 5 – *Obstructive (mechanical) jaundice.* Specimen is colored with hematoxylin and eosin There are concrements of yellow color in bile capillaries and bile ductules. Bile capillaries lumen is dilated, hepathocytes are in fatty degeneration condition. Conjunctive tissue excrescence is observed around portal tracts. Define jaundice type.

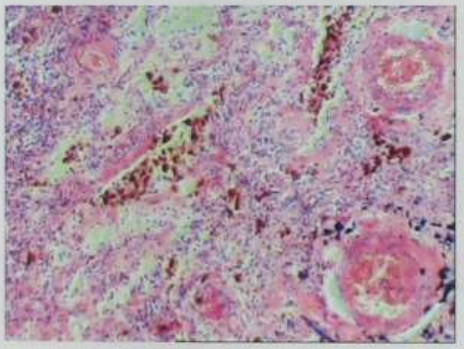


Figure 6 – *Brown (pigment) induration of lungs.* Specimen is colored with hematoxylin and eosin as well as by Pearls. Hemosiderin deposits in alveolar septums, alveoli. Organ stroma is sclerosed. What caused brown coloration of organ and its hardness? What is the origin of blue inclusions in case specimens are colored by Pearls?

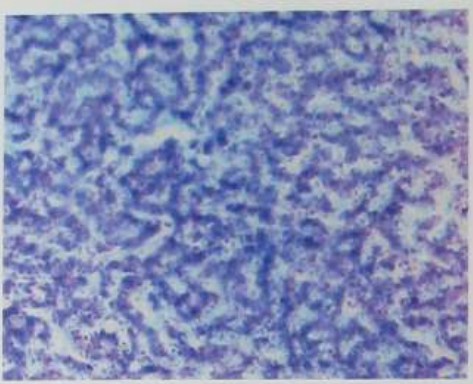


Figure 7 – *Hepatic hemosiderosis.* Specimen is colored by Pearls. What histochemical method is used to reveal iron in tissues? Define the character of its deposit. At what pathology named changes in liver are possible?

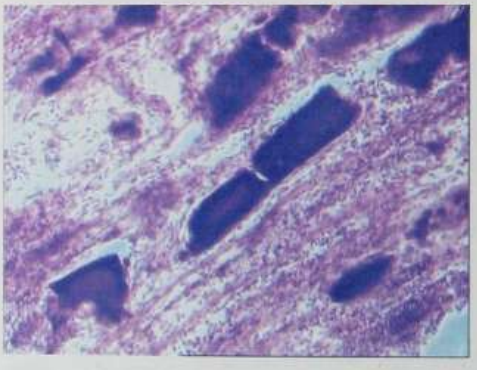


Figure 8 – *Petrificating (calcificating) myositis.* Specimen is colored with hematoxylin and eosin Petrificated myositises are of blue color. Name existing types of pertification.

Theme 4. Cells and tissues damage and death. Necrosis and apoptosis. Pathologic anatomy of organ deficiency. Fundamentals of thanatology. Death, definition, signs of death

Topicality of theme: cells and tissues damage and death in organism are met in organism continuously under keratolysis, blood cells cytothesis, etc. as well as under other diseases and refers to general pathologic processes. This process can take place under tissues or cells metabolic imbalance, under cellular metabolism products or pathologic products of exogenic and endogenic origin uptake, so this theme knowledge is necessary for correct understanding and successful learning of the other subdivisions of general and special pathologic anatomy.

Purpose: to study cells and tissues damage and death etiology, development mechanisms, morphologic manifestation and consequences.

Specific aims: 1 To know variety of necrosis.
2 To learn causes, patho- and morphogenesis, morphologic manifestations, cells and tissues death consequences.
3 To know the essence of apparent death and natural death and terminal conditions characteristic.
4. To learn pathogenetic and morphologic foundations of thanatogenesis.

Basic matters for self-work

Critical alteration of specialized cells. Definition, etiology and consequences.

Molecular mechanisms of cells critical alteration. Concepts of endogenous metabolic catastrophe: cells biological combustion insufficiency, cell acidotic alteration,

plasma membrane transportaion mechanisms injury, activation of cytoplasm lipid peroxidation and cell membranes, injury with free radicals and nitrogen oxide excess, catastrophic increase of free calcium in cell, cell injury with transmitters excess, abnormal proteins accumulation in cell. Critical injury of cell with external factors: external physics-chemical factors, pathogenic infects (ultramicrobs, Rickettsias, bacteria, fungi).

Kinds of specialized cells death in organism.

Cell necrosis: definition, terms and phases of development, morphologic characteristic of coagulation necrosis and cells necrosis, their consequences.

Pathogenic inductive apoptosis: definition, molecular mechanisms, term of development, microscopic manifestation, consequences.

Immune destruction of cells. Immune destruction of cells in organism conditions and designation. Phagocytosis: definition, main cells-phagocytes, phagocytosis mechanisms and microscopic manifestation. Immune cells killing: definition, cytotoxical cells, mechanisms and microscopic manifestations, consequences. Cells destruction with activated complement: definition, mechanisms and microscopic manifestations.

Pathological anatomy of organ insufficiency.

Autoimmune (lymphocytic) destruction of all specialized structures of organ: definition, stages of development, clinical-morphological characteristics, consequences.

Postishemic-markfusional organs injury: definitions, morphogenesis peculiarities, clinical-morphologic characteristics, consequences.

Necrosis of organ or its portion. Morphologic types of tissues necrosis (colliquative, coagulative): definition, causes, pathological anatomy. Organ necrosis: definition, causes,

development stages (ore-necrotic, necrosis and tissues destruction). Post necrotic transformation of organ's sphacelus (necrosis demarcation and encapsulation, regeneration, infection and inflammation, formation of ulcer, cyst, sequester, sclerosis/gliosis foci, calcinosis foci).

Clinical-morphological classification of organ necrosis basic kinds.

Infarction: definition, morphogenesis, pathological anatomy of main types, consequences. Gangrene: definition, morphogenesis, pathological anatomy of dry, wet and anaerobic, consequences. Morphologic characteristics of infarction, gangrene. Decubitus: definition, trophoneurotic necrosis morphogenesis, consequences. Noma: definition, morphogenesis, pathological anatomy, consequences. Morphogenesis, pathological anatomy of liver toxic necrosis and enzymatic pancreatonecrosis. Sequester: definition, morphogenesis, pathological anatomy, consequences.

Fundamentals of thanatology.

Human being birth and death. Organism death from biological, social and medical positions: idea of natural, violent death and death from diseases (untimely and sudden). Intrauterine death definition.

Thanatogenesis. Cause, molecular-metabolic and structural mechanisms of vital parts activity cessation under natural course of disease. Immidiate consequences of heart, lungs, cerebrum, kidneys and liver work cessation.

Clinical-pathological characteristics of the main periods of thanatogenesis. Modern acknowledged periods of thanatogenesis: critical period, apparent death, post reanimation period, natural death. Consequences of vital parts activity cessation.

Critical and agonal periods of disease: definition, clinical-pathological features, consequences.

Clinical death: definition, features and terms of development, idea of cardiopulmonary reanimation and its consequences.

Post reanimation period: definition, molecular and clinical-pathological anatomy features of vital parts injury and their functions recovery.

Natural death: definition, immediate (main) causes and development terms under natural clinical course and under sudden death of a person. Precursory and delayed signs of natural death and resuscitated patient. Morphological characteristic of cadaveric changes. Basic reasons and morphological signs of intrauterine fetal death and neonate death.

I Auxiliary material for self training to prepare to practical class

Critical alteration of specialized cells is manifested with their death being the final result of their damage. The most often cell's death is caused by acute hypoxia or ischemia; physical factors (mechanical trauma, burns, frostbites, radiation, electric shock); chemical substances and medicines; infections, intoxications, immune reactions and other conditions.

Mechanisms of cells damage

Mechanisms of cells damage are extremely various. Under ischemia damage develops in the result of oxygen scarcity in tissues and its free radicals creation causing lipids peroxidation and cellular breakdown. Critical damage can develop under calcium homeostasis disturbance. Under cytolemma hyperpermeability free calcium ions concentration grows causing activation of numerous ferments' damaging cell: phospholipase, protease, ATPase, endonuclease. ATP

content decrease causes cytolemmas damage and induces cell death.

Types of specialized cells death.

Three basic types of specialized cells death in organism are recognized: ischemic or hypoxic, toxic and damage with oxygen free radicals. Hypoxic and ischemic damage occurs in the result of arterial flow cessation. Herewith oxidative phosphorilation is ceased and ATP formation is terminated, anaerobic glycolysis enhances, lactic acid, inorganic phosphate accumulates, intracellular pH decreases, chromatin consenses, cell becomes dropsical, membrane structures destruct. Cell damage by free radicals is caused by membranes lipids peroxidation, autocatalytic reactions development, oxic proteopepsis, DNA damage. Toxic damage occurs under chemical substances action on cell membrane or intracellular organelles.

Two types of local death exists: necrosis and apoptosis. Necrosis (from Greek nekros – dead) which is local death, death is characterized with cells death in living body. Specific cells, a group of cells, the portion of the organ, organ in full can be subject to death.

Cells necrosis

Cell necrosis is cell death under the influence of extreme negative exogenic and endogenic factors and it is manifested with considerable cells edema or cellular breakdown, cytoplasmic proteins denaturation and coagulation, cell organelles breakdown. Three stages are differentiated in necrosis development: pre-necrotic, necrotic and post necrotic. Pre-necrotic stage is characterized with severe degenerative changed which are ended with necrosis. At necrosis stage the following is broken-down and decomposed (kariorrhexis,

kariolysis), cellular cytoplasm (plasmorrhexis, plasmolysis) and intercellular substance – fibrinoid necrosis.

In the post necrotic stage necrosis products are subject to autolysis, meaning dilation or dispersion or organization. *Macroscopically* necrosis region differs from surrounding living tissues. Its of dirty black color in skin and bowels and whitish yellow in the other organs (myocardium, liver, kidneys, spleen).

By etio-pathogenetic principle the following direct necrosis is differentiated: traumatic, toxic and the following indirect ones: trophoneurotic, allergic, vascular.

Microscopic signs of necrosis:

Cell nucleus change: karyopyknosis, karyorrhexis, kariolysis.

Cell cytoplasm chang: plasma coagulation, plasmorrhesis, plasmolysis.

Intracellular substance change: mucoid swelling, fibrinoid swelling, fibers disintegration.

Necrosis classification by etiology: trophoneurotic, toxic, traumatic, vascular, allergic.

Trophoneurotic necrosis occurs under central nervous system and peripheral nerves injury. *Traumatic necrosis* occurs in the result of physical, electrical, chemical, thermal trauma direct action. *Toxic necrosis* occurs in the result of toxins, mostly of bacterial origin influence on tissues. Allergic necrosis develops on condition of tissues hypersensitivity (sensibilization). *Vascular* (ischemic) necrosis occurs in the result of tissues blood supply significant decrease or termination.

Clinicopathologic classification of the main types of organs' and tissues' necrosis

The following types of necrosis are differentiated: coagulation, colliquative, infarction, gangrene, decubitus, sequester.

Coagulation (dry) necrosis is characterized with sphacelus portion deaquation and induration. It includes cheesy (caseation) necrosis under tuberculosis, lues, lymphogranulomatosis as well as cereous myonecrosis under abdominal and flea-borne typhus, cholera, fibrinoid necrosis under allergic and lymphocytic diseases, malignant hypertension as well as adiponecrosis which is distributed into ferment, which occurs under pancreatitis and non-ferment caused by trauma.

Colliquative (wet) necrosis is characterized with necrotic tissue rarefication and fusion in the result of hydrolytic processes activation. It is developed in tissues rich with moisture, for example in cerebrum.

Infarction is necrosis caused by blood supply deficiency. Occurs in the result of thrombosis, embolism, long term arteriostenosis and long term, functional overexertion of organ in hypoxia conditions. By its shape infarction could be wedge-like (spleen, lung, kidneys) and irregular shape (heart, cerebrum). By its appearance it is distributed into white (ischemic), which the most often is found in cerebrum, spleen; red (hemorrhagic) which occurs in lungs, bowel, amphiblestrodes; white with hemorrhagic crown – in heart, kidneys. Infarction form and appearance depends on the features of organ's vascular system, types of vessels branching, anastomosis development, structural-functional features of the organ (for detail see the theme of circulatory disturbances).

Gangrene is death of tissues contacting with air (bowel, extremities). Under the influence of air ferric sulphide is formed from hemoglobin, and this ferric sulphide colors necrotic portion in black. Dry and wet gangrenes are differentiated. *Dry* occurs mostly in the result of insufficient arterial blood supply.

Necrotic portion dries up, densifies, mummifies. *Wet* gangrene occurs in the cases when lymph and black blood outflow is disrupted or when necrosis portion is subject to putrefactive mycronychia action. Necrotic portion is hydropic, diluted, of dirty black color with very unpleasant smell. *Anaerobic gangrene* development is based also on blood outflow disrupted. It is caused by a group of anaerobic activators. During that gases squeeze microvasculature structures.

Decubitus is a kind of gangrene. It is caused by blood supply and nervous trophism disturbance of subiculum in the place of squeezing (sacral bone, bladebones, calx) under seriously ill patient long term decubitus, for example, cerebrovascular accident.

Sequestrum is sphacelus which is not subject for autolysis for a long time. As a rule sequestra are observed in bones under osteomyelitis.

Demarcation line of red color with a tinge of yellow occurs surrounding necrotic portion. This is reactive inflammation characterized with vascular distention in living tissue, edema, leukocytic infiltration, macrophages incipiency. Lytic ferments of heterophilic leukocytes expedite dead zymolyte maceration and resolution similar to the one observed under wet necrosis, for example in cerebrum with cisterns formation and cyst buildup or rejection (*autoamputation*) of external necrotic body parts. In favorable cases mesenhymal origin cells proliferation starts around necrotic portion, spacelous aggregate either grow with conjunctive tissue (*organization*) or encrust with it (*encapsulation*) or are subject to calcification (*petrification*). Sometimes necrotic portion purulence is observed with abscess formation.

Apoptosis

Apoptosis is genetically programmed death of unnecessary or defective cells in living body and the following

causes these cells destruction in the process of embryogenesis and physiologic involution: cutaneous epithelium, white and red corpuscles extinction. Herewith chromatin condensation and fragmentation in cells is observed. In case apoptosis decrease neoplastic process is developed and in case apoptosis increase – atrophy. Apoptosis differs from necrosis in:

- inflammation absence,
- only several cells or their groups are involved in the process,
- cell membrane is saved,
- cellular breakdown is done not by activated hydrolytic ferments, but in participation of special calcium-magnesium dependent endonucleases which cut nucleus into numerous fragments,
- formed cells fragments (apoptosis corpuscles) phagocytized by parenchymatous or stromal cells which are situated nearby.

Apoptosis morphogenesis develops in several stages:

- chromatin condensation and margination, nucleus becomes fragmented,
- intracellular organelles condensation and cells shrinkage,
- apoptosis corpuscles formation,
- apoptosis corpuscles phagocytosis with parenchymatous cells or macrophages .

Under histological investigation apoptosis cells are round or oval particles with intensively colored cytoplasm and dark fragments of nucleus chromatin.

Fundamentals of thanatology

Thanatology is doctrine of organism dying starting from initial signs up to full corruption of the body. In the course of dying organism stays in terminal (critical) condition and is capable for reversible development occur prior to death

coming. Herewith progressive functions decrement of various organism's systems is observed, first of all respiratory depression as well as blood flow organs depression occurs, organism's homeostatic systems incoordination has place: pulmonary edema, arrhythmia, paroxysm, respiration disturbance, constrictors paralyses, etc. Hypoxia and blood circulation disturbance cause pathologic changes in organs and tissues, which are called moribund state. Blood circulation directed to support functions of cerebrum causes microcirculation disturbance on periphery resulting in parenhymal organs structure and functions failure. Energy metabolism switches to anaerobic glycolysis causing lactic acid accumulation, acidosis, hypoxia intensifies. Biologically active substances come into blood causing microcirculation channel paresis and paralysis, increase of vascular permeability, blood clotting, stasis occurrence, clots formation. Terminal condition development and signs depend on pathological process caused death agony. In case dying is going on, terminal condition can be divided into several stages: pre-agony, terminal pause, agony, apparent death, natural death. During pre-agony stage arterial tension gradually decreases, inhibition of sensorium and electric activity of cerebrum. Tachycardia passes into bradycardia, trunkal reflex disturbance occur. In terminal phase temporary breath holding is observed, and periodic asystolia changes bradycardia. Agony is characterized with sudden activation of bulbar centers on the background of cerebral cortex full shutdown. Such disintegration of vegetal centers is accompanied with temporary and short time arterial tension increase, sinus automatism initiation and respiratory movements intensification. Apparent death is characterized with the deepest inhibition of central nervous system which expands also on spinal bulb with blood circulation termination and apnea.

Death, types, signs, postmortem changes

Depending on the causes the following types of death are recognized: *natural* (physiologic) death from age and organism depreciation, *violent* death from trauma or other negative influence on organism which ends with death and *from diseases*. Depending on reversible or irreversible changes in organism apparent death and natural death are specified. *Apparent death* is characterized with apnea, blood circulation termination and lasts for 5-6 minutes until cerebral cells death. Apparent death is reversible process of dying. Reversibility depends on the stage of hypoxic changes in cerebrum. *Natural death* is manifested with irreversible changes development and autolytic processes beginning in all the organs. It has characteristic signs and postmortem changes in tissues: dead body cooling, postmortem rigidity, mummification, blood relocation, postmortem lividity, cadaveric disintegration. In case death process in fast, it is observed liquid blood in the heart and vessels caused by fibrinolysis, postmortem face lividity, ecchymosis in conjunctiva, intensive and wide spread cadaveric lividity, urine, fecal matter discharge as well as red mucus presence in respiratory passages, considerable venous plethora of internal organs, hemicardia engorgement, punctuate hemorrhage on heart, lungs surface.

In case agony comes prior to death dense blood clots are observed in the heart and vessels – red in case of short term agony and yellowish-white or white under long term agony. Following basic vital functions of organism termination, early and late signs of natural death gradually develop in organism. Early signs are as follows: cadaveric lividity (occur in 30 –60 minutes post mortem), cadaveric rigidity (occurs in 2-4 hours), cooling (every hour of death gives 1 degree dead body temperature decrease, desiccation of specific parts of skin and mucous coats (the most clearly it can be seen on opened eye sclera – Lyarshe spots) and

autolysis. Late signs of natural death occur on 2-3 day port mortem. They are ruining (putrefaction, dead body damage by plants, animals) and preserving (grave wax, mummification, turfy tannage, etc.). Putrefaction occurs with microorganisms participation and is characterized with dead body organic substances destruction. This is accompanied with gases formation, tissues mollities and dilution. First signs of putrefaction occur in large bowel in 24-36 hours, abdominal wall derma turns green because of sulfgemoglobin accumulation.

II Algorithm of the practical part of lesson

To learn and to be able to describe in oral form macrospecimens exhibited in the macromuseum

1 *Gangrene of the low extremity.* Low extremity is covered with skin which is on considerable area dark-brown with areas of desquamation of epidermis, wrinkled, dry, diminished in sires in the area of the low third of shin. There are defects of skin of the trophic ulcer type.

2 *Moist gangrene of hand.* Epidermis of hand, particularly forearm on considerable area is desquamated, tissue of hand is swollen, cyanotic colour.

3 *Pancreanecrosis.* Tissue of pancreas is represented by single intacted islets of pale rose colour, other tissue is unstructured, with haemorrages.

4 *Gangrene of small intestine.* The wall of small intestine is swollen, dark-brown colour, mucous layer is dim. In the mesenterial vessels there are thrombi.

5 *Ischemic infarction of the myocardium with haemorrhagy rim.* On the frontal cut of heart in the wall of the left ventricle and interatrial septum ischemic areas, limited by crimson framing are seen. On the transversal cut of left ventricle the area of dark-coloured myocardium which spreads on all layers

of wall of heart is seen. Obturative thrombus of crimson color is seen in clearance of coronary artery.
Haemorragical framing is formed by paretically extended vessels and haemorrhage around the area of infarction. It is a fresh infarction (less than one day) because area of necrosis, changes of haemodynamics in the microcirculatory channel are well expressed. Sings of organization are absent.
6 *Haemorrhagic infarction of lung*. On the cut of lung three-cornered form dense, airless area of crimson colouring is seen. Its basis is returned to the pleura and apex to the hilus of lung. It is haemorrhagic infarction which developed as a result of obturation of pulmonary artery by embolus, and blood that is in alveoli entered the area of necrosis through anastamosises from the branches of bronchial artery.
7 *Infarction of kidney*. On the cut of kidney clear area of cone-shaped form, which differs from surrounding tissue by the changed colouring, is seen.
8 *Ischemic infarction of spleen*. On the crimson background of wedge-shaped form there are white ischemic areas. Infarction of the largest size is fresh because capsule above the area of infarction something projects above the surface of spleen. Infarction of less sizes, which is located higher is on the stage of organization (germinated by connective tissue). Capsule above infarction sinks down. A white scar is seen below, capsule about it also sinks down. It is organized infarction. As a rule source of thromboembolism is mitral and aortic valves of heart. Consequently, such changes in a spleen are characteristic for rheumatism, prolonged septic endocarditis.

To learn and sketch microspecimens advised by teacher and be able to draw the essence of pathological process with proper designation:
1 *Necrotic angina*. Preparation is stained with hematoxilin-eosin. On a considerable area tissue is necrotic, nuclei are

absent, design of tissue structure is effeced and stained in homogenous pink colour, only in places there are centers of infracted lymphatic tissue with follicles in which also areas of neurosis take place. Stratified squamous epithelium on the surface of tonsil is intacted, somewhere in pockets (crypts) there is purulent exudation. Vessels are sharply extended, somewhere there are numerous haemorrhages. Designate: 1 - flat epithelium, 2-areas of necrosis.

