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SHORT COURSE OF GENERAL PATHOLOGY

Part 2

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В93 Короткий курс загальної патоморфології:
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Посібник містить короткий виклад теоретичн матеріалу основних тем загальної патоморфології, що відпові програмі, затвердженій МОЗ України і ЦМК з вищої медич освіти. У посібнику представлені цифрові мікро-та мак фотознімки, викладений їх опис та наведені приклади тестови ситуаційних завдань до кожного заняття.

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

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Content module 3
Immunopathologic processes

Specific aims of module:

- *To explain structural organization of immune system and immune system central and peripheral organs' functioning mechanisms.*
- *To analyze morpho-functional changes of thymus gland under its inherited or acquired pathology.*
- *To explain mechanisms of immune answer to antigen action.*
- *To interpret cell immunity mechanisms.*
- *To interpret immune immunity mechanisms.*
- *To interpret mechanisms of development and morphologic changes under hypersensitivity reaction.*
- *To explain autoimmunization mechanisms.*
- *To analyze clinical-pathologic manifestations of autoimmune diseases.*
- *To explain mechanisms of development and morphologic characteristic of primary and secondary immune inefficiency.*
- *To interpret morphologic manifestations of primary and secondary immune deficiency.*
- *To interpret morphologic manifestations of graft rejection reactions, graft-versus-host disease, reactions on incompatible blood transfusion.*

Theme 11 Immune system pathomorphology. Hypersensitivity reactions and mechanisms

Basic matters for self-training:

Structural-functional organization of immune system: idea of immunocytes and their functions, central and peripheral organs of nervous system structure and functioning.

Thymus (thymus gland) in norm: embryogenesis, morpho-functional characteristics. Thymus diseases. Idea of thymus hyperplasia, thymitis. Thymus changes under immunogenesis failure. Age and accidental involution (transformation). Congenital diseases of thymus: hypoplasia, dysplasia, thymomegalia.

Organism's immune response on antigen action: types and phases of normal immune response. Immunological tolerance: biological significance, mechanisms, factors influencing tolerance induction.

Cellular grounds of immune response. Primary lymphoid organs: thymus, bone marrow. Cells participating in immune response (nomenclature, morphology, functions). Secondary lymphoid organs: lymph glands,spleen, lymphadenoids in mucus tunics. Morphological characteristics, functions. Antigens, ways of their coming to organism. Tissue-specific antigens.

Humoral immunity. Antibody: structure, classes, physical and biological features of immunoglobulin. Regulation of antibodies' generation. Primary and secondary immune response.

Cell-bound immunity. T- lymphocytes (memory cells): functions, subdivisions, classes. Antigen recognition, T-lymphocytes activation, cytotoxic T-cells.

Immunological hyperresponsiveness: definition, classification. Pathogenesis and morphologic characteristic of immediate-type reaction. Pathogenesis and morphologic characteristic of antibody-mediated hyperresponsiveness (destructive and cytokinetic reactions). Pathogenesis and morphologic characteristic of immunocoplex hyperresponsiveness. Pathogenesis and morphologic characteristic of delayed hyperresponsiveness.

Theme 12 Autoimmune diseases. Immunodeficiency states

Basic matters for self-training:

Autoimmune diseases: definition, autoimmunization mechanisms, classification and general clinical-morphological characteristics.

Immunodeficiency: definition, mechanisms of development, general clinical-morphological characteristics of primary and secondary immunodeficiency.

Amyloidosis: structure, physicochemical properties, methods of amyloidosis diagnosis, theories of etiology and pathogenesis, principles of classification. Role of immunologic failures in amyloidosis progress. Systemic amyloidosis: (primary, secondary): morphologic characteristics, clinical implications. Local and endocrine amyloidosis. Amyloid of insenescence: morphologic characteristic, clinical implication.

Immunodeficiency syndromes. Immunodeficiency: idea, etiology, classification.

Primary immunodeficiencies: definition, classification, methods of diagnosis. Clinicopathologic characteristics of primary immunodeficiencies. Causes of death.

Secondary (acquired) immunodeficiencies: definition, etiology, classification.

Acquired immune deficiency syndrome (AIDS): epidemiology, ways of transmission, etiology. Pathogenesis and morphogenesis. Clinicopathologic characteristics: AIDS-associated diseases, opportunistic infections, tumors. Complications, causes of death.

Iatrogenic interventions into immune system. Short characteristic of graft reject phenomena, 'graft-versus-host" reactions, reaction to incompatible blood transfusion.

Practical class 10. Theme: Immunopathologic processes

Topicality of theme: immune system pathology is morphologic ground of rather big group of immune pathologic diseases. Clinical aspects of diseases will be different depending on its localization. However morphologic regularities of their progress are similar. Their knowledge makes it possible to evaluate in correct manner course and consequences of diseases accompanied by immune pathologic processes.

Aim: to learn immune system pathology reasons, classification and consequences for clinical picture.

Task: 1) To repeat immune system structure and functions and its components interaction.

2) To learn morphologic changes in immune system under antigen stimulation.

3) To know immune pathologic processes definitions and classification as well as causes and morphogenesis.

4) To know immunodeficiency conditions and autoimmune diseases classification and morphology.

5) To be able to differentiate clinicopathologic forms of various types of hypersensitivity reactions and interpret their implications.