2 *Necrosis of epithelium of tubules of kidneys.* Preparation is stained with hematoxilin-eosin. In a cortical layer areas, where nuclei of epithelium of curled tubules are absent or are almost absent, epithelium is swollen, cytoplasm stained in homogenous pink colour, pulls in clearance of tubules in glomeruli nuclei are intacted. Designate: 1- clearance of tubules, 2 - necrosis of epithelium, 3 - intacted epithelium of tubules.

3 *Zencer's necrosis.* Preparation is stained with hematoxilin-eosin muscular fibers are fragmented, sarcoplasm is haemogeneous, as "waxen candles", transversal striation and nuclei are absent. A massive haemorrhage and areas of reactive inflammation are seen in endo- end perimysium. Somewhere dark- blue areas of hypercalcification are seen. Designate: 1- haemorrhages, 2 - necrosis of muscular fibers and hypercalcification

4 *Tubercular lymphadenitis.* Preparation is stained with hematoxilin – eosin. Lymphatic tissue and separated follicles are intacted only under the capsule of lymphatic node. On a large area pulp is necrotisated, it is presented by haemogenous, unnuclear mass, which is stained by eosin in intensively rose colour, as a result of coagulation . Designate: 1 -area of necrosis, 2 - lymphatic follicle,

5 *Haemorragic infarction of lung.* Preparation is stained with hematoxilin – eosin In tissue of lung area necrosis is seen. Lung tissue in necrotic area is changed. There are erythrocytes

in clearance of alveoli and interalveolar septa. On the periphery of infarction discirculatory disorders are observed, haemorrhages, red thrombi in clearance of vessels. Designate: 1 - area of necrosis of interalveolar septa, 2 – haemorrhages , 3 - thrombi in vessels.

6 *Ischemic infarction of myocardium with haemorrhagy rim.* Preparation is stained with hematoxilin – eosin. Stained in intensive rose colour area of myocardium is seen. Cardiomyocytes in that area are without nuclei, sarcoplasm is homogenous, pink colour, transversal striation is absent. Eosinophylia is characteristic for necrotic tissues. Absence of nuclei is an evidence of the fact that from beginning of necrosis few days passed (about a week). Designate: 1- necrosis of cardyomyocytes, 2 - cellular infiltration, 3 –haemorrhagy.

7 *Ischemic infarction of kidney.* Preparation is stained with hematoxilin – eosin. Area of kidney parenchyma stained in intensive rose colour is seen. Epithelium of tubules, glomerular structures in that area are without nuclei, cytoplasm is homogenous, pink colour, that is characteristic for necrotic tissues. Absence of nuclei in cells an evidence of their necrosis. In neighboring areas of parenchyma of kidney intacted, undamaged areas are seen, in clearance of arteria thrombus is seen. Designate: 1- necrosis of tubular epithelium, 2 -necrosis of glomeruli, 3 - intacted kidney structures.

Situation tasks

1 Patient ill with coronary heart disease, 60 years old, dies with acute heart failure signs. On section it is seen that the heart is increased in size, in the left ventricle wall there is a portion of 2 to 3 cm size, irregular shape, of greyish-brown color, with hemorrhage on periphery. There is blocking thrombus of red color in the left coronary artery lumen. Name clinical-morphology form of necrosis, process etiology and development mechanism.

2 Patent with gastric cancer who stayed in bed for a long time in forced position (lied on back), skin along vertebral column in certain portions became dark-brown, soft tissues with signs of edema, keratolysis occurred, liquid with bad smell appeared. What clinical-morphology form of necrosis developed with patient? Name its type.

3 Patient K., 83 years old, suddenly lost consciousness, on the background of which death came. Autopsy: atherosclerosis of aorta, heart coronary vessels, kidneys, cerebrum. There are separate scars in kidneys; there is injury zone of irregular shape in cerebrum left hemisphere, full of grey color mush. What clinical-morphology form of necrosis developed with patient? Name necrosis type depending on etiology.

4 After considerable exposure to cold patient's lower extremities expanded, specific portions of skin became black, keratolysis occurred in some places. At knee joints section derma became red, hot by touch. What clinical-morphology form of necrosis developed with patient? Name necrosis type depending on etiology.

Answers to situation tasks

1 In this case vascular necrosis developed – myocardium infarction. The cause is acute ischemia in the result of coronary artery blocking thrombus. Mechanism of infarction development is indirect.

2 Decubitus developed with patient, this is trophic-neurotic necrosis.

3 Cerebrum infarction developed. By etiology necrosis is divided into vascular, trophic-neurotic, toxic, allergic and necrosis caused by physical or chemical factors.

4 Frostbite developed, this is necrosis caused by low temperature action.

Test tasks

1 Patient of declining years suffered of low extremities vessels' atherosclerotic injury. Suddenly pain in right foot occurred. Under examination it was found that foot is expended, tissues are flaccid, of black color, macerated. Demarcation zone is not distinct. Name pathological process.
A. Coagulation necrosis. **B.** Sequestrum. **C.** Mummification necrosis (dry gangrene). **D.** Humid gangrene.
E. Mummification.

2 Patient died of acute heart insufficiency. Autopsy showed lungs edema, there is a focus of necrosis of yellowish-grey color in the heart, and thrombus in coronary artery. Name pathologic process in the heart:
A. Myocarditis. **B.** Cardiosclerosis. **C.** Hyalinosis.
D. Amyloidosis. **E.** Infarction.

3 9 years old child was operated for osteomyelitis. In the portion of injured bone a piece of necrotic bony tissue, which lays loose in marrowy channel cavity. What kind of necrosis is it?
A. Infarction. **B.** Sequestrum. **C.** Gangrene. **D.** Colliquative.
E. Coagulative.

4 Needle biopsy of liver found that some hepatocytes are destroyed into small fragments with nucleus remnants. These cells have safe membrane. There is no inflammation reaction. Name pathologic process.
A. Necrosis. **B.** Plasmorrhaxis. **C.** Plasmolysis. **D.** Apoptosis.
E. Kariorhexis.

5 In extracted lung tissue of patient ill with tuberculosis necrosis of the following kind developed:
A. Coagulative. **B.** Colliquative. **C.** Caseation. **D.** Fibrinoid.

E. Patchy (perifocal).

6 Patient 36 years old died of cholera. Under dead body examination it was found that upper and lower extremities are sharply crouched. It was a hard job to turn extremities back to anatomical position. What changes developed in patient?
A. Cadaveric emphysema. **B.** Cadaveric degradation.
C. Cadaveric cooling. **D.** Cadaveric rigidity. **E.** Cadaveric imbibition.

Answers to test tasks.

1. D. 2. E. 3. B. 4. D. 5. C. 6. D.

Illustration to theme

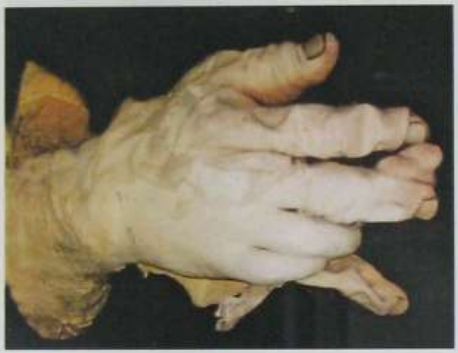


Figure 1 – Wet gangrene of the hand. Epidermis of hand and partially forearm is rejected, hand tissue is edematous, bluish discolored.

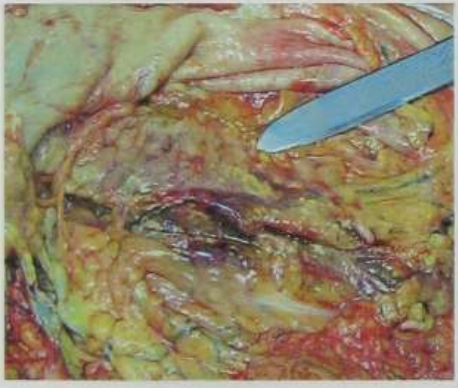


Figure 2 – Pancreonecrosis. Pancreas tissue is represented with individual safe islands of pale-red color, remaining part of tissue is instructural with hemorrhages.

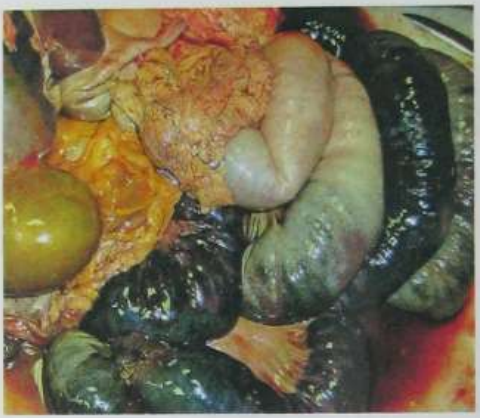


Figure 3 – Gangrene of small bowel. Small bowel wall is edematous, of dark-brown color, serous coat is matt. There are ruffs, thrombus in vessels.

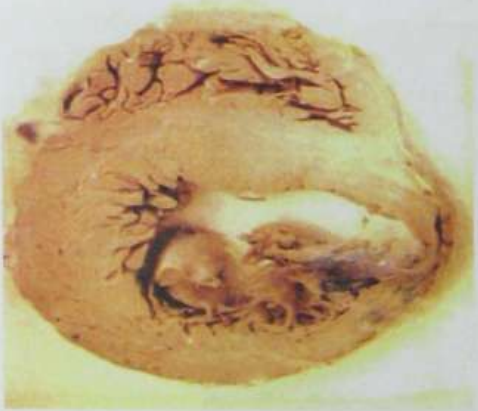


Figure 4 – Ishemic myocardium infarction with hemorrhagic crown. On left ventricle transversal section it is seen of dark colored myocardium portion which spreads on the full thickness of cardiac wall. In coronary artery lumen obturating thrombus of dark-red color is seen.

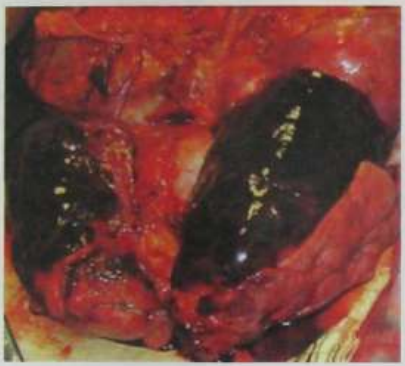


Figure 5 – Hemorrhagic infarction of lung. On lungs section it is seen free of air portion of triangle shape of dark-red color, the base of which is turned to pleura and its cupola – to lungs entry. This is lung hemorrhagic infarction, which developed because of lung artery branch blocking with embolus and blood in alveoli came into necrosis zone through anastomosis from bronchial artery branches.

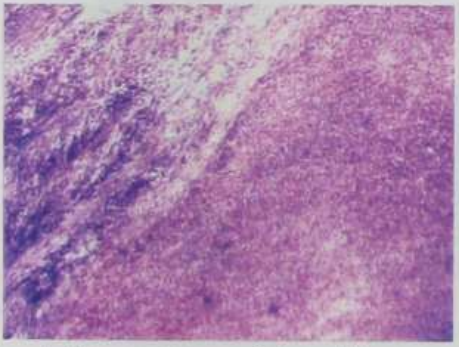


Figure 6 – Necrotic tonsillitis. Specimen is colored with hematoxylin and eosin. Tissue is spacelous in considerable area: nucleus are absent, tissue structure is defaced and in case subject to coloration is colored in homogenous pink, lymphoid tissue pockets are safe here and there.

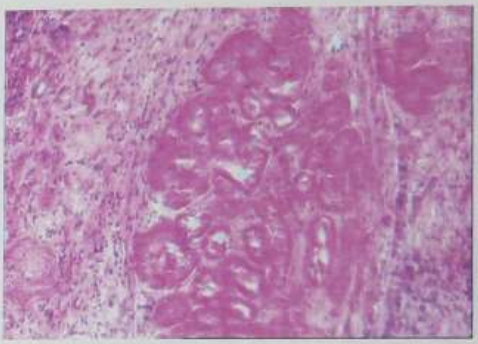


Figure 7 – Kidney tubules epithelium necrosis. Specimen is colored with hematoxylin and eosin. Convoluted renal tubules epithelium nucleus are absent, epithelium is edematous, cytoplasm is colored in homogenous pink.

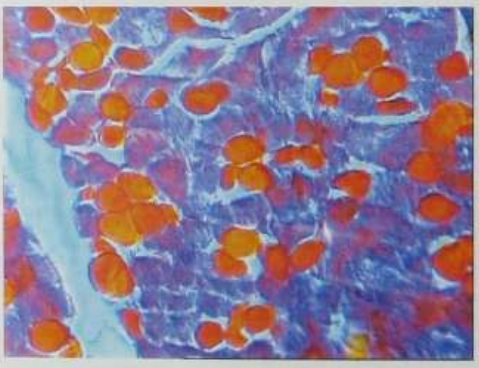


Figure 8 – Zenker's degeneration. Specimen is colored by Malori's technique. Muscle fibers are fragmented, sarcoplasm is homogenous, looks like "wax candles".

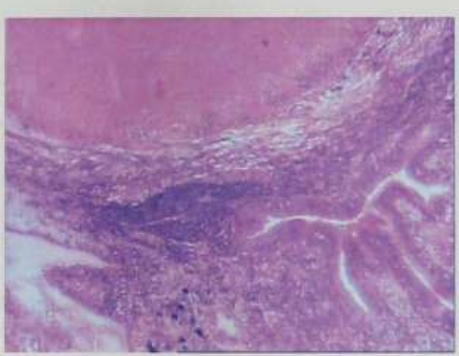


Figure 9 – Tuberculosis peritonitis. Specimen is colored with hematoxylin and eosin. Lymphoid tissue and separate follicles are intact only under lymph gland capsule. In the big area pulp is necrotized and represented with homogenous nuclear - free mass, which is intensively colored in pink with eosin.

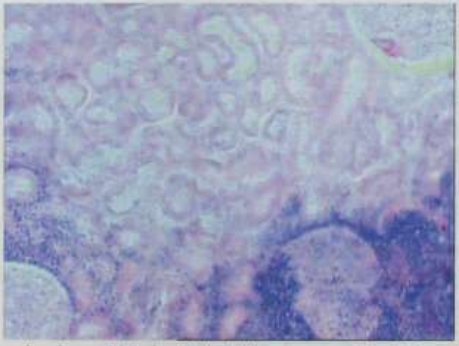


Figure 10 – Ishemic infarction of kidney. Colored with hematoxylin and eosin. Kidney parenchyma portion is seen colored in intense color. Renal tubules epithelium, glomerule structures in this portion is free from nucleus, cytoplasm is homogenous, of red color, which is attributable to necrotized tissues. Nucleus absence in cells testifies their necrosis. In kidney parenchyma adjoining portions safe and intact structures are seen.

Practical class 5

Theme 5 Skills. Autopsy.

Autopsy procedure and methods in medical and preventive treatment facilities

Dead body stays in the ward for two hours after the fact of natural death is established by in-patient hospital's physician. Surname, name, father's name, date and time of death, department are to be written on the hip with brilliant green. Usually rubber-coated label on which above mentioned passport data is written is fixed to the arm. The latter method is better to use in those medical and preventive treatment facilities in which sporadic death cases occur.

Under body lift and its further examination it's necessary to keep all moral-ethical and professional requirements. Ethical requirements include medical secrecy keeping regarding everything revealed at autopsy (thanatopsy). It's also should be taken in mind that dead body serving for science has relatives and family. For example, Professor V.Gruberg required from students and those working in autopsy room to take off hats, as "hats wearing does not correspond the credit of the room". It's advised to warn junior health professionals of the fact that cadaveric hypostasis can disfeature the face in case body stays dorsum upwards. It should be kept in mind that after natural death fact is etsbalished it's necessary to close eyes, fasten up lower jaw, to cover the body with clean linen, etc. Simultaneously with diseased body completely filled-in medical records should be submitted to mortuary.

Prior to deceased body autopsy anatomist studies all the data regarding patient's life, disease and death which can be found in medical card of hospital patient, asks attending doctor missed facts relating to course of disease and dying. Sometimes it's useful to clarify some data from relatives,

especially in case patient's short term stay in the hospital. The following should be carefully investigated: laboratory, tolls and other methods of investigations, methods of treatment, medicines potions taken by patient, diagnosis written on title page of medical records as well as all working diagnosis written in log books. All this circumstances study pursues one more important aim – to exclude or to find out medicolegal aspect.

It's desirable that anatomist examining all necessary data independently formulated diagnosis which can differ of attending doctor diagnosis. Doing this, as P.Kalitiyevskyi mentions, anatomist in a certain manner puts her/himself in the position of attending doctor, which is really important for mutual understanding between anatomist and clinician.

There is certain algorithm in autopsy fulfillment:

1 To carry out autopsy in day light as artificial lighting changes color transfer.

2 To put on gown and rubberized apron and oversleeves. It's advisable to use anatomical gloves. This will ensure contagious diseases prevention, as well as cadaveric alkaloid penetration through possible defects of skin.

3 External examination of diseased body. The following should be established: sex, body-type, nutrition, state of integumentum, existence of death signs, eruptions, hematomas, wounds, ulcerations, edema, etc. It's desirable that attending doctor could confirm passport data of diseased.

4 Main incision. It's necessary to watch to prevent it coming through after surgical sections, cicatrix and other defects.

5 Detailed examination of cavities establishing the position and interlocation of organs, presence of joints, exudates, transudate, foreign objects, etc.

6 Organs' withdrawal from the cavities and their investigations (size, weight, color, consistency, shape, etc.) with simultaneous necropsy taking and, depending on tasks set for

anatomist, material for bacteriologic, serologic, biochemical and virology investigations. Sometimes X-ray examination of bones is done.

7 Short summary incorporating paragnosis, the cause of death, possible discrepancies between clinical diagnosis and paragnosis, accessory matters clarification which are of interest for clinicians.

8 Cadaver toilette.

9 Autopsy records keeping.

First autopsy methods were described in details by R.Virhov. Later on it was improved by Kiary, L'Etule, O.Abrykosov, G.Shore. methods of two last ones are the most widely used in anatomists' practice.

O.Abrikosov offers to investigate organs by cavities. First organs of cervix and thoracic cavity are removed in totality. Then separately intestinal tract, liver, stomach and dodecadactylon in one set, urinary tracts and genital organs in totality.

G.Shore suggested organs full evisceration method, which means removal of cervix, thoracic cavity, abdominal cavity and small pelvis as single total complex. This method is rather convenient to be used under investigation of those deceased bodies who died of after surgery complications. In this cases it's reasonable to search in details field of operation area, namely state of surgical sutures, vessels, exudates presence and character, correctness of surgery fulfillment.

Autopsy recording

Autopsy recoding should be done in autopsy document – records of post mortem examination (autopsy). It consists of the following parts: passport, descriptive, paragnosis and clinical autopsy epicrisis. Passport portion includes data regarding deceased' surname, name and father's name, his/her age, address, number of in-patent's observation records, profession and specialty, the date of admission to the hospital

and date of death, diagnosis. Autopsy records should contain also brief extract from observation records regarding features of etiology, clinical implications, tools and laboratory results, methods of treatment. Take into consideration that it's advisable to indicate specialty instead of writing "retired", as well as characteristic features of disease which made it possible to make diagnosis mentioned in clinics.

There are various procedures to fill-in descriptive part. At present there is a tendency to simplify it, to go apart from classical form of presentation. It's unacceptable to use general terms, for example "atherosclerosis", "adenoma", "pneumosclerosis", etc. instead of pathologic signs or to compare the size of pathologic changes with such objects as English walnut, pea, egg instead of accurate statement of dimensions. It should be remembered that autopsy records is legal document in which minor changes, which, to the opinion of anatomist, are not critical could be of first priority under further examination. Moreover it's not feasible to use autopsy records in which the character of pathologic changes is only emphasized. This way often causes mistakes, which are hard to correct. Making pictures and audio tape recording are also considered to be ancillary methods of recording. The basic requirement imposed to descriptive part of records is sufficient completeness and distinctness combined in case possible with briefness of presentation.

The following forms of pathologicoanatomic changes registration are widely used in autopsy practice:

- by anatomic systems of organism;
- by the way of autopsy fulfillment;
- by preliminary defined place of system injury in conformance with peculiarities of the case, and further on - by the way of other systems examination.

It's always recommended to start descriptive part from body appearance description, registration of nutrition, status of

skin integuments, mucus tunic, eyes, hair, nails, character of edema, etc. These features are sometimes sufficient to assume this or that pathology presence. It's advisable to make records immediately following autopsy and do not defer that on the next day, it's better to make records at dictation by stages of autopsy carrying out or using voice recorder.

Pathologoanatomic diagnosis formulation follows descriptive part of records, based on macroscopic diagnostics and in case necessary using express-methods. Diagnosis formulation is advised to be done in attending doctors presence prior to the body toilette.

Pathologicoanatomic diagnosis structure and composition

Diagnosis is medical conclusion regarding pathologic state of health of the person under examination, presence of disease (trauma) or the cause of death expressed in terms, provided by International classification of diseases, traumas and causes of death. Making diagnosis is the final stage of the data of anamnesis, clinics, laboratory-tools investigations, macro- and microscopic morphology examination results analysis.

The following variants of diagnostic process are differentiated depending to its stages:

- diagnosis under long term health condition observation by territory or family physicians, and prophylaxis observations
- diagnosis at admission to medical-diagnostic establishment;
- clinical diagnosis by which treatment is carried out; This is final clinical diagnosis which is to be made by attending doctor at patient's release from the hospital or in case of death;
- pathologoanatomical (legal) diagnosis made by anatomist (medical examiner) based on sectional and biopsy material examination .

Up-to-date clinical and pathologoanatomic diagnosis

should represent nosology, etiology, pathogenesis, morphofunctional manifestations and prognosis of disease. That is to say pathologoanatomic diagnosis should include all the stages of cognitive process: observation, morphofunctional characteristic of pathologic changes, disease nosology attribute definition (formal diagnosis), describe etiology, interrelationship and sequence of morphologic manifestations occurrence taking into consideration data of anamnesis, clinical signs and complex of laboratory-tools and morphologic intravital analysis results (clinical diagnosis of this patient or deceased), as well as prognosis in case diagnosis making based on biopsy examination.

It should be kept in mind that each nosology unit contains the reason as well as probable consequence which realize in certain conditions only. Cause and effect are interconnected with possibility and reality, contingency and probability. At this connection between the cause and contingency incorporates consequence variability on the same cause and possibility of cause transfer into effect is defined by probability.

Under pathologoanatomical diagnosis making it's necessary to take into consideration as follows:

- one reason can cause one consequence;
- one reason can cause a number of consequences;
- one consequence can be caused by a number of reasons;
- patient's death can be caused by reason and consequence (consequences);
- reason and consequence (consequences) can change disease manifestations (pathomorphism).

It's often that attending doctors and anatomists interpret and understand the same phenomena in a different way, as well as their place among the other processes found at patient from the point of view of cause and effect, their significance in the course of disease, as well as of diagnostic positions. Clinicians

often establish as basic nosology unit manifestation of disease or complication on which their curative or reanimation actions were directed. This is the ground to understand that without unified principles of pathologic anatomy processes interpretation and registration collaboration of attending doctors and prosectors will be inefficient and will not be useful for clinical practice and doctor's skills improvement which should be its result.

Final diagnosis is the result of complicated process of numerous facts comparison and apprehension, collected by doctor in the process of treatment which is based on formal and dialectical logic's laws. Diagnosis defining is not formal stage, but the conclusion of doctor's mentation expressed in written form. In such a way there should be accurate principles of its expression understandable for attending doctor, prosector as well as comprehensible under statistic analysis of population death rate.

Clinical analysis and paragnosis consist of divisions

1 Principal diseases.
2 Principal disease complications.
3 Concurrent diseases.

Principal disease should be nosologic form which by itself or through pathogenically connected complications caused functional diseases lead to patient's clinical picture and afflicted death. For example, peptic ulcer diseases, lung cancer, croupous pneumonia, rheumatism, etc. Herewith it's not feasible to list symptoms and syndromes to substitute nosologic unit.

Clinical-pathology anatomical epicrisis is the most complicated autopsy records division to be formulated. This is synthesis of the clinical course of disease and the data found under morphologic examination, determination of etiology,

morphogenesis and mechanism of death. Prosector states in it his/her view on the features of this specific case.

Clinical-pathology anatomical epicrisis should cover the following matters:

1 Substantiation of diagnosis: principal disease, complications, concurrent disease.

2 Clarification of thanatogenesis links and primary and immediate causes of death establishment;

3 Pathomorphism manifestations analysis (medical actions influence on disease clinical-morphological manifestations);

4 Diagnosis comparison by headings (principal disease, its complications and concurrent diseases) mentioning the cause of diagnosis discrepancy;

5 Clarification of diagnostics and patient's admission expediency evaluating this factor influence on curative process and disease consequence.

There is not any distinct scheme of clinical-pathological anatomy epicrisis which is caused by the fact that specific approach is possible for every specific case. In the other words, this is subjective prosector's view on disease with morphological analysis utilization. However, taking into consideration that major part of it content is devoted to clinical picture and treatment analysis, possibilities of early pre-hospital and hospital diagnosis, necessary diagnostic measures use, timely patient's admission, diagnostic process dynamics, surgery feasibility, characteristic of therapy, reanimation measures, these principal matters are advisable to be peer reviewed, under attending doctors active participation, during medical session, clinical-pathology anatomical conference. Only in such a way it's possible to express medical cogitation errors and failures of treatment-prophylaxis work in every specific case.

Notional module 2

Morphology of blood supply and limphokinesis disturbance

Lectures – 4 hours

Practical classes – 8 hours

Student's self-work – 7 hours

Form of student's individual self-work – thesis or library-research papers

Specific objects of the module

- *To explain the causes and consequences of ion-osmotic and water balance disturbances.*
- *To analyze the role, causes and consequences of renin-angiotension-aldosteron system function disturbance.*
- *To explain mechanisms of development, morphologic manifestations and consequences of the following kinds of circulation disorders: arterial and venous plethora, ischemia, hemorrhages, stasis, plasmorrhagia, shock, embolism.*
- *To explain lymphokinesia disturbance development mechanisms, morphologic manifestation and consequences.*
- *To describe structural-functional components of hemostasis system.*
- *To analyze hemorrhagic syndromes` reasons, morphologic manifestations and consequences*
- *To analyze thrombosis reasons, morphologic manifestations and consequences*
- *To analyze thrombosis reasons, morphologic manifestations and consequences*

Disseminated intravascular blood coagulation syndrome.

Theme 8 Ion-osmotic and water balance disturbances

Basic matters for self-training

Ion-osmotic and water balance disturbances The causes, pathogenesis of hyposmolar and hypersmolar comas, their consequences and patients' death causes. Hyper- and hypopotassemia: definition, causes of development, role in thanatogenesis. Water balance disturbance, hypo- and hyperpotassemia: causes of development, role of intercellular and cellular dehydration in thanatogenesis. Transsudate, cavities hydrops, viscus edema (lungs, cerebrum): patho- and morphogenesis, clinicopathologic characteristics.

Renin-angiotension-aldosteron system. Life incompatible blood pH disturbance: definition, role in thanatogenesis. Osmotic pressure, oncotic pressure: characteristics, regulation. Potassiou metabolism disturbance. Hypopotassemia, hyperpotassemia: mechanisms of development, clinical manifestations.

Theme 9 Blood circulation disorders: plethora, ischemia, infarction, hemorrhage, bleeding, stasis, plasmorrhagia. Embolism. Shock. Lymph flow disturbance

Basic matters for self-training

Plethora (plethora). Arterial plethora. Causes, types, morphology. Venous plethora: general and local, acute and chronic. Venous (passive) congestion in small circle of blood circulation system: patho- and morphogenesis, clinicopathologic characteristics, consequences. Blood circulation disorders under chronic myocardium cardiac decompensation. Heart and lungs disorders pathomorphology under chronic right ventricle and left ventricle cardiac insufficiency (cardiac decompensation). Venous plethora in portal vein system (portal hypertension): pathogenesis and clinicopathologic manifestations.

Ischemia (ischemia): definition, causes, mechanisms of development, morphologic characteristic and methods of diagnostics, clinical meaning. Collateral blood circulation role. Acute and chronic ischemia. Infarction: definition, causes, classification, morphologic characteristic of various kinds of infarctions, complications, consequences.

Hemorrhage: external and internal, bleeding. causes, kinds, clinicopathologic characteristics. Hemorrhagic diathesis. Stasis: causes, mechanism of development, kinds, clinicopathologic characteristics, consequences. Pre-stasis, slagging phenomenon. Bleeding. Plasmorrhagia: causes, mechanism of development, kinds, morphologic characteristics, consequences causes. Lymph flow disturbance. Lymph flow insufficiency. Causes, kinds, morphologic manifestations. Lymphedema – acute and chronic, general and regional. Lymphostasis, elephantiasis. Lymphorrhea – external and internal (chylous ascites, chylothorax). Importance of lymph flow disorders.

Shock: definition, causes, pathogenesis and stages of development, pathologic anatomy manifestations of acute disorders of blood circulation and their consequences with patients died of shock. Postischemic-reperfusion organs injuries: causes, pathogenesis, clinicopathoanatomic features and their consequences.

Embolism: definition, kinds, causes, morphologic characteristics. Orthograde, retrograde and paradoxical embolism. Thrombo embolism: causes of development, clinical significance. Pulmonary artery thrombo embolism, acute cor pulmonale. Thrombo embolism syndrome: clinicopathologic characteristic.

Theme 10 Hemostasis disorders. Thrombosis, disseminated intravascular coagulation syndrome

Basic matters for self-training

Idea of hemostasis system structural-functional components. Pathogenetic classification of hemostatic disorders.

Hemorrhagic syndromes: definition, basic causes, principal pathogenetic kinds, pathoanatomic manifestations, consequences.

Thrombosis. Internal and external systems of coagulation. Fibrinolysis. Cells and factors participating in coagulation and fibrinolysis. Thrombocyte aggregate formation. Concept of coagulation cascade. Local and general factors of thrombus formation. Thrombus, its types, morphologic characteristic. Venous thrombosis. Arterial thrombosis. Thrombosis in cardiac cavities. Varicose veins. Thrombophlebitis and phlebothrombosis. Thrombosis significance and consequences. Disseminated intravascular coagulation syndrome. Definition, kinds, mechanisms of development, stages, morphologic characteristic, clinical manifestations.

Practical class 6-7

Theme: Water-electrolytic balance disorders and blood circulation disturbances. Hemostasis disorders. Thrombosis. Disseminated intravascular coagulation syndrome

Theme topicality Disorders of water-electrolytic balance, hemostasis and blood circulation cause cells and tissues' structures damage, expressed in tissue and cell metabolism change, meaning various types of degeneration development, up to necrosis. They are found in organism

permanently under various diseases, can develop in specific as well as in all organs and cause their functions decrease, so they belong to general pathological processes. First of all these disorders intrinsic to all cardiovascular system diseases. Their knowledge makes it possible to evaluate correctly dynamics of clinical course and foresee diseases' consequences.

Purpose: to learn water-electrolytic balance, hemostasis and blood circulation disorders' etiology, mechanisms of development, morphologic manifestations and consequences.

Specific aims:

1 To know the kinds of plethora, ischemia, stasis, hemorrhages, shock, embolism, thrombosis, disseminated intravascular coagulation syndrome.

2 To learn the causes, patho- and morphogenesis, morphologic manifestations of plethora, ischemia, stasis, hemorrhages, shock, embolism, lymph flow disorders, thrombosis, disseminated intravascular coagulation syndrome.

3 To be able to differentiate various clinicopathologic kinds of blood circulation distrubance.

4 To learn pathogenetic and morphologic fundamentals of ion-osmotic and water balance disorders.

I Auxiliary material to prepare for practical class

Blood circulation disturbance causes tissue (cell) metabolism decrease, causing tissue (cell) structure damage in the form of degeneration or necrosis, as well as activates ibroblasts causing sclerosis development.

Ion-osmotic and water balance disturbance

It is manifested with tissue fluid content and ions concentration in cell or extra cellular change. Tissue liquid content decrease causes dehydration or exicosis. At that organs and tissues grow down, atrophies, capsule shrinks, Serous and mucus tunics surface becomes dry, blood thickens and darkens. Tissue liquid content increase causes edema. At that transsudate accumulates in tissues, which is a liquid containing max. 2% of protein. Depending on reasons edemas are differentiated as congestive, cardiac, renal, degenerative, marantic (cachectic), inflammatory, allergic, toxic, neuropathic, traumatic edemas. Congestive edemas occur under disorders of venous outflow (trombophlebitis, phlebothrombosis, veins compression), lymphostasis. Cardiac edemas develop under cardiac activity decompensation. Renal edemas develop under renal diseases, but their development pathogenetic mechanisms are various: under nephrotic syndrome it is hypoproteinemic edemas, under glomerulonephritis edemas are caused by sodium holdup. Degenerative and marantic edemas are connected with blood oncotic tension decline. Inflammatory, allergic, toxic, neuropathic, traumatic edemas are caused by vascular membranes hyperpermeability. In case liquid uptake in subcutaneous fat anasarca develops, in cardiac pouch cavity – hydro pericardium, in pleural cavity – hydrothorax, in abdominal cavity – ascites. The most dangerous for organism is cerebral and pulmonary edema, which often cause patients' death. Edema consequences could be favorable – liquid resorption or unfavorable - parenchymatous cells degeneration and atrophy followed by sclerosis.

The following kinds of blood circulation disorders are differentiated: plethora (arterial and venous), ischemia (ischemia), infarction, stasis, thrombosis, embolism, hemorrhages, shock, disseminated intravascular coagulation

syndrome, plasmorrhagia. Some of them are of general and some of the are of local character.

Arterial plethora

Arterial plethora is organ or tissue intensified blood filling caused by excessive arterial flow.

It could be acute or chronic, physiological or pathological, general or local. ***General plethora*** develops under circulating blood volume increase (plethora) or number of erythrocytes increase in blood (erythroemia, Vaquez's disease). Skin, visible mucus tunics redness (plethora), blood tension increase is observed at that.

Local arterial plethora. Local arterial plethora could be physiological and occur under shame, heavy manual labor, organs hyperfunction (work plethora) and pathological. The following kinds of local pathological arterial plethora are differentiated:

1 Angioneurotic (neuroparalytic plethora) is observed under vasodilatating nerves irritation or vasoconstrictor nerves paralysis. Skin, mucus tunic becomes red, slightly swollen, warm or hot by touch. This plethora could occur on certain body portions under innervation's failure, sympathetic nervous system nodes failure. For example same side face skin redness is observed under croupous pneumonia. As a rule this plethora passes without trace.

2 Collateral plethora occurs because of blood flow hindrance in main artery lumen of which is closed with thrombus, embolus or artery is squeezed with tumor. Blood comes to bloodless portion by collateral vessels, lumen of which is reflex dilated. In case collaterals insufficient development tissue and ischemia or even necrosis develops.

3 Plethora after ischemia (post ischemic) occurs in cases when the cause of artery squeezing (tumor, ligature, liquid accumulation in cavity) is eliminated rather quickly. Under

these circumstances vascular lumen of former bloodless tissue is sharply dilated and overfilled with blood which can cause its rupture and hemorrhage. Besides that ischemia occurs in the other organs because of blood redistribution, for example cerebrum ischemia can occur with vertigo. So ascetic liquid should be slowly released from abdominal cavity. In case vertigo caused by cerebrum ischemia occurred in the result of blood redistribution it's necessary to place patent's body in such a way to provide low position of the head.

4 Vacant plethora is caused by atmospheric pressure decline. General vacant plethora occurred with divers and pilots under fast lift from high pressure into low pressure area. In such cases it is combined with gas embolism. An example of local vacant plethora is redness in the place of gallipots.

5 Inflammatory plethora is caused by action of biologically active substances – inflammation mediators, for example, histamine, serotonin. At this in the place of injury arterioles are dilated after short time reflex spasm of them. Most of all it relates to postcapillares and venules lumens, local redness and temperature rise. Plethora facilitates metabolism intensification in inflammable zone tissue, neutrophilic leucocytes (microphages) migration in tissues, microorganisms elimination, that is of defensive character.

6 Plethora based on arteriovenous fistula occurs in those cases when, for example under gunshot wound or tumor injury joint between artery and vein is formed and arterial blood overfills venous vessels because of tension difference.

Venous plethora

Venous plethora is organ or tissue blood filling increase caused by slow (hindered) blood outflow, blood flow at that is not changed or decreased. Venous (passive) congestion causes dilation of veins, venules, capillaries, blood flow slowing down in them causing development of hypoxia, capillaries wall

penetrability increase, edema and tissue trophism disorder. Venous plethora could be general or local.

General venous plethora

General venous plethora occurs under cardiac pathology causing heart failure. Under acute cardiac insufficiency (myocardium infarction, acute cardiac decompensation) plasm extravasation (plasmorrhagia), edema, punctuated diapedesis bleeding occurs, degenerative and necrotic changes in parenchymatous elements, for example in lungs under left ventricle infarction. Chronic venous plethora occurs under chromic cardiac (cardiovascular) insufficiency, which develops under congenital and acquired cardiac malformations, myocarditis, cardiosclerosis. At that chronic hypoxia occurs causing not only plasmorrhagia, edema and punctuated bleeding but also tissues and organs atrophy and sclerosis.

Sclerotic changes are caused by the fact that hypoxia stimulates collagen synthesis by fibroblasts; simultaneously parenchymatous elements atrophy occurs. In such a way parenchyma is substituted with conjunctive tissue, organs and tissues thicken – their epiduration occurs.

Skin, especially legs' skin under general venous plethora becomes cold and of bluish color (cyanosis). Blue color is caused by the reduced hemoglobin (without oxygen) which is of bluish color. Veins and cutis lymphatic vessels are dilated, overfilled with blood, derma and subcutaneous fat are edematous. Conjunctive tissue enlargement is manifested with skin induration. Inflammation pyogenic abscesses and trophic ulcers occur in skin quite often which are long lasting.

Liver under general venous plethora is enlarged, Hard. Section surface is striped – dark red spots are seen on grey-yellow background, looking similar to nutmeg section - nutmeg liver. Nutmeg liver development morphogenesis is

rather complicated. Under general venous plethora blood outflow from the liver is hindered, hepatic veins are dilated. Central veins of the parts and central sections of sinusoids supplying blood to the central veins also dilates. Dilated central veins and central sections of sinusoids create "bloody lakes" in the center of the parts causing dark-red spots. In case plethora intensification hemorrhages occur in the center of the parts. Hepatocytes situated in the center of the lobules (centroclinal) atrophy because of dilated vessels' compression, degenerative changes and necrosis develops in them. At this parts periphery hepatocytes compensatory hypertrophy. In the result of hypoxia adipose degeneration occurs in hepatocytes, causing grayish-yellow color of liver. Hypoxia facilitates conjunctive tissue excrescence, due to that sinusoids walls thicken causing hepatocytes hypoxia extension. Venous plethora intensification causes hepatic sclerosis (fibrosis) progress which is finalized with congestive (nutmeg) hepatic cirrhosis. In such a way as time passes hepatic insufficiency joins cardiac insufficiency.

Under chronic venous plethora brown hardening (induration) develops in lungs. Pulmonary venous blood congestion occurs on condition that right ventricle of heart pumps blood into lungs and left ventricle can not provide this blood pumping from the lungs into aorta. It is caused by mitral or aortic valves failure or left ventricle cardiomiocytes injury. Blood accumulates in pulmonary artery pond, hypertension occurs in lesser (pulmonary) circulation. As a result of hypertension microcirculation channel vessels dilate and capillary walls permeability increases. Besides that capillary walls permeability is caused be intensifying hypoxia. Blood liquid phase sweats from capillaries accumulating in alveoli's lumen, pulmonary edema develops. As hypoxia and hypertension intensify in lesser circulation capillary walls permeability becomes more expressed - numerous diapedetic

hemorrhages occur, meaning erythrocytes' sweating from vessels lumen into surrounding tissues. Out of vessels they are treated by tissues as foreign and are absorbed by macrophages. Hemoglobin transforms in them into hemosiderin (ferrum containing pigment). Further on macrophages are destroyed and hemosiderin under insufficient lymph flow deposits in stromal tissues. Lungs obtain brown color. Macrophages in which hemosiderin forms are called siderophages. Alveolocytes also have macrophage function and those of them which are found in patients' with cardiac decompensation sputum are called cardiac failures' cells. Thus, rusty-brown color of lungs under chronic venous plethora is caused by hemosiderin which situates in macrophages as well as in interalveolar partitions, alveolar lumens, bronchi' walls and lumens, lymphatic vessels and lymph nodes.

Lungs thickening (induration) under chronic venous plethora is caused by conjunctive tissue' increased effuse in lungs. Three factors contribute that:

1 Tissue hypoxia activates fibroblasts, latter actively fissure, synthesize collagen fiber and intracellular substance causing conjunctive tissue growth leading lungs' thickening.

2 Under lungs' venous plethora lymphatic system's absorption and dynamic insufficiency causing congestion of fluid in tissues and tissues proteins accumulation takes place. Tissue fluid accumulation enhances hypoxia, that in its turn leads to sclerosing.

3 Free hemosiderin also contributes tissues sclerosing.

In such a way lungs become large, thick, of rusty-brown color on surface and in section. Thus lungs insufficiency joins cardiac decompensation.

Kidneys under chronic general venous plethora become large and cyanotic (cyanotic induration), the most plethoric are cerebral layer veins and intermediate area veins. Cyanotic color is caused by organ's overfilling with venous blood.

Enhancing hypoxia causes parenchymatous elements degeneration and conjunctive tissue excrescence, leading to organ's hardening. Similar changes develop in spleen, cerebrum and other organs. Skin, especially legs' skin, becomes cyanotic, cold to touch, hard.

Local venous plethora

Local venous plethora develops in case hindrance of blood outflow from specific organs or parts of the body, caused by vein lumen obstruction with clot, embolus or vein contraction by tumor, enlarged neighbour organ. For example, acute venous plethora of gastrointestinal tract occurs under portal vein thrombosis. Under hepatic veins' thrombosis or in case their obliteration caused by thrombophlebitis nutmeg liver disease (Budd-Chiari syndrome) develops. Kidneys' venous plethora can develop under thrombosis of their veins. Under local venous plethora venous blood outflow partially goes through collaterals.

Sometimes collateral veins are so much overfilled with blood that their varicose develops. Such varicose nodes (knots) can burst because of their wall atrophy, causing hemorrhage, sometimes fatal. For example, under portal vein blood congestion at hepatocirrhosis port-canal anastomosis develops causing varicose of low one-third of esophagus veins. Varicose node burst causes significant hemorrhage, sometimes fatal.

Ischemia

Exsanguination or ischemia (from Lat. ischo – block) is organ, tissue or part of the body blood filling' reduction caused by insufficient blood inflow. Complete exsanguinations is possible. Ischemic tissue becomes pale, flaccid, organ decreases in size, its capsule shrinks.

Under ischemia tissue' oxygen shortage (hypoxia) occurs, metabolism slows down, reductive-oxidative ferments activity decreases, mitochondrion destroy, glycogen disappears, degenerative and necrobiotic changes develop, in first turn of parechymatous elements. Tempo of described changes depends on ischemia development (acute and chronic ischemia). Under complete blood supply cessation ischemised portion necrosis occurs (infarction). Under chronic ischemia parenchymatous elements degeneration and atrophy develops as well as conjunctive tissue enhanced excrescence (sclerosis). Depending on courses and conditions of origination the following types of ischemia are differentiated:

1 Spastic (reflex) – arteriospasm under painful stimulation, negative emotions.

2 Obstruction – partial or complete obstruction of artery with thrombus, embolus, spalled atherosclerotic plaque, conjunctive tissue grew after arterial wall inflammation (obliterating endarteritis).

3 Compressive – artery contraction with tumor, exudates, ligature, tourniquet.

4 Ischemia caused by blood redistribution. Under ascitic fluid drain blood outflows to abdominal cavity and brain ischemia develops. Blood outflows in lower situated portions of the body in cases person tries to stand up quickly, brain ischemia occurs with giddiness, orthostatic shock develops, that is loss of consciousness.

Stasis

Stasis (from Latin stasis – arrest) – blood circulation arrest in microcirculation channel vessels, mainly in capillaries.

Blood circulation arrest is preceeded by blood circulation slowing down which is pre-stasis condition or pre-stasis. In stasis development mechanism changes of blood flow characteristics expressed with enhanced erythrocytes' intracapillary aggregation are of main importance. It leads

blood capillary flow hindrance, slowing down and arrest. Under stasis hemolysis and blood coagulation doesn't occur. Erythrocytes aggregation is called slage-phenomenon. Erythrocytes stick together forming so called coin columns causing blood viscosity increase. The causes are as follows: blood clotting under capillary walls increased permeability, occuring under plethora, hypoxia, vasculitis, high and low temperature's action, allergic diseases. Stasis is reversable phenomenon. Condition after its release is called post-stasis. Irreversable condition leads to distrophy and tissue and organ cells' necrosis.

Plasmorrhagia

Plasmorrhagia is plasma going out blood circulatory channel, causing plasma leakage of vessel wall and degenerative changes development in it up to fibrinoid necrosis.

Epithelium edema and hardening takes place, choroids fissure dilates, basal membrane integrity is crippled. The causes are as follows: nerve-vascular failures (spasm) – hypertension disease, tissue hypoxia – decompansated cardiac diseases, immunopathologic reactions – autoimmune reactions, vasoactive substances (serotonin, histamine) amount increase in blood - infection, infection-allergic diseases, coarsely dispersed proteins, lipoproteins – atherosclerosis. Plasmorrhagia consequence is transcapillary metabolism failure and fibrinoid necrosis development or vessels' hyalinosis.

Hemorrhage

Hemorrhage (haemorrhagia) is blood outcome from vessels lumen or heart into environment (external) or into body cavities (internal).

External hemorrhages are lung (hemoptysis) – haemoptoe, nose – epistaxis, blood vomiting– haematemesis,

blood in excrements – maelena, from uterus – metrorhagia. Internal hemorrhages are as follows: blood accumulation in heart cavity hemopericardium, pleura – hemothorax, abdominal cavity – hemoperitoneum.

Extravasations are accumulation of blood run out from vessels in tissues.

Kinds of extravasations: hematoma, fruise, petechia, echymosis, hemorrhagic infiltration. Hematoma is clotted blood accumulation in previously damaged tissue. They are the most dangerous in cerebrum, adrenal glands. Fruise (hemorrhage) – flat hemorrhages in skin and mucous tunics. Petechias, echymosis are small spot hemorrhages. Massive infiltration of tissue without basic and structural components destruction is called hemorrhagic infiltration.

The causes of blood outgo from blood circulatory system are as follows: break (haemorrhagia per rhexin), erosion (haemorrhagia per diabrosin), vascular walls' permeability increase (haemorrhagia per diapedesis).

Hemorrhages caused by vascular' wall or heart rupture (haemorrhagia per rexin). Could be of traumatic (mechanical) or pathological origin. The latter is mostly caused by necrosis, inflammation or tumor. For example, under myocardial infarction, rupture of aorta's outgoing portion (over valve), under hypertension disease, necrosis of mid layer of aorta wall (medionecrosis), syphilitic mesaortitis. Sometimes rupture of cardiac aneurysm or aorta or other organs is observed caused by considerable increase and overdistension of their capsule (enlarged spleen rupture under leucosis). Such ruptures occur even with minor trauma, for example, rough palpation.

Hemorrhages caused by vascular walls erosion (haemorragia per diabrosin) occurs under inflammation, malignant tumors, necrosis. For example, proteolytic ferments

action under inflammation, gastric juice, chorion villous growing-in under chorioepithelioma.

Hemorrhages caused by vascular walls increased permeability (haemorrhahia per diapedesis). Mostly shows up under arterioles, capillaries, venules injury. The causes of microcirculatory channel vessels' walls increased permeability are as follows: hypoxia (cardiac, pulmonary insufficiency, ischemia; vascular walls inflammation (vasculitis) under flu, measles, epidemic typhus, meningococcosis, secondary syphilis, sepsis, scarlatina , avitaminosis – deficiency of vitamin – scorbutus. Diapedetic hemorrhages are also observed under blood flow features and blood coagulability characteristics change, haematogenic organs failure (thrombocytopenia or Werlhof's disease, hemophilia, leucosis, ischemia). Diapedetic hemorrhages taken systemic character it's called *hemorrhagic syndrome*. Multiple spots hemorrhages are called hemorrhagic purpure or hemorrhagic diathesis.

Consequences of bleeding, hemorrhages – blood resolves more often, sometimes cysts are formed (cerebrum). Their content and walls are of chocolate color (chocolate cysts), the color is caused by hematogenous pigments. Sometimes blood coagulates and grows with conjunctive tissue – organization.

Hemorrhages significance. In case aorta wall rupture death comes fast of heart ventricles filling deficiency caused by intracardial pressure sharp drop, even under minor blood loss. The condition of cardiac systole is sufficient intracardial pressure, as it is not made, heart stops in diastole. Autopsy shows in blood sags in endocardium (Minakov's spots), which occurs because of adhere by suction heart action (like after cupping glasses). In cases cardiac rupture its pressurization with blood comes - cardiac tamponade. Under considerable hemorrhage up to half mass of blood (2-2,5l) death comes from loss of blood. Long term hemorrhages

repeating periodically under gastric ulcer disease, ulcerative colitis, menstrual period's failures, etc. lead to chronic ischemia, posthemorrhagic ischemia. The most dangerous is cerebral haemorrhage, and pulmonary hemorrhage at which death comes because of asphyxia as lumens of bronchi and trachea are obturated with blood.

Thrombosis

Thrombosis *is antemortem blood coagulation in lumens of vessels or heart. Formed grume is called thromb.* Intravascular grume of lympha is also called thrombus.

Local factors of thrombus formation are as follows: endothelium damage, blood flow laminarity slowing down and abnormality. ***To general one:*** imbalance between coagulative and anticoagulative blood systems and change of its composition. The following processes underlie the process of thrombs formation: thrombocytes agglutination, fibrin formation, erythrocytes agglutination, blood plasma proteins' precipitation. Thrombocytes agglutination and their coagulation close to the wall is one of important stages of thrombs formation. Under thrombocytes denaturation thromboplastic substances are segregated: active thromboplastin or thromboplastin which in the presence of calcium ions activate prothrombin which transforms into trombin. Futher on agglutinated thrombocytes degranulation takes place. Fibrin formation goes on caused by coagulation or protein (fibrinogen) coagulation. Thrombin influences fibrinogen and fibrin-polimer forms. The process of blood coagulation proceeds in the form of cascade reactions.

Thromb morphology. Thrombus consists of head, body and tail. With its head it is fixed to vascular wall in the place of its damage, exactly where the process of thrombus formation started. Thrombus is thick unlike postmortem grume, its

surface is stripped (Tsan's transverse lines) because of thrombocytes and fibrin rhythmic precipitation. Postmortem grume's surface is smooth, shining.

Depending on regular elements of blood domination, white, red, mixed and hyaline thrombus are differentiated. In *white* – dominate leucocytes, thrombocytes and fibrin, which form slowly under fast blood flow in arteries. *Red*, apart from white, contains bigger amount of erythrocytes, forms fast under blood slow flow, more often in veins. *Mixed thrombus*, in which leucocytes are alternated with erythrocytes and fibrin layer-by-layer occur in heart cavities, aneurisms, varicose veins. *Hyaline thrombus* does not contain fibrin, consists of destroyed erythrocytes, leucocytes, blood plasma proteins, forms in microcirculation channel vessels. In respect to vessels lumen thrombus could be mural and obturating.

Thrombi can form in arteries, veins, cardiac cavities, in heart's and vessels'в aneurisms. The most important practical meaning has thrombus appearance in cardiac cavities and venous network. The causes of thrombus formation in veins are progressive cardiac insufficiency, immovability after complicated surgeries, severe oncology pathology, serious infections, veins inflammation (phlebitis), veins catheterization. Thrombus formation in cardiac cavities occurs more often in atriums, in atrial auricle portion, in chronic aneurisms, on cardiac valves. The cause is: cardiac insufficiency and cavities dilation, myocardial infarction with endocardium damage, valves injury under endocarditis. Thrombi formation in arteries are observed under atherosclerosis plaques' ulceration, arterial aneurisms, vasculitis. Thrombi growth goes on by thrombosis masses stratification in the direction of blood flow or against blood flow direction. Thrombi which grows fast is called progressive. There is also a concept of "migrating thrombosis", when many

thrombi in various places of human body form in case blood ability to coagulate is increased. Thrombi in aneurism are called dilative. Thrombi formed under blood flow general slowing down, under cardiac insufficiency are called marantic or congestive. Thrombi formed in the place of the vessels branching are called thrombus-riders.

Thrombosis consequences are favorable and unfavorable. Aseptic autolysis and organization belong to the first ones. Thrombi dissolve owing to blood anticoagulative system activation and leucocytes' proteolytic ferments which are destroyed in the thrombi. Thrombi disappear without a trace. Big thrombi are rare to dissolve, more often they grow with conjunctive tissue, that is called organization. Conjunctive tissue growing in starts from the head. Cracks (channels) form in it in which blood circulation can recommence - recanalization of vessels. Surface of such channels is paved with endothelium. Later on they convert into vessels containing blood – "thrombus vascularization". Besides that vessels can grow in from intima side. Sometimes thrombi could carbonize (phlebolits).

Unfavorable consequence is septic autolysis under pyogenic infection influence. In such cases thrombi disintegration into parts is observed, these parts are carried with the blood in various organs and tissues causing inflammation generalization and sepsis development.

Thrombosis significance. The defensive one is determined by hemorrhage stop from damaged vessel. Unfavorable – development of necrosis, thromboembolism, thrombophlebitis.

Embolism

Embolism is circulation in blood or lymph particles which are not met there as normal. Emboli mostly move in blood or lymph flow direction (orthograde), sometimes – rethrograde (against the flow), for example in case veins (lymphatic vessels) valves insufficiency under their lumen dilation (venous stagnation, lymphostasis). Sometimes paradoxical embolism is possible when under defects presence in interatrial septum or interventricular septum, embolus, passing lungs, comes from left half of heart to the right one.

Depending on emboli nature the following kinds of embolism are differentiated: thromboembolism, fat, air, gas, tissue (cellular), microbial embolism, embolism by foreign objects.

1 Thromboembolism – is the most often kind of embolism. The most often thrombi of greater circulation veins' become emboli or those formed on valves under endocarditis. From greater circulation veins they come into small branches of pulmonary artery. Under that, as a rule, hemorrhagic infarction of lungs occurs. Under thromboembolism of pulmonary artery large branches sudden death comes caused by pulmocoronary shock development. The essence of shock lays in the fact that as the result of pulmonary artery intima irritation by embolus, which is rich with nerve receptors, especially in the place of its branching, sudden spasm of bronchi, pulmonary artery branches and cardiac coronary vessels occurs. Thromboemboli from lungs, mitral and aortal valves comes to aorta and through its branches – into various organs, where they obstruct vessels and contribute infarctions development. Thromboemboli from intestines veins migrate in liver portal vein system. Under migrating thrombosis thromboembolism is diversified, in such cases we speak of thromboembolism syndrome.

2 Fat embolism – emboli are fat drops. It develops under traumatic injury of subcutaneous fatty tissue, tubular bones fracture, massive fermentative necrosis of fatty tissue (pancreonecrosis), mistaken injection in vessels oily medicines. Oil, as a rule, comes into veins and pulmonary artery branches. Death comes in case two third of its branches are obstructed, from acute pulmonary-cardiac insufficiency. In case less amount of vessels are obstructed, fat emulsifies, lathers and resolves with lypophagues, sometimes pneumonias' development is observed.

3 Air embolism occurs in case neck veins injury in which negative pressure exists in case uterus veins are not diminished in its postnatal atony, pneumothorax, accidental air injection in vein together with medicines. Massive air embolism of lesser circulation vessels causes sudden death. At that air accumulates in right heart cavities. With the aim of its preliminary diagnosis right heart is subject to sticked submerged in the water. First pericardium should be dissected and filled with water, after right ventricle of the heart sticking air bubbles are coming out. Blood in right heart cavities is foamy.

4 Gas embolism **occurs mostly under** fast change of high atmospheric pressure to the low one (fast depressurization of airplane cabin, space vehicle, pneumatic work). Under fast decompression nitrogen dissolved in blood could not be taken out by lungs and its bubbles occur in blood - "blood boils". Gas emboli appears in arterial blood, obstruct capillaries of all organs and tissues, especially in capillary vascular network structure. The most affected are cerebrum and spinal cord,, kidneys, knee joints, eye retina. The portions of ischemia and necrosis appear in organs with further multiple spot hemorrhages and microthrombi, which is characteristic for decompression (caisson) sickness

5 Tissue (cell) embolism occurs under tissue damage with trauma or pathologic process causing a piece of tissue (cells)

coming into blood circulation. It's mostly apply to malignant tumors, cells of which penetrate into lumens of blood (veins) and lymph vessels causing metastatic disease, pieces of heart ventricles under ulcerable endocarditis, aorta walls under atherosclerotic plaques ulceration, cerebrum tissues under head trauma, as well as (neonates) under birth craniocerebral trauma. Embolism with amniotic water in purtunent women also refers here.

*6 **Microbial embolism*** occurs when pathogens' colonies obstruct vessels lumens (capillaries). It could be fungus, protozoa, zooparasites. Quite often microbial emboli forms under thrombi' suppurative melting. In obstruction place metastatic pyogenic abscesses form.

*7 **Embolism with foreign objects*** occurs in case fragments of bullets, mines and other objects come into vessels lumen. Heavy foreign objects move close, sometimes against blood flow – rethrograde embolism. Here relates also embolism with a pieces of petrificates, atherosclerotic plaques' cholesterol crystals.

Significance of embolisms: infarctions development, metastatic diseases of tumors, pyogenic abscesses metastaic diseases with sepsis, thromboembolism syndrome development, sudden death of pulmocoronary shock.

Infarction

Infarction is a fire of necrosis, caused by blood supply stop, in other words, ischemia. It belongs to vascular and ischemic kind of necrosis. Infarctions occurs of wedging shape in organs with mainline type of arteries branching (spleen, lungs, kidneys) and of irregular shape in organs with scatter type of arteries branching (cerebrum, heart). White infarction (spleen), which infarction with red shell (myocardium, kidneys) and red infarction (lungs, bowel) are differentiated.

White infarction is well separated from surrounding tissue necrosis portion of white-yellowish color. Occurs mostly in organs with collaterals insufficient development (spleen).

White infarction with hemorrhagic dressing is a portion of white-yellowish color necrosis separated from surrounding tissue with dilated collateral vessels and diapedetic hemorrhages. The shell is the result of spasm conversion into paretic dilation of vessels and increase of vessels permeability.

Hemorrhagic infarction is a portion of necrosis soaked with blood. Its development is caused by organ's angioarchitecture – dual type blood supply with anastomosis presence. For example, lungs obtain venous blood through pulmonary artery system and arterial – from bronchial artery system. In conditions of pulmonary artery branch lumen obstruction which is often facilitated with thrombi formation on venous stagnation basis, blood through anastomosis comes to necrosis portion from bronchial artery, burst capillaries and accumulates in alveoli.

Morphology of infarctions

Organ	Type of infarction	Type of necrosis
➢ Heart	➢ White with hemorrhagic dressing	➢ Coagulation with secondary colliquation
➢ Lungs	➢ Red	➢ Coagulation
➢ Kidneys	➢ White with hemorrhagic dressing	➢ Coagulation
➢ Cerebrum	➢ White and red	➢ Colliquation
➢ Spleen	➢ White	➢ Coagulation
➢ Bowel	➢ Red	➢ Colliquation

Three consequential stages are differentiated ***in infarction morphogenesis*** – pre-necrotic (ischemic), necrotic and post-necrotic (infarction healing, cicatrization). Pre-necrotic stage is characterized with growing degenerative changes. Tissue structure yet conserved. Glycogen disappears in ischemic portion, breath ferments activity decreases, intracellular organelles swell and destroy. Necrosis stage is clearly manifested in 18-24 hours from the beginning of the process development. It is characterized with tissue decay (nucleus disappear, cytoplasm dissolve) and its melting (autolysis). In the place of infarction with time passing by conjunctive tissue cicatrix is formed. Petrification and cyst formation (cerebrum) also relate to favourable consequences. Dangerous one is suppurative melting which is often found under bacterial embolism.

Shock

Shock is generalized acute failure of hemodynamics caused by super strong irritation of organism with cardiac-vascular system neurohumoral regulation disorder manifested with acute decrease of blood supply into tissues, their hypoxia and vitally important functions of organism depression.

Shock pathogenesis

In shock development pathogenesis erectile and torpid phases are differentiated. In the first phase generalized excitation of nervous system is observed, metabolism intensification, sympathoadrenal system activation, catecholamines' amount increase in blood, endocrine glands function increase, generalized spasm of the vessels, arterial-venous anastomosis opening, blood re-distribution in venous channel past capillaries, venous pressure increase, failure of blood outflow from capillaries, blood depositing in internals, hypovolemia, blood portion exclusion from general circulation,

blood minute volume decrease, circulation speed decrease, hypodynamia development, energy metabolism change on anaerobic way. In the second phase considerable slowing-down of central nervous system functions is observed as well as cardiovascular system function failure, respiratory compromise and hypoxia development.

Etiopathogenetic classification of shock

By etiology the following types of shock are differentiated – from exogenous factors action: traumatic, burn, from electric trauma; from endogenous factors action under internal diseases: abdominal, cardiogenic, nephrogenic; - caused by humoral failures: anaphylactic, hemotransfusion, hemolytic, endocrine, toxic (bacterial, infection-toxic). By endopathogenous principle shock is divided into septic, cardiogenic, anaphylactic, hypovolemic, neurogenic.

Shock morphology

Shock morphology: fluid condition of blood in vessels, disseminated intravascular blood coagulation, hemorrhagic syndrome, blood depositing in microcirculatory channel, blood circulation bridging, glycogen mobilization in tissues' depots, degenerative changes in parenchymatous organs. Fluid condition of blood occurs under instantaneous death and is caused by postmortem fibrinolysis as the result of consumption coagulopathy under DIC-syndrome which the most often occurs under bacterial shock. Blood depositing macroscopically is manifested with the features of hypovolemia: there is no blood in the heart, small amount of blood is in big venous vessels. Blood circulation bridging is manifested with kidneys cortex ischemia, juxteglomerular zone and renal pyramids plethora, interstitial edema of lungs. Fast glycogen mobilization from depot is manifested with light (shock) hepatocytes presence: first glycogen disappears, then

fatty (adipose) degeneration develops. Hemodynamic changes at shock are as follows: venous hyperemia, sludge-syndrome, stasis, thrombosis, diapedetic hemorrhages, pulmonary edema. Certain morphologic features of changes in internals depending on shock type were found.

Septic or bacterial (endotoxic) shock occurs under bacterial toxins accumulation in organism and cytokines level increase in blood. Basic manifestation of this shock is increased vascular permeability and enhanced intravascular blood coagulation. The following develop at that: thrombosis of kidneys' microvessels, DIC-syndrome, adrenal glands, adenohypophysis with corresponding necrotic changes in these organs with their insufficiency development.

Cardiogenic shock occurs in the result of considerable sudden cardiac activity depression, observed under myocardial infarction, acute myocarditis, arrhythmias, cardiac valves perforation, massive pulmonary thromboembolism, pericardial tamponade. Morphologic manifestation is even venous plethora of capillaries and venules, or untimely death features: venous plethora of internals, big venous vessels overfilling with fluid blood and merged hemorrhages on serous tunics, pulmonary edema.

Disseminated intravascular clotting (DIC) syndrome (Disseminated intravascular blood coagulation syndrome) *or DIC-syndromw or thrombohemorrhagic syndrome or consumption coagulopathy is grave terminal condition characterized with fine thrombi (fibrin, erythrocyte, hyaline) widespread formation in microcirculatory channel with simultaneous non-coagulation of blood causing multiple hemorrhages.*

The most often thrombi are observed in microvessels of lungs, kidneys, liver, adrenal glands, hypophysis, cerebrum, etc. Simultaneously multiple hemorrhages develop in these

organs, degenerative and necrotic changes, and thrombocytopenia in blood causing pathologic bleeding disease. Owing to such changes multisystem insufficiency develops and patients' death. The cause of syndrome development is unknown. The most often DIC-syndrome develops under endotoxic shock caused by massive injury of endothelium with bacteria, virus, rickettsia, immune complexes or cytokines, under premature detachment of placenta and embolism with amniotic fluid and intrauterine death of fetus; under snake bites, under promyelocytic leukemia, etc. Syndrome is grounded on blood coagulative and anticoagulative systems function failure.

Lymph flow disorders

Lymph flow disorders are manifested with mechanic, dynamic and resorption insufficiency. Mechanic insufficiency develops when lymph flow hindrance exists (squeezing, lymphatic vessels congestion, lymph nodes' block by malignant cells, lymphatic vessels' or thoracic duct's surgical ablation, lymphatic vessels valves insufficiency). Dynamic insufficiency occurs under capillaries' enhanced filtration. Resorptive insufficiency is observed under decreased permeability of lymphatic capillaries. Morphologic manifestations are as follows: lymph flow slows down and lymph vessels dilation, lymph congestion, collateral lymph flow development, lymphatic vessels reconstruction, lymphangiectasias appearance, lymphedema (local or general) development, development of chylous ascites, chylothorax, lymph stasis, elephantiasis, sclerotic changes in tissues.

II Algorithm of the practical part of the class

To learn and to be able to describe orally macrospecimens on the theme which are exhibited in macromuseum of the Chair

1 *Brown induration of lung* (see the theme violations of pigment metabolism).

2 *Nutmeg liver*. Organ is enlarged, dense. Parenchyma on a cut is pied, has the appearance of nutmeg: on the light – yellow background there are dark-brown clots. The light – yellow colour of hepatocytes. Dark – brown spots are bloody lakes (extended central veins and sinusoids).Nutmeg liver is by morphological expressions an example of total venous plethora. At progress of cardiac insufficiency indicated changes in liver ends by nutmeg portal cirrhosis of liver.

3 *Cyanotic induration of kidney*. Organ is enlarged, dark-blue colour prevails on a cut, especially sharply shown in intermedial zone (on a border between cortical and medullar layer). Cyanosis is conditioned by kidney congestion by venous blood. The oxidized haemoglobin (arterial blood) is of purple-red colour and is reduced (without oxygen, venous blood) blue-red, therefore at venous stagnation cyanosis takes place. In the conditions of hypoxia process of collagen formation by fibroblasts is activated, and consequently sclerosis develops (induration, densing)

4 *Attached to the wall (nonobturative) mixed thrombus of aorta at atherosclerosis a blood clot partly fills clearance of aorta.* The surface of blood clot is striped (Tsan's lines), colour is red. A heart, body and tail of blood clot are seen. Intimae of aorta is rough in favour of ulceration of atherosclerotic plaques. In destruction of endothelium of aorta tissue thrombocinasa frees. Process of adhesion of thrombi with their next agglutination in the area of damage of endothelium (ulcers) is observed. Damage of thrombocytes is accompanied by release of trombocytic thrombocinasa. Active plasmic thrombocinasa forms from nonactive tissue and thrombocytic thrombocinases,

that starts next phases of blood coagulation. Obturative thrombus of aorta is fatal complication of atherosclerosis.

5 *Obturative red thrombi in the regions of aorta's bifurcation. Thrombus-rider.* Clearance of artery in the region of its bifurcation is filled by thrombic masses. The surface of blood clot is striped (Tsan's lines). The consequences depend on localization of thrombus of thrombus – rider. It is seen on preparation, that branches of artery of large calibre are obturated – common iliac arteries, therefore consequences are inauspicious – gangrene of the low extremity. Such case was described at first by Lerish and is named Lerish's syndrome.

6 *Rupture of the wall of uterus.* Uterus is enlarged. Large transversal rupture of its front wall is seen. Enlarged size of the organ indicate that it is uterus of pregnant woman. Transversal rupture arises at surplus contraction of uterus during births, often at disparity of size of foetus and pelvis (narrow pelvis, big foetus). Consequently, bleeding from the ruptured vessels develops.

7 *Tamponade of pericardium (haemopericardium).* It is seen on frontal cut of pericardium, that pericardium is filled with blood, which is coagulated. On the lateral wall of left ventricle, near its basis, crimson area of myocardium, irregular form and sinuous chink are contoured. Crimson colour is conditioned by that necrotic area of myocardium is saturated by blood. Blood got into a cavity of pericardium through the chink in region of infarction which takes all layer of wall of left ventricle (transmural infarction) and haemopericardium develops. Tamponade of pericardium is fatal complication of infarction of myocardium.

8 *Broken tubular pregnancy.* Though opening in an uterine tube, which appeared as a result of rupture of its wall, blood clot is seen. In a blood clot which is in abdominal cavity, an embryon is seen. Chorion fibers are bordered by throphoblast, cells of which have high lytic (destructive) activity. At tubular

pregnancy fibers on 8-12th week germinate all relatively thin wall of tube, and it ruptures as a result of corroding (eating away) and growth of foetus.

9 *Thromboembolism of lung (Pulmonary) artery (TELA).* An extraneous body is seen in clearance of the exposed pulmonary artery. It is thromboembol, not attached to the wall of vessel. It is of red colour with a smooth surface. Largeness of thromboembol is explained by that after thromboembolism develops, embolus grows as progressive thrombus, it means that fresh thrombic masses accumulate on it. The source of thromboembolism is the veins of large circle of blood circulation. Thromboembolism of pulmonary artery may lead to patient's death, that is seen on this macropreparation, and development of pulmo-coronary shock. At irritation of very rich on nervous endings intimae even by small embolus, especially in the region of its bifurcation, spasm of bronchi, pulmonary and coronary arteries of heart develops.

10 *Haemorrhage in a cerebrum.* In a right hemisphere haematoma with destroy of brain tissue is seen. Borders of haematoma are unclear. Name possible causes of haemorrhage, mechanism of bleeding, consequences.

11 *Embolismic purulent nephrite.* On the surface of kidney and in cortical layer on the cut small yellow abscesses surrounded by red rim are seen. What is the morphogenesis of abscess of kidney?

12 *Metastases of cancer to the liver.* In parenchyma of liver on cut white, different sizes nodes of tumor are seen in capsule of liver above tumor, navel-shaped pullings. What is the type of embolism in this case? By what vessels acid metastasmation pass?

13 *Thrombosis of heart chambers.* Filled with thrombic masses chambers of both ventricles are seen on a frontal cut. Specify causes of that thrombi formation. What are possible outcomes?

To learn micropreparations from a theme and be able to draw the essence of pathological process with proper designations

1 *Hyperaemia of lung.* Staining with hematoxilin-eosin Pulmonary tissue is presented by alveolar cells and bronchioli. Clearance of interalveolar capillaries, peribronchial vessels are extended, filled in with blood. Presence of blood in clearance of alveoli and bronchioli is marked. Epithelium of bronchioli and bronchi is desquamated; layers of it are in the clearance of bronchi. Bronchial wall is infiltrated by neutrophiles, lymphocytes, is swollen. Somewhere interalveolar septa are very thin; clearance is extended (emphysema). It is inflammatory hyperaemia. Blood enters the clearance of alveoli and bronchioli as a result of increased permeability of wall of vessels in inflammation. Designate: 1 –alveoli, 2 – bronchiole, 3 – vessel, 4 - inflammatory infiltrate.

2 *Venous plethora of liver. Nutmeg liver.* Staining with hematoxilin-eosin. At small magnify of microscope mainly central parts of hepatic lobules are plethoric (red colour). At total venous plethora outflow of venous blood from liver is impeded, so central veins of lobules extend, and central of sinusoids also extend (blood lakes) to the measure of increasing of plethora haemorrages appear at the center of lobules, hepatocytes atrophies from pressure there, and undergo (give way to) dystrophy, conditioned by hypoxia, and die. Hepatocytes of periphery of lobules are compensative hypertrophied. Nutmeg liver is morphological expression of total venous plethora. Designate: 1- central vein, 2 – sinusoids, 3 - hepatocytes of the centre of lobule, 4 - peripheral hepatocytes

3 *Organized thrombus with phenomena of recanalisation and revasculation.* Staining with hematoxilin-eosin. Artery in transversal cut is presented on the micropreparation. The wall of artery consist from adventitia (external membrane), external elastic membrane, smooth muscle layer, internal elastic

membrane and intimae. Endothelium is absent. Clearance of vessels is filled by thrombic masses on the stage of organization. On the periphery of thrombus germination of connective tissue from the wall of vessel into thrombus is seen, many nuclei of different form (round, oval, oblong), that are the nuclei of cells of granular tissue. Centered accumulation of erythrocytes. Bounded by endotheliocytes. That are places of germination of vessels into thrombus, (vascularisation of thrombus). Dark-blue spots are seen under intimae of artery. That are areas of liming, that is an evidence of atherosclerotic changing of arterial wall. So,atherosclerosis of artery with damaging of intimae, stipulate formation of obturative thrombus, which organizates. Designate: 1- wall of the vessel, 2 -atherosclerotic plaque with liming, 3 - granular tissue, 4- capillaries in thrombi.

4 *Fatty embolism of vessels of lungs*, preparation of lung of animal, to which oily suspension was injected intravenously. Staining with sudan III. Clearance of vessels of microcirculatory channel of lung sudanphilic substance yellowish-rose colour is seen. Beside embolus vessels are congested by blood, going out of erythrocytes into clearance of alveoli is observed. Fatty embolia of vessels of lung is dangerous for life at embolism of 2/3 and more capillaries of lungs. As a rule, in insignificant embolism fat in capillaries of lungs emulgates, saponificates and resolves by lipophages, sometimes pneumonia develops. Designate: 1- alveoli, 2- bronchioli, 3-vessels, 4-drops of fat.

5 *Mixed thrombus in artery*. Fibers of fibrin, big numbers of erythrocytes, remains of leucocytes are seen in structure of thrombus, in head of thrombus, which is attached to the wall of vessel, haemosiderophages and elements of connective tissue are founded. Designate: 1-wall of vessel, 2- haemosiderophages, 3-thrombus

6 *Shock kidney*. In epithelium of proximal tubules granulation of cytoplasm is expressed. Some cells are without nucleus, and cytoplasm has homogenously-pink colour, vessels of cortical layer are extended, plethoric. Designate: 1-proximal tubule, 2-necrosis of epithelium, 3-dystrophy of cytoplasm of epithelium
7 *Shock lung*. Areas of shrinking of alveoli (athelectasis), serously-haemorrhagic edema of interalveolar septa, fibrin deposition in clearance of alveoli, microthrombi, stasis in capillaries are seen. Designate: 1-stasis in capillaries, 2-clearance of alveoli, 3-fibrin in alveoli.
8 *Stasis in capillaries of cerebrum*. On subject glass two serial cuts of brain are stained with hematoxilin-eosin (pink) and according to Gidagin's method by hydrochloric acid haematin (black). On preparation, stained by haemotoxilin-eosin plethora of vessels of cerebrum, edema around vessels and cells, swelling of matter of cerebrum. On preparation, stained according to Gidagin, black colour erythrocytes are seen. Find an area, where capillaries of brain filled with chains of black erythrocytes are expressly seen. *Designate*: 1-plethora of vessels, 2-edema of brain, 3-stasis
9 *Haemorragical infarction of lung* (see class 3).
10 *Brown induration of lungs* (see class 2).

Situation tasks

1 Patient suffered from rheumatic cardiac failure with left atrioventricular opening stenosis prevalence. Death came from chronic progressive cardiac decompensation. Name morphologic changes in lungs, liver, cerebrum, kidneys, spleen.
2 Patient ill with alcoholic liver cirrhosis died from hemorrhage caused by esophagus dilated veins' rupture. What caused esophagus veins' dilation?
3 10l of ascitic fluid was fast removed from patient's abdomen, collapse developed, patient to lost. Why unconsciousness

occurred? What are the changes in cerebrum? What is the prognosis?

4 Patient undergone a number of myocardial infarctions. Right now short breath, acrocyanosis; ascites are observed. Indicate morphologic changes of skin and internals.

5 Patient has a tumor of diaphragm which pinches hepatic veins. Indicate morphologic changes in liver.

6 Patient, 52 years old, was treated in-patient in cardiologic section because of rheumatic heart failure with circulation disorders (cyanosis, edemas). Pain in left leg muscles occurred. Measurement showed that left shin circumference is 5 cm bigger than right shin. Name reasons and morphogenesis of changes in leg tissues.

7 Section showed: aorta abdominal portion intima has numerous ulcerous atherosclerotic plaques, it is dense homogenous red color mass in aorta lumen, which crumbles, conjoint with intima, surface is corrugated. Indicate the essence of pathologic process.

8 Section showed foreign body in inferior vena cava lumen, which fills-in vascular lumen. Surface is bright, of red color, of elastic consistency, didn't attached to vascular wall. Name foreign object nature.

9 Increased spleen of patient ill with leucosis was palpated by 10 students. After examination patient's condition sharply took a turn to worse – paleness, thready pulse, tachycardia, blood pressure decrease. Name probable reason of patient's condition taking turn to worse.

Answers to situation tasks

1 Brown pigment induration of lungs, nutmeg liver, cyanotic induration of kidneys, cerebrum vessels venous plethora and brain edema, cyanotic induration of spleen.

2 Under liver cirrhosis portal hypertension develops, porto-caval anastomosis dilate, esophagus dilated veins' wall

atrophies. Under their rupture hemorrhage occurs, sometimes fatal.

3 Under fast removal of ascitic fluid in abdomen organs hyperemia appears after ischemia. At the same time cerebrum exsanguinates because of blood re-distribution in organism, vertigo develops. It is necessary to lay patient horizontally and symptoms of cerebral ischemia will disappear.

4 Under chronic cardiac insufficiency legs edema, cyanosis, legs tissues' atrophy and sclerosis are developing, in internals cyanotic induration, nutmeg liver are observed.

5 Under renal vein squeezing nutmeg liver develops.

6 On heart insufficiency background leg veins thrombosis developed, obstructing blood outflow, tissues swell so leg become thicker.

7 Mural thrombus formed in aorta in the place of atherosclerotic plaque.

8 There is postmortem grume in vein lumen.

9 Under rough palpation enlarged spleen capsule burst and internal hemorrhage developed.

Test tasks

1 During autopsy of suddenly died person it was found irregular blood filling of myocardium. Electronic microscopically – glycogen content decrease and mitochondrions destruction. Name likely blood circulation disorder.

A. Angioneurotic arterial hyperemia **B.** Vacant arterial hyperemia. **C.** Acute venous hyperemia. **D.** Chronic ischemia. **E.** Acute ischemia.

2 During traffic accident driver's neck was injured with broken glass. Hemorrhage was minor but in few minutes undergone died under acute asphyxia signs. What pathologic process could be thought of?

A. Pulmonary embolism. **B.** Pulmo-coronary reflex. **C.** Air embolism.
D. Acute posthemorrhagic ischemia. **E.** Gas embolism.

3 12 l of liquid was fast removed from patient with ascites abdomen by paracentesis method. As a consequence collaps developed with consciousness loss, and hyperemia occurred in abdome. Indicate type of peritoneum arterial hyperemia.
A. Angioneurotic hyperemia. **B.** Vacant local. **C.** Collateral. **D.** Hyperemia caused by arteriovenus bridge functioning. **E.** Hyperemia after ischemia.

4 During autopsy of the deseased from long term cardiovascular decompensation mixed trombi were found in atrial auricles. What kind this thrombus belongs to in confomance with pathogenetic classification?
A. Progressive. **B.** Inflammatory. **C.** Dilative. **D.** Migrating. **E.** Stagnant

5 Under dead body section in left auricle it was found red color tissue, elastic, bright, covered with tender net of fibrin, which was not fixed to heart walls, and which repeats their relief. What is the nature of this tissue?
A. Postmortem grume. **B.** Mural thrombus. **C.** Obturating thrombus. **D.** Migrating thrombus. **E.** Progressing thrombus.

6 Boy, 8 months old, died of severe form of influenza under cerebral coma features. Microscopically in cerebrum was found edema, swelling numerous spot hemorrhages. In microcirculatory channel vessels lumen thrombi are observed which look like homogenous thick mass colored with eosin in pale-red color. Thrombi fill vascular lumens. Your consideration regarding changes observed in vascular lumens.
A. Viruses colony. B. Blood stasis. C. Hyaline thrombi. D. White thrombi. E. Postmortem grumes.

7 Patient ill with hypertension disease died under features of stroke from cardiac insufficiency. Microscopically in

cerebrum it was edema, numerous spot hemorrhages. Name mechanism of spot hemorrhages development.

A. Vascular walls corrosion. B. Erythrodiapedesis. C. Vascular wall rupture. D. Microaneurisms' rupture. E. Erythrocytes agglutination.

8 Patient died of sepsis, developed as right hip soft tissues phlegmon complication. Section showed the features of systemic inflammative response syndrome. Mixed thrombus was found in right hip vein lumen, which with his head is fixed to intima on the level of hips' upper third part and its tail is situated in inferior vena cava on renal veins level. Indicate this thrombus name.

A. Obturating. B. Progressive. C. Congestion. D. Dilative. E. Mixed.

9 After mechanic trauma of the head portion turned blue and intumescense in temporal part occurred. Exploratory puncture showed that in the place of trauma cavity formed filled with blood. Indicate the name of pathology.

A. Fruise. B. Ecchymosis. C. Hematoma. D. Thrombi. E. Hemorrhagic infiltration.

10 Patient ill with tertiary syphilis suddenly died. Section showed aorta ascending part rupture, Minakov spots in the heart, blood loss equaled to approximately 0,5l. Name immediate cause of death.

A. Blood loss. B. Hypoxia. C. Cerebrum exsanguination. D. Acute posthemorrhagic ischemia. E. Heart ventricules filling shortage.

Answers to test tasks

1. E; 2. C; 3. E; 4. E; 5. A; 6. C; 7. B; 8. B; 9. C; 10. E.

Illustrations to theme

Figure 1 – *Nutmeg liver.* Parenchyma at section is stripped, has nutmeg appearance: dark brown spots on light yellow background. Light yellow color of liver is caused by hepathocytes' adipose degeneration, dark brown specks – blood lakes (dilated central veins and sinusoids). Nutmeg liver is morphologic expression of general venous plethora. Under cardiac insufficiency progress named changes in the liver are ended with nutmeg portal liver cirrhosis.

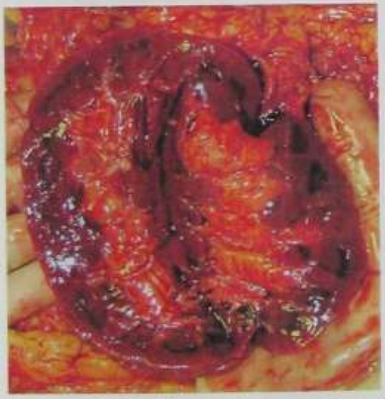


Figure 2 – *Cyanotic induration of kidney.* Dark-blue color dominates on section (it is the most full-blown in medullar layer). Cyanosis is caused by the fact that kidney is overfilled with venous blood. Oxidized hemoglobin (arterial blood) is of purple-red color, and reduced hemoglobin, that is without oxygen (venous blood) is bluish-red, so cyanosis takes place under venous congestion. In conditions of hypoxia the process of collagen formation by fibroblasts activates, so sclerosis occurs (induration, thickening).

Figure 3 – *Rider-thrombus*. Vein lumen in its branching place is filled with thrombi masses. Thrombus surface is stripped (Tsane's lines). Consequences depend on rider-thrombus localization. It is seen on specimen that thrombus obstructed vein branches are of big size, so consequences are unfavorable.

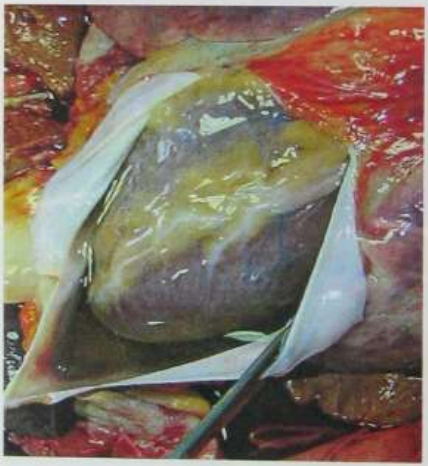


Figure 4 – *Hemopericardium*. There is blood accumulation in pericardium lumen. The most likely reason is myocardium rupture.

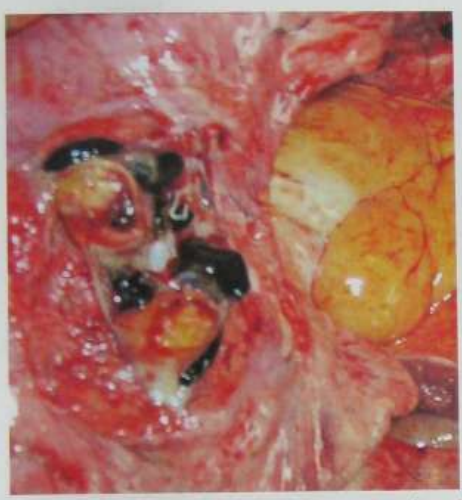


Figure 5 – *Pulmonary embolism*. In the opened pulmonary artery lumen foreign object is seen, which is thromboembolus not fixed to vascular wall. It is of red color with smooth surface. Big size of thromboembolus is explained by the fact that after thromboembolism development embolus grows similar to progressive thrombus, that is to say fresh thrombus masses deposit on it. The source of thromboembolism is greater circulation veins. Pulmonary embolism can cause patient's death as the result of pulmonary artery lumen obstruction, which is seen on this macrospecimen, and pulmo-coronary shock development. When even small embolus irritates very rich to nerve-ending intima of pulmonary artery, especially in the place of bifurcation, spasm of bronchi, pulmonary and cardiac coronary arteries occurs.

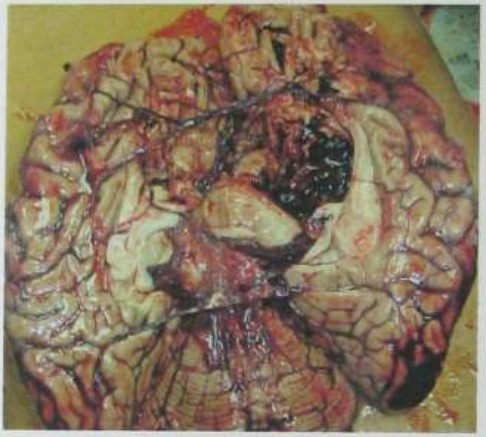


Figure 6 – *Cerebral hemorrhage.* Hematoma with brain tissue destruction is seen in the right-brain. Hematoma's boarder is not distinct. Indicate possible reasons, mechanism, consequences of hemorrhage.

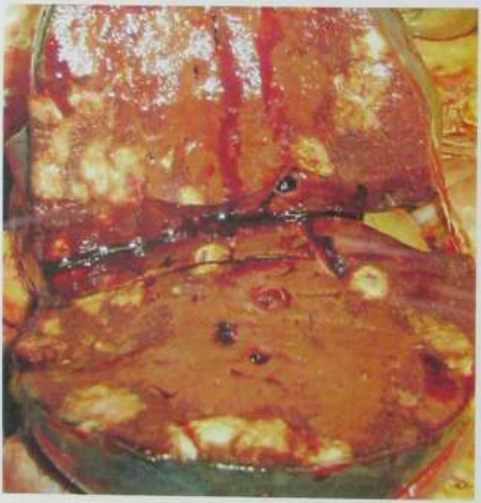


Figure 7 – *Liver metastasis.* On section white color tumor nodes of various sizes are seen in liver parenchyma. What type of embolism is in this case? What vessels cancer metastasis passed through?

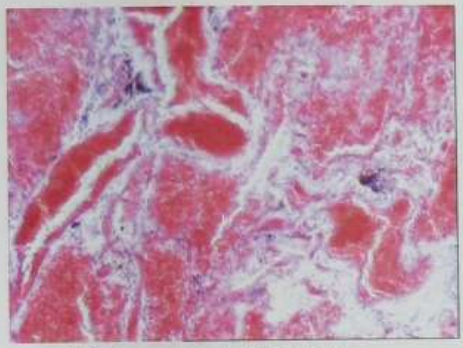


Figure 8 – *Lung hyperemia*.. Colored with hematoxylin and eosin. Arteries' and capillaries' lumens are dilated, plethoric. Erythrocytes situate also in alveoli's lumen. This is inflammable hyperemia. Blood comes into alveoli's lumen in the result of vascular wall permeability increase under inflammation.

Figure 9 – *Organized thrombus*. Colored with hematoxylin and eosin. Artery in transverse section is shown in microspecimen. There is no endothelium. Vascular lumen is filled with thrombus masses on the stage of organization.

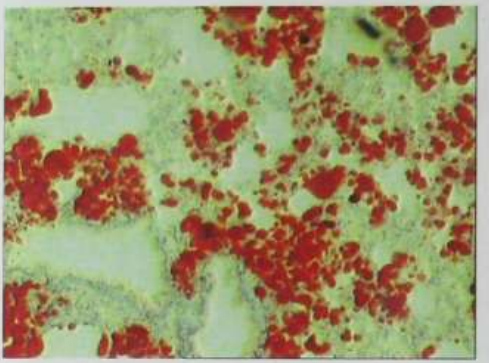


Figure 10 – *Pulmonary vessels fat embolism.* The specimen of animal's tissue after oil suspension intravenous injection. Colored with sudan III. Sudanefill substance in lungs microcirculatory channel lumen is of yellow-red color.

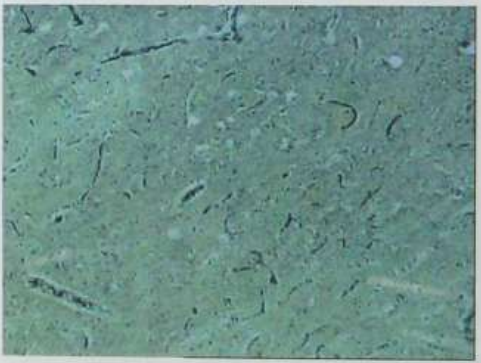


Figure 11 – *Stasis in cerebrum capillaries.* Specimen is colored by Gendeigain's method with muriatic hematoxylin (black). Erythrocytes are of black color. Find the portion where cerebrum capillaries are clearly seen filled with erythrocytes in the form of black erythrocytes chain – stasis.

Content Module 2
Inflammation

Lectures – 2 hours
Practical classes – 4 hours
Student's self-work – 2 hours
Form of student's individual work – thesis or reports

Specific objects of module:

- *To define the essence and biological sense of inflammation.*
- *To explain the ethiology, pathogenesis of inflammation, role of plasmic and cellular mediators.*
- *To analyze stages and kinetics of inflammatory response.*
- *To analyze morphologic characteristics, clinical significance of varieties of exudative inflammation.*
- *To analyze the ethiology, pathogenesis, morphologic characteristics and consequences of proliferative inflammation.*
- *To analyze the ethiology, development mechanism, morphologic and clinical characteristics and consequences of granulomatous inflammation.*
- *To explain cellular kinetics of granuloma.*
- *To analyze specific and non-specific granuloma and granulomatous diseases.*

Practical class 8

Topic 9 General conception about inflammation. Exudative inflammation. Morphology of exudative inflammation

Importance of the topic: *Inflammation is a morphological basis for a large group of diseases. Depending on their localization there are various clinical presentations of diseases. Thus, morphological mechanism of its development is always the same. Knowledge of its development mechanism allows evaluating the anamnesis and consequences of diseases which are accompanied by inflammation. Purpose: to study causes, nosotaxy, morphologic presentations and consequences of inflammation.*

Specific goals: 1) To know causes and morphogenesis of inflammatory process.

2) To learn how to diagnose inflammation on macro- and microscopic levels.

3) To learn how to differentiate morphological and clinical forms of inflammation and explain its presentations.

Basic matters for self-work

Inflammation: its definition, essence and biological sense. Problem of local and common concerning inflammation. History of studies of inflammation (Celse, R. Verkhov, D.F. Kongame, P. Erlich, I. I. Mechnikov). Clinical characteristics and sympthoms of inflammation (local and systemic ones).

Ethiology and pathogenesis of inflammation. Mediators of inflammation. Common features. Plasmic mediators: system of blood coagulation, system of kinin, system of complement (ways of activation). Cellular mediators. Vasoactive amines (histamine, serotonin), metabolites of arachidonic acid (prostaglandins, leukotrienes), activation factor of platelets,

tumor necrosis factors, interleukins, interferon. Significance of lysosome components, free radicals of oxygen, neuropeptides. Stages of inflammatory response.

Kinetics of inflammatory response.

Cellular and molecular processes at inflammation. Mechanism of increase of vascular penetration. Mechanisms and stages of leukocyte migration. Chemotaxis. Phagocytosis (stages), complete and uncomplete phagocytosis. Mechanisms of development of macrophage infiltration at chronic inflammation.

Exudative inflammation: serous inflammation, fibrinous (croupous, diphtheritic) inflammation, suppurative (phlegmon, abscess, empyema) inflammation, catarrhal inflammation, hemorrhagic, combined inflammation. Morphological characteristic and clinical significance.

I Pre-auditorium self-training to practical lesson

Inflammation is a typical pathologic process which appears as an answer to action of damaging agent and shows in three interrelated reactions – alteration, microcirculation disorder together with exudation, emigration and proliferation.

This universal vascular-mesenchymal reaction has been developed during the process of phylogenesis and has a protective-adaptable significance. It is aimed at elimination or deactivation of pathogenic agent and restoration of damaged tissue. That is its biological sense. Celse and Halen were the first who described clinical presentations of inflammation: swelling, pain, reddening, temperature increase, function disorder. Virkhov showed the significance of cellular reaction in development of inflammatory reaction in parenchyma and stroma of organs. I.I. Mechnikov discovered the phenomenon

of phagocytosis in the process of inflammation. D.F. Kongame showed that the vascular reaction is of great importance in the development of inflammation, as well as vascular penetration increase, outlet of plasma and cellular elements from the vessels which determines swelling.

Ethiology and pathogenesis of inflammation, mediators of inflammation

Inflammation is the organism's answer to influence of numerous agents of external and internal surroundings. Among external (exogenous) causes the biological agents come first - viruses, bacteria, rickettsia, fungi, protozoa, and helminthes. Among physical causes there are traumas, radiant energy, high and low temperatures which are the most important, among chemical ones – acids and alkalis. Internal (endogenous) factors are the structures of proper tissues and cells, as well as metabolic products which changed their properties as a result of necrosis, tumor decay, hemorrhage, thrombosis, salt deposits. Immune complexes also belong hereto.

Kinetics of inflammatory response. Cellular and molecular processes at inflammation. Inflammation is developed in histion. This term determines the morphofunctional unit of connective tissue which includes cellular elements, fibers, ground substance, nerves and nerve endings, hemomicrocircular channel and lymphatic viae. Traditionally, inflammation has three *stages* which cannot be clearly demarcated - stage of alteration, stage of blood circulation disturbance with exudation and emigration of cellular elements and stage of proliferation.

One can distinguish the following clinical presentations of inflammation: fever, reddening, swelling, pain, function

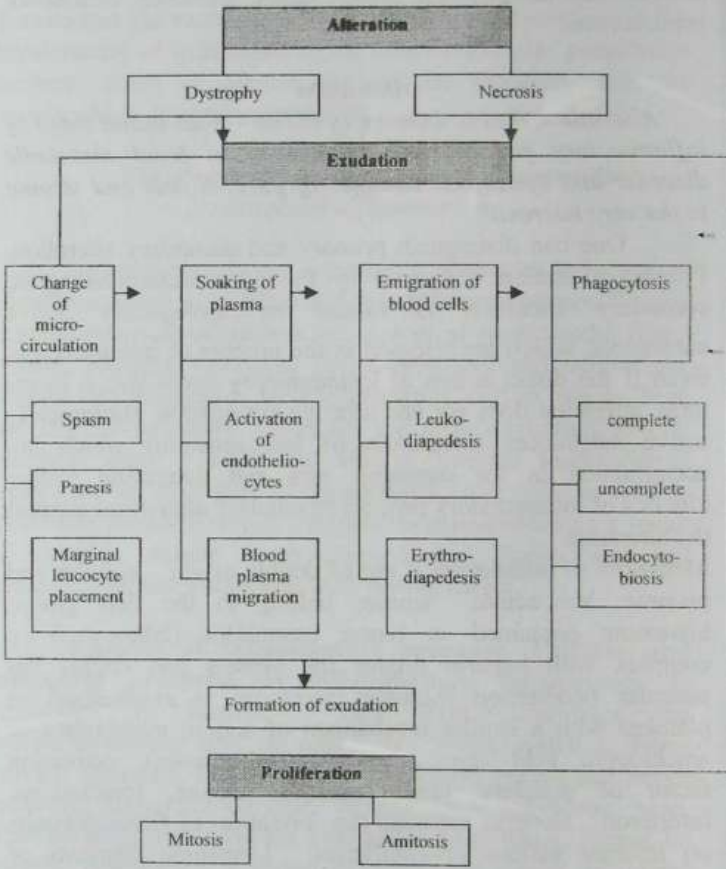
disorder and morphologic presentations: alteration, exudation, proliferation.

Alteration

Alteration, that is damage of tissue - is an initial stage of inflammatory process. Its essence is in local metabolic disorder and dystrophic changes of parenchyma and stroma to the very necrosis

One can distinguish primary and secondary alteration. Primary alteration is caused by the most hazardous agent; secondary alteration is caused by biologically active substances, which are released in the process of inflammation. Even if the direct action of inflammatory agent was a short-term, alteration does not end after its elimination. Biologically active substances (mediators of inflammation) which are accumulated in the damaged area and determine further kinetics of inflammatory process (secondary alteration) support the alteration.

Mediators of inflammation are of double origin – cellular and plasmic. Vasoactive amines belong to the first group: histamine contained in tissue basophiles (labrocytes) in complex with heparin dilates the vessels and causes the vascular penetration increase; serotonin is synthesized in platelets with a similar mechanism of action; metabolites of arachidonic acid (prostaglandins, leukotrienes); activation factor of platelets, tumor necrosis factors, interleukins, interferon. Heparin prevents the formation of fibrin deposits on internal surface of capillaries. Lysosome ferments of granulocytes, monocytes, tissue macrophages and basophiles – protease, esterase, collagenase, elastase - play a key role in mechanisms of secondary alteration.


Alteration
Dystrophy
Necrosis
Exudation
Change of micro-circulation
Soaking of plasma
Emigration of blood cells
Phagocytosis
Spasm
Paresis
Marginal leucocyte placement
Activation of endothelio-cytes
Blood plasma migration
Leuko-diapedesis
Erythro-diapedesis
complete
uncomplete
Endocyto-biosis
Formation of exudation
Proliferation
Mitosis
Amitosis

Exudation

The essence of the secondary stage of inflammation is in disturbance of blood and lymph circulation in microcirculation channel - arterioles, capillaries, venules. At first a short-term reflex spasm of arterioles appears. It is changed into the arterial hyperemia, which is developed as a result of accumulation of mediators of inflammation, as well as hydrogen ions and potassium ions in the nidus of inflammation. The following stage of vascular changes is venous hyperemia. Accumulation of exudation in extracellular space results in compression of veins and slowing down the blood outflow. Then pre-stasis comes, which is characterized with pendular and jerky movements of blood and eventually there is an entire circulatory arrest (stasis).

Blood circulation disturbance is accompanied by exudation and emigration of cellular elements.

Exudation – is an outflow of liquid phase of blood (water, proteins, and electrolytes) out of the bounds of bloodstream.

It is tightly connected with emigration, which is the outlet of platelets. Exudation is determined by three causes:

a) increased intravascular pressure at arterial or venous hyperemia;
b) increased vascular wall penetration under influence of mediators of inflammation, hydrogen ions and potassium ions, adenosine triphosphate, lactic acid and others;
c) increased oncotic pressure outside the vessels in consequence of decomposition of molecules of proteins and outlet of albumins.

For a long time the mechanism of plasma and form elements' migration through endothelial cover and basic vascular membrane was unknown. According to electron

microscope tests it is clear now that endotheliocytes are adjacent to each other, just in some areas connected through desmosomes. Owing to their location above membrane colloid mass these cells are able to contract, to change form, to migrate. As a result of such migration the fissures are generated between endotheliocytes. At the initial stages of inflammation water, molecules of proteins and electrolytes penetrate mainly by means of pinocytosis, not so often they penetrate through fissures between endotheliocytes. First of all water penetrates with soluble salts and small quantity of low molecular weight proteins (to 2 %) – albumins. At further increase of penetration content of proteins 3-5 % runs up due to outlet of globulins and fibrinogen. This inflammatory liquid is called exudation. Depending on quantitative predominance of its components one can differ serous exudation, purulent effluent, fibrinous exudate, hemorrhagic exudate, mixed exudation. Macroscopic examination shows that tissues swell, and their color depends upon stage of inflammation and type of exudation.

Emigration of leucocytes occurs in venules in parallel with exudation. Their outlet out of the vessel includes three periods – marginal placement, vascular wall penetration, motion in tissue.

The period of marginal placement is represented by stratification of form elements of blood. Erythrocytes move in the middle of vascular lumens (axon), and leucocytes move to the layer of plasma, closer to vascular wall.

Internal surface of vessels is covered by bordering layer, which consists of glycosamineglycanes, glycoproteins, fibrin and other components. First of all polymorphonuclear leukocytes (neutrophils, eosinophils) adhere to this border, later – monocytes and lymphocytes. They migrate to the inflammatory nidus in the same order.

Among the mechanisms of marginal placement the formation of bands of fibrous tissue in vascular lumens and

reduction of electric charge of leucocytes and endothelial cells are also important.

In order to migrate out of the vessel the leukocyte should surmount two obstacles – monolayer of endothelium and basic membrane.

The mechanisms of this transition are known. When two adjacent endotheliocytes contract, the fissure is generated between them, where the leukocyte pseudopod penetrates.

By means of it the leukocyte rapidly pours cytoplasm through the fissure under endotheliocyte which exfoliates from the basic membrane. The opening is closed. This way of emigration is called interendothelial. It is peculiar to neutrophils, eosinophils. Monocytes and lymphocytes are able to penetrate directly through endothelial cell (transendothelial emigration).

The next obstacle – basic membrane - the leukocyte overcomes due to phenomenon of thixotropy that is transfer of membrane gel into sol at its contact with ferments – elastase, collagenase, hyaluronidase. The leukocyte easy penetrates the sol and appears in tissue outside the microvessel, and membrane is restored into the dense gel.

After penetration of venule wall, the leukocyte continues its motion to the centre of inflammation due to chemotaxis with a promotion of its negative charge because positively charged H^+- and K^+-ions are accumulated in inflammatory tissues.

The monocytes leave bloodstream the same way as the neutrophils do.

They turn into macrophages outside the vessel. Eosinophils as neutrophils are accumulated in connective tissues of intestine, lungs, skin, and external genitals at local allergic reactions. They are slow-moving and have low phagocytic activity concerning bacteria.

Eosinophilic chemotaxis factor excreted by T-lymphocytes, basophiles, and mastocytes determines their motion to the area of allergic inflammation. Eosinophils are also accumulated in areas of histamine placement digesting granules released by labrocytes.

Moreover, they are able to excrete on the surface of parasite their lysosomal enzymes.

That is why there is a diagnostic significance of eosinophilia. Basophiles are also accumulated in areas of inflammation and take part in allergic reactions. They contain more than a half of blood histamine. Its release has a systemic character and may cause a circulatory collapse and death.

T-lymphocytes and plasmocytes which penetrated inflammatory tissue function for immune protection.

Infiltrate is an accumulation of cellular elements of hematogenic and local origin, liquid phase of blood and chemical substances in the area of inflammation.

"Inflammatory edema" is a term for tissue soaking just with a blood plasma without mixture of cellular elements.

Depending upon cell composition there are infiltrates of polymorphonuclear leukocytes, round-cell, macrophage, eosinophilic, hemorrhage infiltrates. Their characteristic features are increase of tissue volume, increased tissue density, pain, as well as change of color. Polymorphonuclear leukocytes determine gray-green color, lymphocytes – light gray, erythrocytes – red.

Erythrodiapedesis is a migration of erythrocytes outside the vessel. Cellular composition depends upon character of pathogen, area of inflammation, duration of process, physical-chemical changes of tissue medium, reactivity of the organism.

Polymorphonuclear infiltrate predominates at bacterial infection, eosonophilic and limphocytic infiltrate – at allergic and chronic inflammations. Basic functions of infiltrate cells

are phagocytic, barrier, and enzymatic ones, which are tightly connected.

Phagocytosis – is an ability of some cells of the organism to absorb and digest various particles of biotic and abiotic environment. All phagocytes are divided into two groups – microphages (neutrophils, eosinophils) and macrophages. Microphages absorb mainly pathogens of acute infection, macrophages – dead cells and their rests.

Four stages can be distinguished at the process of phagocytosis – approach, adhesion, absorption, and digestion. Approach of phagocyte to the object is connected with positive chemotaxis. It is created by chemotaxis factors of T-lymphocytes, labrocytes, basophiles, components C_3 and C_5 of complement system, products of vital activity of microorganisms and tissue destruction. The object of phagocytosis adheres to the leukocyte in that area where surface tension of its coat decreases and the cytoplasm protrudes. If the leukocyte and the phagocytic particle have unlike charges, it contributes to adhesion. Adhered particle can be absorbed by two ways – its retraction inside of the phagocyte (invagination), or encapsulation by pseudopods from all sides.

In both cases it turns to be in a closed space circled by the membrane of phagocyte (phagosome).

Digestion is performed by means of hydrolytic enzymes of lysosomes, which circle phagosome and merge into a united food vacuole (phagolysosome).

Total destruction of the absorbed particle is a characteristic feature of a complete phagocytosis. Though, there are conditions when the phagocyte does not contain a sufficient number of enzymes or antibacterial cationic proteins, then the absorbed object isn't digested. There is an uncompleted phagocytosis. Sometimes phagocytic bacteria may find favourable conditions for their intracellular

development and reproduction (endocytobiosis). As a result the phagocyte dies and microorganisms are distributed with stream of lymph.

There could be the following causes of uncompleted phagocytosis – hereditary disturbances of generation and maturing of phagocytes: hereditary hypogranulocytosis, at which reproduction of neutrophils is blocked; Chédiak-Higashi syndrome, based upon defect of generation of lysosomes; Alder syndrome, at which the metabolism of polysaccharides in leukocytes is blocked; NADF oxidase enzyme deficiency which catalyses generation of hydrogen peroxide. The phagocytosis becomes incompleted at persons with radiation sickness, after long glucocorticoid treatment, at proteinic starvation, at aged persons.

Proliferation

Proliferation is the third final stage of the process of inflammation, at which there is a cessation of damages and there is a renovation of damaged tissues. At this period the concentration of active substances grows which slow down destructive processes. The cellular composition of the infiltrate is changed. At the nidus of inflammation the processes of reproduction of cells start to prevail, both local cells (cells-residents) and cells-emigrants which came from blood and adjacent tissues.

There is an increase in quantity of auxesis. It is generated in platelets (platelet-derived growth factor), monocytes (interleukine 1), hepatocytes (somatomedin), and other cells.

Mesenchymal (cambial), adventitional cells, endotheliocytes, lymphocytes and monocytes are propagating themselves. Cambial cells of mesenchyma differentiate into

fibroblasts and then into fibrocytes. The hypoxia developed as a result of thrombosis and stasis is significant for their proliferation. Monocytes are able to be transformed into tissue macrofages, which are able to differentiate into epithelioid cells and giant cells. B- lymphocytes generate plasmocytes, T-lymphocytes, evidently, are not able to differentiate. Fibroblasts and endotheliocytes are of the most importance in the proliferative processes.

Fibroblasts synthesize collagen and glycosaminoglycans, and endotheliocytes provide the appearance of new blood and lymphatic vessels.

Consequences of inflammation

Consequences of inflammation depend upon ethiology, anamnesis, structure of the organ, in which it appeared. Typical consequences are as follows:

a) enzymatic decomposition, phagocytic resorption and resolution of decomposition products with a complete renovation of structure and function of the organ;

b) renovation of structure of the organ by means of substitution (cicatrization);

c) conversion to chronic form;

d) death of vitally important organs and the organism.

Terms of inflammation

In most cases name of inflammation is formed by means of addition of ending "itis" (pleuritis, appendicitis, and conjunctivitis) to the Latin or Greek name of organ or tissue. Sometimes the special term is used (angina, pneumonia).

At classification of inflammation ethiology, anamnesis, character of tissue reaction, predomination of one of the phases are taken into consideration. According to the ethiology the

inflammation could be classified for ordinary inflammation, which is caused by physical, chemical and biological factors and specific one (tuberculosis, syphilis, leprosy, glanders, rhinoscleroma). According to anamnesis there are fulminant, acute, subacute and chronic inflammations. Both ordinary and specific inflammations have two morphological forms: exudative and productive.

Exudative inflammation

Exudative inflammation – the type of inflammation, in which exudation prevails over alteration and proliferation.

By the type of exudation there could be serous, fibrinous, suppurative, putrid, hemorrhage, catarrhal, mixed inflammations. The nature of exudation depends upon stage of penetration of vascular wall. First of all proteins, salts and water penetrate (serous inflammation), then fibrinogen comes (fibrinous inflammation), later – leukocytes (suppurative inflammation) and at the highest degree of penetration the erythrocytes come (hemorrhage inflammation). The last form of exudative inflammation is the hardest one. Putrid, catarrhal, mixed inflammations are not considered to be independent forms.

Serous inflammation has an acute form. It is developed at action of thermal, chemical and biological agents (microbacteria of tuberculosis, diplococci of Franckel, meningococci, shigels), autointoxications (thyrotoxicosis, uremia). The exudation contains about 2% of proteins. It is accumulated in serous cavities, between leaves of soft brain tunic, in perisinusoid and perivascular spaces, in the intersticium of the organs, Shumlyansky - Bowman's capsule, in the epidermis and under, generating vesicles, in alveoles' lumens. It causes pressure upon the organs and tissues, disturbs

their functions. Most of all there is a favourable consequence of serous inflammation (resolution), the sclerosis appears not so often (e.g., cardiosclerosis, hepatocirrhosis at thyrotoxicosis).

Fibrinous inflammation is also characterized by acute course. The exudation is rich in fibrin which is generated from fibrinogen of blood plasma. The tissue alteration with releasing of thromboplastin promotes thereto. It appears at uremia, mercuric chloride poisoning, as well as a result of action of biological agents (diplococcus of Franckel, streptococcus, staphylococcus, microbacteria of tuberculosis, pathogens of diphtheria, dysentery, and influenza). It is developed on mucous and serous membranes, as an exception in the organ (croupous pneumonia). There are two subtypes of the inflammation - croupous inflammation and diphtheritic inflammation. Morphologically they are identified by the stage of easiness of fibrinous membrane removal. If it is easy to remove the membrane so it is croupous inflammation, if it is difficult –so it is diphtheritic inflammation. Close contact of fibrinous membrane depends upon depth of necrosis. The deeper and bigger the area of necrosis of mucous or serous membranes is, the more tissue thromboplastin is excreted and more fibrin threads are accumulated. At exfoliation of the membrane the ulcers, hemorrhage, bleeding appear. Diphtheritic inflammation always appears on mucous membranes covered by multilayer pavement epithelium (tonsils, esophagus, groin, neck of uterus), as well as on skin (do not mix with diphtheria inflammation, which determines ethiology but not the morphological characteristic of inflammation).

It is determined by the fact, that multilayer pavement epithelium unlike the single-layer prismatic epithelium is closely adjacent to underlying connective tissue. At the same time the fibrin threads penetrate between epithelial cells, and it

is difficult to remove the membrane. At macroexamination the mucous or serous membranes are dark, shaggy, as if they are covered with hair coat. It is clearly demonstrated at presence of fibrinous pericarditis (hairy heart), fibrinous pleurisy.

Clinically it determines noise of friction of pericardium or pleura. Fibrinous inflammation causes intoxication by products of tissue dissociation or toxins of microorganisms accumulated under membrane.

Under influence of neutrophils the membrane could be dissolved or turn off. At diphtheria it could cause aspiration and asphyxia. After tearing off the granulation tissue is generated at areas of ulcers, then scars, especially at diphtheritic inflammation.

Often the fibrinous membranes could be organized by means of invasion into granulation tissue which brings to commissures generation or cavities obliteration (obliterating pleurisy or pericarditis), organs' deformation (stenosis of bowel). At deposits of chloride of lime "the stone heart" (pericardium petrification) could be developed.

Suppurative inflammation has an acute or a chronic course. The exudation of a green tint contains dead neutrophils (suppurative corpuscles), lysed tissues and cells with mixture of lymphocytes, macrophages and erythrocytes. It is developed mostly in response of action of pyogenic microorganisms – staphylococcus, streptococcus, gonococcus, meningococcus. Not so often diplococci of Franckel, typhoid fever bacteria, microbacteria of tuberculosis, fungi could cause the suppurative inflammation.

Sometimes it appears at action of chemical substances (aseptic inflammation). There are two morphological types of suppurative inflammation – phlegmon and abscess. Moreover, there are such special forms as empyema and edema.

Suppurative inflammation starts with a local infiltration by exudation without generation of a cavity. For example, the inflammation of hair follicle and oil gland (furuncle) appears this way. Carbuncle is the fusion of several furuncles. The perifocal suppurative inflammation is developed around the foreign body, fungi, parasites, colony of microorganisms, necrotic tissue. At this stage the process may be ended or changed into phlegmon or abscess.

Phlegmon – is a vast suppurative infiltration, through which the exudation is distributed diffusely between tissue structures dividing them into layers.

In some cases the tissues are fused under influence of proteolytic enzymes (soft phlegmon), in other cases they come under influence merely of necrosis (hard phlegmon).

Necrotic tissue is rejected and changes into sequestrum. Cellulites (suppurative inflammation of fibro-fatty tissue) is distinguished as a separate form of phlegmon.

The transformation of local suppurative infiltration into a phlegmon is observed in the organs of layered structure which consist of layers of fatty tissue, fasciae, vascular and nerve trunks.

Their mobility (peristalsis, tractions of skeletal muscles) is of a special importance. As a practical matter the fact is important that the exudation is able to be distributed from nidus of primary local infiltration to remote areas and be accumulated at clusters of soft tissue. The edema appears in such a way with corresponding clinical presentations. For example, after postinjection suppurative infiltration of a buttock the edema appears in popliteal space or around the Achilles' tendon.

The second consequence of suppurative infiltration is an *abcess* – a local inflammation generating cavity filled with pus. As a rule, it could be developed in organs with lack of soft layers (brain, liver, kidney, lungs). The abscess is developed as follows: under influence of proteolytic enzymes the leukocytes

of tissue in the area of local suppurative infiltration are lysed and separated from neighbor structures by means of granulation bank of granulation tissue which creates the pseudocoat. Its internal surface is rich in capillaries and produces suppurative corpuscles (pyogenic membrane). Gradually the granulation tissue of external surface becomes mature and passes on to the membrane of connective tissue (encapsulation).

The abscess takes its chronic course. The suppurative inflammation of hollow organs or serous cavities with pus accumulation is called *empyema*.

The most favourable consequences of suppurative inflammation are resolution and scar formation. Often they determine generalized intoxication with dystrophic processes in other organs, especially and organism emaciation, especially at chronic course.

After dissolution of the capsule the pyogenic abscesses may burst open outside or to adjacent cavities. The fistulas are generated, the inflammation is continued as pleurisy or pericarditis. As a result of contact perifocal expansion of the process the reactive inflammation is observed, e.g. pleurisy or pericarditis. The pus may be distributed by the vessels (even to the development of sepsis) at patients with suppurative lymphangitis, phlebit, phlebothrombosis. The chronic suppurative inflammation causes amyloidosis of internal organs.

Hemorrhage inflammation is mainly acute. It is developed at special danger infectious diseases (plague, anthrax, smallpox) and viral infections which are accompanied with significant increase of vascular penetration. The exudation contains erythrocyte that is why it has a rusty tint.

Putrid inflammation is accompanied with tissue destruction and excretion of gases with objectionable odor. It is caused by putrefactive bacteria. The exudation looks like ichor.

Catarrhal inflammation is developed on mucous membranes. The exudation consists of mucus, cast-off epithelium and blood elements. Depending upon its constituents prevalence there are serous (thin), mucous (thick, viscous) exudations, purulent effluent (of green tint), putrid (with objectionable odor, e.g. at ozena), hemorrhage (rusty, e.g. at influenza) exudations.

The inflammation has an acute or a chronic form. At first one there is a predominance of hypertrophy of mucous membrane (hypertrophic catarrh), at second one – atrophy and sclerosis (atrophic catarrh). Most often there are the following causes: infectious agents, thermal and chemical agents, autointoxication, allergy.

Mixed inflammation is observed at action of various agents, particularly mixed infections, when one exudation (serous-suppurative or serous-fibrinous) supplements another one, especially often it is observed at changed reactivity of the organism.

II Algorithm of the practical part of lesson

To learn and be able to describe orally macropreparations in the Chair macromuseum

1 *Abscess of cerebrum.* A cavity 2x2 in size is seen on the cut of cerebrum. Its internal surface is covered by festering exudates. The abscess of cerebrum develops more frequent as haematogenous complication of purulent otitis, abscesses of face, suppurative pneumonia.

2 *Diphtheria of respiratory tract.* White fibrinous pseudomembranes cover mucous of glottis, pseudomembrane is fastened closely, under it ulcers are seen. It is diphterical inflammation, as though mucous of larynx upper glottis is represented by stratified squamous noncornificated epithelium white colour fibrinous pseudomembranes are also seen on the surface of mucousa of trachea, mucousa is sharply hyperaemied. Fibrinous pseudomembrane is fastened friable, so fibrinous inflamunation of thrachea is croupous.

3 *Fibrinosly – purulent pericarditis.* Pericardium is rough covered by the fibrin fibers "cor villosum". On mucous membranes, including pericardium, fibrinous inflammation is croupous. Along with this mesothelium, as a rule, is damaged, so its fibrinolitic function disappears. As it is so, fibrinous exudates is organized in most cases, germinates by connective tissue along with this comissures between thickened layers of pericardium appears, sticking pericarditis develops. Sometimes in organized fibrin in comissures lime salts can deposit – petrification, "armour heart" develops. Fibrinous pericarditis is observed at rheumatism, uremia (salts of urinary acid, excreted by mucous cells, irritate them). Fibrinously purulent pericarditis is observed at empyema of pleura, madiastinitises, diaphragmitises

4 *Cerebrospinal purulent leptomeningitis.* Hemisphere of cerebrum is represented in the preparation. Greyish – green

colour masses which cover unequable tissue of brain, are seen on the surface of brain membranes (meninges).
5 *Diphtheritic colitis*. Preparation of intestine. Fibrinous pseudomembranes are seen on the surface of mucousa, and also areas of ulceration, which contain rests of pseudomembranes
6 *Croupous (lobar) pneumonia. (stage oof grey hepatization).* Cut of the lung is on preparation. In lower lobe grey-colour dense part with clear boundaries is seen. If put such piece lung into the water, it will drown. Fibrinous stratifications are seen on the surface of lung.

To learn micropreparations from a theme and be able to draw the essence of pathological process with proper designations
1 *Croupous (lobar) pneumonia.* (stage of grey hepatization.) staining with haemotoxilin – eosin. Considerable amount of fibrin, with separate lymphocytes and alveolar macrophages among it, is in the clearance of all alveoli. Interalveolar septa are thickened as a result of infiltration by cellular elements. Blood vessels of lung are plethoric. Designate: 1-filled with fibrin alveoli, 2-blood vessels, 3-bronchi.
2 *Chronic abscess of liver.* Staining with haemotoxilin – eosin.The cavity of abscess is partly filled with purulent masses, which are represented by dead neutrophiles, tissue detritus. The wall of abscess is represented by an internal pyogenic membrane, layer of granulative tissue and mature connective tissue. Intacted parenchyma of liver is placed on periphery. Designate: 1-hepatocytes, 2-pyogenic membrane, 3-granulative tissue, 4-connective tissue.
3 *Exudative tissue reaction in lungs at tuberculosis (caseous pneumonia).* Preparation is stained with haemotoxilin – eosin. Diffuse affection of pulmonary tissue is seen: caseous necrosis which prevails over other inflammatory changes, represented by homogenous pink unnuclear mass perifocal inflammations is seen on periphery. At the large magnifying single oval nuclei

of some greater sizes, are seen and more poorly stained epithelioid cells. Small round intensively stained nuclei prevail (lymphocytes). Serous exudates is in the clearance of alveoli (homogenous pink mass). So exudative reaction takes place. Vessels are plethoric. Designate: 1- caseous necrosis, 2-lymphocytes, 3-perifocal exudative inflammation.

4 *Fibrinously – purulent pericarditis*. Preparation is stained with haemotoxilin-eosin infiltration of tissue by polynuclear cells, pink colour fibrinous masses are seen in the preparation. Designate: 1-fibrinous masses, 2-inflammatory cellular infiltration, 3-cardiomyocytes.

Situation tasks

1 The diffused infiltration of all wall layers by leukocytes is detected at vermiform appendix, taken out at surgical procedure. What is the type of inflammation?

2 The patient V. suffered from thyrotoxic goiter for a long time. She died of cardiac decompensation. At histological study of heart the diffuse cardiosclerosis was detected. What is the morphogenesis of cardiosclerosis?

3 Two-year-old child was taken ill with influenza. He died in a day of respiratory failure. Which changes in lungs caused respiratory failure?

4 Three-year-old child was taken ill with diphtheria. He died at asphyxia. What is the cause of asphyxia?

5 At histological study of tonsils taken out at surgical procedure the hyperplasia of lymphoid tissue, leukocytic infiltration, lack of cell nuclei of surface layers of tonsils are detected. What is your diagnosis?

Answers to situation tasks

1 Phlegmonous appendicitis. The phlegmon is a diffuse soaking of all layers of the organ at suppurative inflammation.

2 At thyrotoxicosis the thyrotoxic heart is developed, it is expressed in hypertrophy of heart and presence of serous myocarditis. The last one brings to development of cardiosclerosis.

3 At influenza there is a possibility of quick development of hemorrhagic pneumonia, which could determine respiratory failure.

4 At diphtheria the fibrinous membranes appear in the throat, spasm of larynx occurs, which causes asphyxia – "true croup".

5 Necrotic tonsillitis.

Illustrations to theme

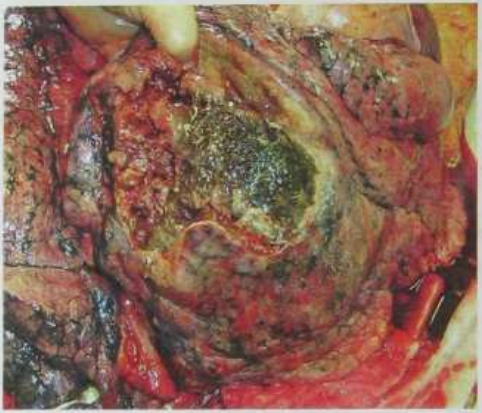


Figure 1 – Abscess of lung. Cavity filled by festering exudates is seen on a cut of lung. The wall of it is thickened, sclerosed, consequently it is chronic abscess.

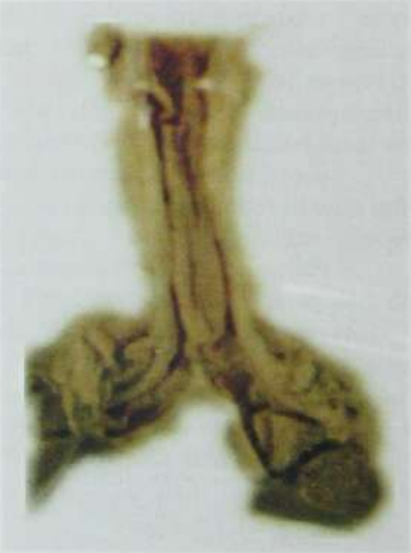


Figure 2 – Diphtheria of respiratory tract. Clearance of trachea and bronchial tubes is filled with fibrinous pseudomembranes.

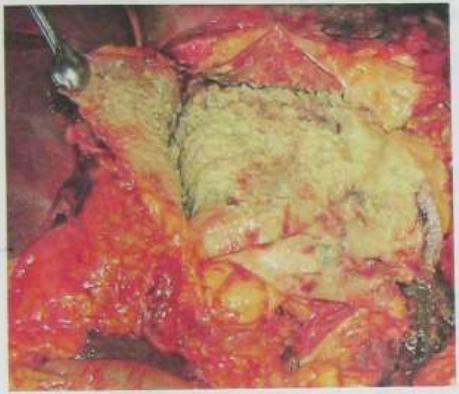


Figure. 3 – Fibrinously-festering pericardisis Pericardium is rough covered by fibers of fibrin. It is "pilose heart". On serous membranes, inflammation is croupous. Mesothelium, as a rule, is damaged, so its fibrinolytic function disappears. In communication with that fibrinous exudate is organized in most cases, germinated by connective tissue.

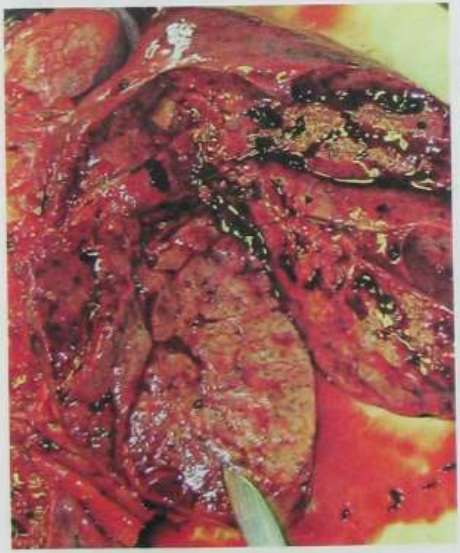


Figure 4 – Croupous (lobar) pneumonia. Lung is grey colour on a cut. Rough. As exeption fibrinous inflammation develops in parenchyma of organ. It is croupous pneumonia.

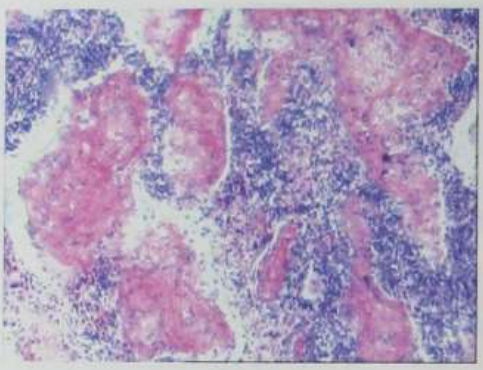


Figure 5 – Croupous pneumonia (stage of grey hepatization). Staining with haemotoxillin-eosin in clearance of alveoli mere is considerable amount of fibrin, among which there are separate leucocytes and alveolar macrophages. Interalveolar membranes are thickened as a result of infiltration by cellular elements.

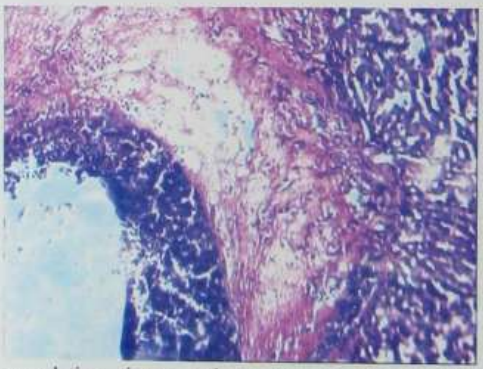


Figure 6 – Chronic abscess of liver. Staining with haemotoxilin-eosin. The cavity of abscess is partly filled with purulent masses, which are represented by dead neutrophiles, tissue detritus. The wall of abscess is represented by an internal pyogenic membrane, layer of granulative tissue and mature connective tissue. Well-kept hepatic parenchyma is on periphery.

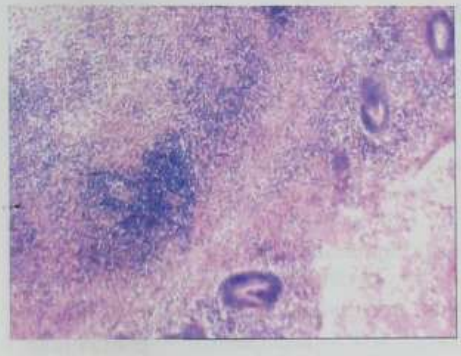


Figure 7 – Flegmonously – ulcerous appendicitis. Staining with haemotoxilin-eosin. Ulcers of mucousa are present. The wall of appendix is along the whole length infiltrated by neutrophiles, swollen.

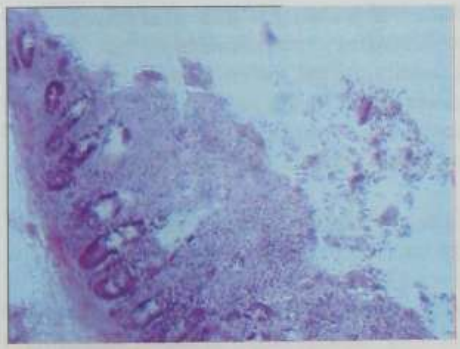


Figure 8 – Fibrinously-ulcerous enteritis. Mucousa is with phenomena of alteration process of necrosis and layings of fibrin are present.

Practical class 9

Topic 10 ***Proliferative inflammation. Specific inflammation. Granulematosis***

Basic matters for self-work

Productive inflammation. Etiology, pathogenesis, cellular cooperations (macrophages, lymphocytes, plasma cells, eosinophils, fibroblasts and others). Morphological features, consequences.

Granulomatous inflammation. Etiology, mechanisms of development, clinical-morphological characteristic and methods of diagnostics, consequences. Cellular kinetics of granulomas. Specific and nonspecific granulomas. Granulomatous diseases.

I Pre-auditorium self-training to practical lesson

Productive (proliferative) inflammation, at which predominance of proliferation of cells with formation of focal or diffuse infiltrates takes place in the area of damage. They can be polymorphocellular, roundcellular (limphocytic-monocitic), macrophagal, epithelioid or plasmocellular. Are found in all tissues.

Three types of it are distinguished: interstitial, with formation of polypuses and pointed condiloms and granulematous.

Interstitial inflammation is characterized by formation of cellular infiltrates in stroma of organ (interstitial myocarditis, interstitial pneumonia, interstitial nephrite). Progress of it can be acute (rheumatism, glomerulonephritis) or chronic. Chronic progress is ended in development of focal or diffuse sclerosis (cardiosclerosis). New growth connective tissue sometimes is undergone dystrophy (hyalinosis). If it is gone with structural alteration of organ (regenerative nodes,

bronchoectasises) and its deformation, then they say about sclerosis.

Productive inflammation with formation of polypuses and pointed condyloms is characterized by simultaneous drawing stroma and epithelium into inflammatory process.

Polypuses grow in the places, where glandular epithelium (stomach, intestine) is situated. Stratified flat epithelium which is placed near prismatic (anus, genitals) in reply to the permanent irritation at a gonorrhoea or syphilis proliferates, forming together with stroma protuberances which are named condyloms.

Granulematous inflammation is the special form of productive inflammation, which develops in reply to persistent irritant of organic or inorganic, often immune nature and is morphologically expressed in forming cellular accumulations (granulomas) of macrophages and their derivative the most frequent granulematous inflammation has chronic progress and very rarely is acute, for example, at spotter fever, rabies (hydrophobia). There phases of granulomas formation are marked out:

Accumulation in foci of damage of young mononuclear cells.

Their transformation into macrophages.

Forming of mature granuloma.

Depending on reactivity of organism three types of tissue reaction in granulomas are observed productive, exudative and alterative productive reaction with formation of resistance of organism. Such granulomas more frequently are completed by scarring. Alterative-productive and exudative-productive reactions prevail when granuloma is formed in weakened organism.

Connected with intensive exudative and emigrant processes it is pierced by plasma proteins polymorphonuclear leucocytes and is undergone necrosis.

Granulematous inflammation		
Non-specific		Specific
Acute	Chronic	Tuberculosis
Enteric fever (typhoid)	Rheumatism	Syphilis
Spotted	Brucellosis	Leprosy
Rabies (hydrophobia)	Tularemia	Rhinoscleroma
	Sarcoidosis	Glanders

Macroscopically granulomas have sizes from barely perceptible by eye nodes to tumular formations (syphilis, tuberculosis). At presence of necrosis they are yellow, at its absence – grey. Granulomas are formed around vessels or alongside them. The damaged vascular wall and mesenchimal cells are the basic components of node.

At a number of diseases (tuberculosis, syphilis, scleroma, leprosy, glanders) granulomas assume specific structural cellular features. In such cases after the whole complex of specific morphologic features it is possible with a certain extent of authenticity to define etiology of disease. Such granulomas are named specific.

Morphological signs of specific **granulomas at tuberculosis**: presence of epithelioid cells, lymphocytes, single plasmocytes, giant Pirogov-Langhans' cells, necrosis in a center.

Morphological signs of specific **granulomas at syphilis**: presence of epithelioid cells, lymphocytes, big number of plasmocytes, giant Pirogov-Langhans' cells, vasculitises, necrosis in a center.

Morphological signs of specific **granulomas at leprosy**: presence of epithelioid cells, lymphocytes, big number of plasmocytes, giant Virhovs' cells, fibroblasts.

Morphological signs of specific **granulomas at glanders**: presence of epithelioid cells, neutrophiles, microabscesses, necrosis with kariorrhexis, granulative tissue.

Morphological signs of specific **granulomas at rhinoscleroma**: presence of epithelioid cells, lymphocytes, big number of plasmocytes, giant Mikulichs' cells, hyaline spheres.

In granulomas at rhinoscleroma light, with foamy cytoplasm and presence of pathogene Mikulichs' cells are founded. In leprosy granuloma there are Virhovs' cells, in which clepsiella Gansen are founded.

Accumulations of polymorphonuclear leucocytes with the phenomena of kariorrhexis are the specific signs of glanders granuloma, are from histiocytes and epithelioid cells is formed around glanders granulomas. Structure of tubercular and syphilitic granulomas is very similar: necrosis, bank of epithelioid cells, accumulation of lymphocytes and Pirogov-Langhans' cells. But in syphilitic granulomas plasmocytes prevail and necrosis always develops around vessels.

II Algorithm of the practical part of lesson

To learn and be able to describe orally macropreparations in the Chair macromuseum.

1 *Miliary pulmonary tuberculosis*. Numerous white colour nodules are seen on the crimson backgrownd of cut of the lung. White colour of granuloma is stipulated by presence of caseous (curdled) necrosis in the centre. Term "miliary" means millet-like. If granulomi are of equal size, that is acute miliar tuberculosis. It means that granulomi developed at the same time. At chronic granulomi are of different sizes. The new ones are big, other, on the different stages of sclerosis, are smaller.

2 *Solitary gumma of liver*. Densed grey colour node, as hen's egg in size is in liver tissue. Coliquous necrosis is in its center.

Necrotic masses are viscid, as though gum(glue), therefore the name is "gumma"

3 *Echinococcus of the liver*. Tumour – like dense node which has cellular structure is seen in the thickness of organ. Node consists of cicatricely connective tissue. Small chitinous blisters of parasite are founded in cells. What is the type of inflammation in this preparation?

4 *Polyposis of small intestine*. Polyps from a pea to a kidney bean, which sit on a thin leg are seen on the surface of mucousa. What is the type of inflammation in this case?

To learn micropreparations from a theme and be able to draw the essence of pathological process with proper designations

1 *Tubercular lymphadenitis*. Preparation is stained with haemotoxilin – eosin. Tissue of lymphatic node is almost fully replaced by pink homogenous mass – curdled necrosis which is bounded from surrounding lymphoidic tissue by the bank of perifocal inflammation. Epithelioid cells, lymphocytes and giant Pirogov – Langhans' cells are revealed in the last. Designate: 1-curdled necrosis,

2-epithelioid cells, 3-lumphocytes, 4-giant Pirogov – Langhans' cells.

2 *Tubercular granulomi of lungs* (miliar pulmonary tuberculosis). Preparation is stained with haemotoxilin – eosin. Tubercular humps are seen in pulmonary tissue: caseous necrosis is represented by homogenous pink unnuclear mass, cellular bank is on periphery (nuclei are stained in a dark-blue colour). At the large magnifying single oval nuclei are seen, epithelioid cells are of some greater sizes and more poorly stained. Small round intensively stained nuclei (lymphocytes) prevail. In granulative bank of some tubercular humps at small magnifying giant Pirogov – Langhans' cells (large multinuclear cells) are seen. Their cytoplasm is stained in intensively rose colour, nuclei are round, hyperchromic, placed on periphery as

a half moon or ring, sometimes at the centre of the cell, number of nuclei is from 3 to 20 and more. Caseous necrosis prevails in tubercular humps, perifocal reaction is expressed poorly, that testify low resistance of the organism. Tubercular humps are numerous, they often merge together. In addition, extended small bronchi, filed by serous exudates with admixture of cracked epithelium are seen in lungs. Separate bronchioli are quite or partly deprived mucosa, and in clearance of alveoli there is serous exudates (homogenous light-pink), that is exudative reaction take place vessels are plethoric. Designate: 1-caseous necrosis, 2-epithelioid cells, 3-lymphocytes, 4-giant Pirogov – Langhans' cells.

3 *Mesaortitis in Syphilis*. Preparation is stained with picrofuscin. There is an inflammatory process, which spreads from the side of intimae and adventitia on a middle layer, in the wall of aorta. Accumulation of lymphoid, plasmatic and giant cells of the Pirogov – Langhans' type takes place. An inflammatory process destroys elastic fibers of middle layer. Designate: 1-intimae, 2-adventitia, 3-inflammatory infiltrate.

4 *Solitary gumma of liver at syphilis*. Numerous massive haemorrhages, areas of necrotic changes in hepatocytes, about what disappearance of nuclei in hepatic cells testifies, are marked in parenchyma of liver. There are places of substitution of parenchyma by connective tissue, and also infiltration by lymphocytes, plasmocytes, macrophages areas of necrosis take place near vessels.

Designate: 1-necrosis of parenchyma, 2-lymphocytic infiltration, 3-wall of gumma, 4-hepatocytes.

5 *Scleroma's granuloma*. Excrescence of distinctive dense granulative tissue, represented by vascular component and numerous cellular elements is seen on preparation : accumulation of plasmatic cells with the admixtures of two-bit of fusiform epithelioid elements. Among these cells there are typical large cells with a transparent cytoplasm the so called

Mikulichs' cells. Somewhere in granulative tissue so called Russels' bodies are exposed – hyaline bullets of pink colour, which are placed by small groups. Part of them is in cells, more lie freely between cells. Designate: 1-Mikulichs' cells, 2-bodies of Russel, 3-Granulative tissue.

6 *Cardiosclerosis*. Preparation is stained with haemotoxilin-eosin. Diffuse excrescence of connective tissue, infiltration by histiocytes is seen in preparation, separate cardiomyocytes are hypertrophied, other atrophied. Designate: 1-areas of excrescence of connective tissue, 2-cellular infiltration, 3-hypertrophied cardiomyocytes.

7 *Micronodular cirrhosis of liver*. Preparation is stained with haemotoxilin-eosin. Expрescence of connective tissue is seen in tissue of liver, that stipulates violation of lobular structure of liver, infiltration by histiocytes, separate hepatocytes proliferate with formation of regenerative nodes.

Designate: 1-areas of excrescence of connective tissue, 2-cellular infiltration, 3-regenerative nodes of hepatocytes.

Situation tasks

1 At a tubercular spondilitis patient a tumular formation to 7 cm in diameter, with fluctuation appeared on the lateral surface of thigh. The formation does not hurt. Skin above it is unchanged. Make your diagnosis.

2 At the diagnostic express-biopsy of lymphnode of the patient with the cancer of lungs curdled necrosis, surrounded by epithelioid cells, lymphocytes and single multinuclear giant cells. Make your diagnosis.

3 Little dense nodes exposed in a skin of a patient. At histological analysis accumulation of epithelioid cells, Virhovs' cells, and lymphocytes is exposed. Make your diagnosis.

Answers for situation tasks

1 Accumulation
2 Exposed changes are specific for tuberculosis
3 Tuberculoid form of leprosy.

Tests

1 Acute adrenal insufficiency developed during surgery of strumectomia, patient died from it. At examination of thyroid Bazeds' goiter was exposed, in adrenals there were haemorrhages. Histologically, in a heart and liver: edema of stroma, insignificant perivascular lymphoplasmocytic infiltration, intracellular edema. What inflammation takes place in a heart in a liver?
a) serous, b) fibrinous, c) suppurative, d) haemorrhagic,
e) catarrhal.
2 A patient with a chronic pyelonephritis died from chronic kidney insuffiency. In life time phenomena of "noise of friction of pericardium" is marked at auscultation. It is exposed on dissection that epicardium is dim, rough as though covered by a hair cover. What pericarditis after character of exudates takes place?
a) Festering, b) putrid, c) serous, d) croupous, e) diphteric.
3 Boy of 5 years old, in few minutes after the sting of bee has sharp pain, swelling and reddening appeared in the region of right hand, temperature rose locally. What morphological substratum lies in basis of the changes?
a) purulent inflammation, b) fibrinous inflammation,
c) haemorrhagic inflammation, d)serous inflammation,
e) granulomatous inflammation.
4 At dissection of body of girl, died of asphyxia, it is exposed that mucous of trachea and bronchial tubes is covered by white-grey pseudomembrane which is not densely connected with inferior tissues and is easily taken off by pincers. Clearance of segmental bronchi is filled with loose masses of

white-grey colour. What tracheobronchitis after character of exudates is marked at dissection?
a) catarrhal, b) croupous, c) diphteric, d) purulent, e) putrid.
5 At examination of tonsils of patient with acute leucosis necrosis of mucous with formation of defects and laying of brownish-green amorphous masses are marked. Necrotic changed tonsils are black, pastous, bleed. An unpleasant smell is felt. Specify the form of quinsy.
a) catarrhal, b) purulent, c) fibrinous, d) gangrenous,
e) ulcerative-pseudomembranous.
6 Gastrobiopsy was performed at patient with chronic helicobacter-associated gastritis. Thinning of mucous, transformation of integumentary cylinder epithelium into cube, decrease of amount of glands, excrescence of connective tissue and diffuse lympho-plasmocytic and neutrophiles infiltration is marked histological. Specify morphological form of inflammation.
a) serous catarrh, b) mucous catarrh, c) putrid catarrh,
d) hypertrophy catarrh, e) atrophic catarrh .
7 Child, after a quinsy has sharply enlarged lymphatic nodes: paratracheal, bifurcational, neck. At microscopic examination of neck lymphatic node foci of necrosis, limited by lymphocytes, epithelioid cells and Pirogov-landhans' cells are exposured. Specify the most reliable pathology.
a) sarcoidosis, b) rhinoscleroma, c) tuberculosis, d) glanders,
e) syphilis.
8 Girl in age 1 year 8 months died of pneumonia. On a section – upper lobe of left lung densed, visceral pleura is covered by thin coating of fibrin, surface of cut of affected part is small-granulated, grey colour, pieces of lung sink in water. Microscopically – in clearance of alveoli there is fibrinous exudate with the admixtures of plenty of neutrophiles leucocytes. Specify, what pneumonia led to childs death.
a) festering, b) croupous, c) necrotic, d) putrid,

e) haemorrhagic.

9 Granuloma, in which cellular infiltrate of epithelioid cells, plasmocytes lymphocytes, single giant Pirogov-langhans' cells took place around focus of necrosis was exposed at the biopsy of inguinal lymphatic node. The productive cellular reaction spreads alongside vessels. Make your diagnosis.

a) tuberculosis, b)leprosy, c)syphilis, d) glanders,

e) hydrophobia (rabies).

10 Excrescences appeared on the back wall of nasopharinx of 3 years old child which is sick in chronic catarrh of mucous of upper respiratory tracts. Histologically: excrescences are built of granulative tissue on different stages of ripening, single glands with thick infiltration by neutrophiles and lymphocytes. Make your diagnosis.

a) papilloma, b) inflammatory polypus, c) glandular polypus, d) stromal polypus, e) tonsillitis.

Answers for the tests

1) a; 2) d; 3) d; 4) b; 5) d; 6) e; 7) c; 8) b; 9) c; 10) b.

Illustrations to theme

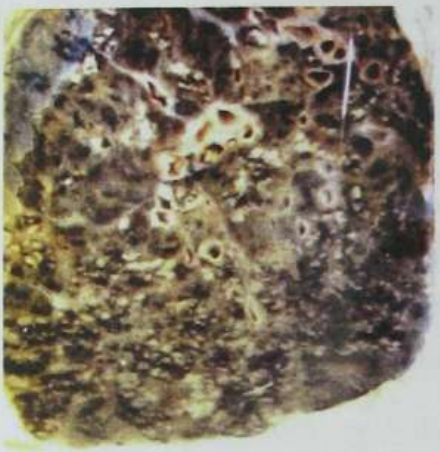


Figure 1 – *Miliary pulmonary tuberculosis.* Numerous nodes of white color of millet grain size are seen on dark red ground of section. White color of tuberculous granuloma is caused by caseous (caseation) necrosis presence in the center. The word "miliary" means millet-like. In case granulomas are of same size it evidences acute miliary tuberculosis, that is granulomas developed simultaneously. At chronic one glanulomas are of various size. Fresh are of bigger size, those which are on various stages of sclerosis are of smaller size.

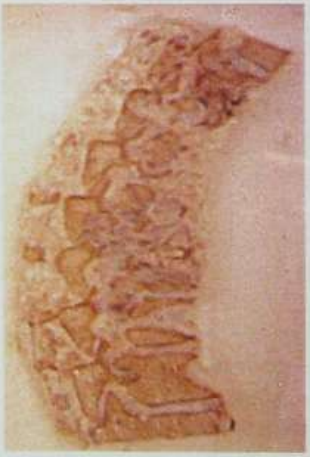


Figure 2 – *Tuberculous osteomyelitis.* Tuberculous process injured vertebral bodies causing kyphosis progress.

Figure 3 – *Ascending portion of aorta aneurysm.* Intima is shrunken, resembles shagreen leather. The most like cause of aneurysm is syphilitic mesaarthritis.

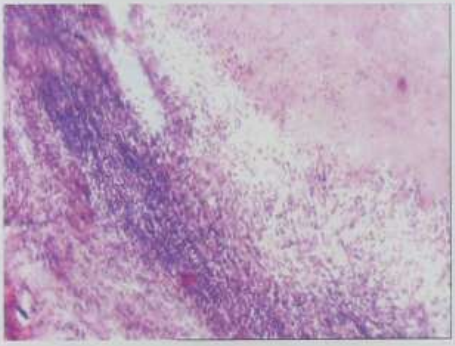


Figure 4 – *Tuberculors lymphadenitis.* Specimen is colored with hematoxylin and eosin. Lymphatic node tissue practically completely is substituted with red homogenous mass – caseous necrosis, which is separated from surrounding lymphoid tissue with perifocal inflammation bank. In the latter epithelioid cells, lymphocytes are observed.

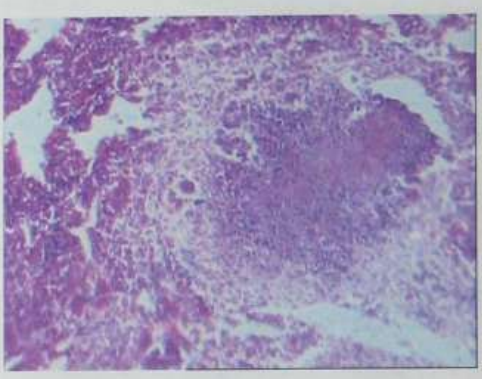


Figure 5 – *Tuberculous granulomas of lung (miliary pulmonary tuberculosis).* Specimen is colored with hematoxylin - eosin. In pulmonary tissue tuberculous gibbus are seen: caseous necrosis in the center is represented with homogenous red nuclei-free mass, cellular bank is on periphery. Small instensively colored nuclei of round shape – lymphocytes prevail. In tuberculous gibbus granulation bank Pirogov-Langerhans' giant cells are seen. Caseous nectosis prevails in tuberculous gibbus, perifocal productive reaction is poorly expressed.

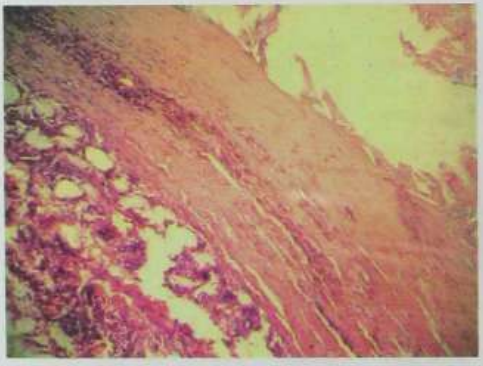


Figure 6 – *Syphilitic mesaarthritis.* Specimen is colored with picrofuchsin. Inflammatory process is observed in aorta wall, which extends from intima side and adventitia on middle membrane. Lymphoid, plasmatic cells accumulation takes place.

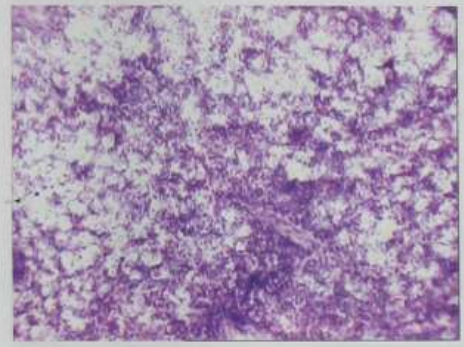


Figure 7 – *Rhinoscleroma*. In specimen it is seen specific hard granulation tissue excrescence, which is represented with vascular component and numerous cellular elements: aggregation of plasma cells with admixture of minor quantity of spindle-shaped epithelioid elements. Among these cells typical large cells with transparent cytoplasm are met, so called Mikulich' cells.

CONTENTS

Навчальне видання

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