I Pre-auditorium self-training for practical lesson

Structural-functional organization of immune system, cellular grounds of immune response

Immune system provides organism protection of infection agents and biologic substances with antigenic features. It includes the following peripheral organs: lymph nodes, pharyngeal tonsils, lymph follicles in intestine wall, lymphocytes in peripheral gland, spleen and central organs – thymus, marrow. Immune protection is done by lymphocytes

(immunocytes) forming in the marrow from lymphoid embryo. Two types of immune response are differentiated: cellular and humoral. ***Cellular immunity*** is provided by T-lymphocytes (T-killers, T-suppressors, T-helpers). They are formed in thymus. Significant role in cellular immunity realization belongs to cytotoxic cells (T-killers) carrying out direct injury of cells by their lysis. Besides that T-cells synthesize lymphokines (cytokines): interleukins, interferon and others which regulate macrophages and other lymphocytes function. Important role in this process is given to T-helpers (CD4) and T-suppressors (CD8). ***Humoral immunity*** is carried out by B- lymphocytes, which transform into plasmacytes and synthesize immunoglobulin (antibodies). Immunoglobulin has antigenic specificity and differs from each other by amino acid composition. Several classes of antibodies are differentiated: IgA, IgG, IgM, IgD, IgE. Immunoglobulin molecules consist of light and heavy chains. Each chain has permanent and temporary chains comprising corresponding receptors to antigens providing their contact and annihilation. Immune response to antigen could be primary and secondary. Primary response occurs in case immune system first contact with antigen. It is realized in several days while B-lymphocytes transform in plasma cells and start to synthesize IgM. Secondary response occurs after immune system repeated contact with antigen and develops fast (in 2-3 days) with IgG assistance.

Thymus disease

The most often *thymus disease* shows itself with inherited pathology: aplasia, hypo- and dysplasia, atrophy, thymomegalia as well as accidental involution, hyperplasia from lymphoid elements or neoplastic processes. Under aplasia, hypo- and dysplasia of thymus, as well as under it senile accidental involution or atrophy cellular or combined

immune deficiency develops quite often. Thymomegalia (inherited or acquired) is also accompanied with immunodeficiency state progress causing severity of infection diseases course and sometimes even fatal consequences of them. Thymus hyperplasia from lymphoid elements is characteristic for autoimmune diseases.

Immune response of the organism for antigen action

Immune response of organism for antigen action is done by organism's lymphoid system and is characterized with specificity (action is directed on specific antigen), potentiation (action enhancement under repeated introduction of antigen) and immunological memory (recognize antigen in considerable time period between its penetration into organism). Phases of immune response: lymphocytate antigen recognition, T- and B- lymphocytes transformation and proliferation, Types of immune response are as follows: primary and secondary. Primary immune response occurs under the first time meeting with specific antigen. At it IgM is produced, further on IgG appear. Secondary immune response occurs under repeated antigen getting into organism and is accompanied with IgG accumulation. Immune tolerance means immune system's insusceptibility to own tissues which are antigens, this is natural tolerance developing in fetal life.

Immunological hypersensitivity

Immunological hypersensitivity is one of the evidences of dysimmunity, occurring in sensitized organism and is connected with humoral and cellular immunity. Immediate and delayed type hypersensitivity are differentiated which are morphologically shown with acute or chronic immune

inflammation. Reactions of hypersensitivity could progress by four types of scenarios.

Hypersensitivity of the Ist (immediate) type develops at participation of tissue basophils and blood basophils which produce IgE in case antigen (allergen) getting into organism. This reaction takes place at eczemas, dermatitis, allergic rhinitis and gastroenteritis, atopic asthma – local manifestations, anaphylactic reactions and shock - systemic manifestations. Immediate type hypersensitivity reaction progresses very fast, at it alterative and vascular-exudative changes prevail: plasma escape, mucoid and firbrinoid swelling, fibrinoid necrosis, accumulation of coarsely dispersed proteins, fibrin, immune complexes, cellular elements – erythrocytes, neutrophils, eosinophils. These are so called reagin reactions in which allergic antibodies or reagins participate, fixing on tissue basophiles membrane and blood basophiles. In case repeated antigen coming these activated cells separate vasoactive substances – histamine and various ferments, which starts bloodstream exudative reaction. In the place of this reaction development intensive eosinophilic infiltration is found which is able to reduce allergic response.

Hypersensitivity of the IInd type (antibody-mediated hypersensitivity) develops under antibody (IgG or IgM) interaction with antigen on cells surface, with their further damage by lysis, phagocytosis by microphages, T-lymphocytes cellular cytotoxicity, cells' function change. An example of these reactions could be reactions with erythrocytes destruction after hemotransfusion, hemolytic disease of neonates, reactions with neutrophils', thrombocytes', etc. destruction.

Hypersensitivity of the IIIrd type (immune complex hypersensitivity) develops in the result of immune complexes formation after antibody and antigen interaction, causing complement activation and acute inflammation and necrosis

progress. Immune complex hypersensitivity could be systemic - serum sickness, erythematosus or local – Arthus phenomenon after repeated antigen introduction at vaccination.

Hypersensitivity of the IVth type (delayed-type hypersensitivity) is realized under participation of cells - sensitized lymphocytes and macrophages, which could behave cytotoxically directly (T-killers) or secret lymphoquins. This reaction develops in 24-72 hours after antigen introduction in sensitized organism and is characterized with granulomatous inflammation with caseous necrosis. . Clinicopathologic manifestations of delayed-type hypersensitivity include tuberculine-type reaction in skin for antigen introduction, contact dermatitis, autoimmune diseases, immunity under viral, fungal and some bacterial infections (tuberculosis. brucellosis).

Autoimmune diseases

Autoimmune diseases occur in case disorder of immune system natural tolerance to own antigens, which is formed in embrional period. Autoimmunization is formed, in the other words autoantibodies, circulating immune complexes aggression, which contain autoantibodies to antigens of the own cells of organism. In autoimmune diseases development significant role is assigned chronic viral infections, radiation, genetic abnormalities. At it a number of cells damage mechanisms are differentiated occurring under humoral or cellular hypersensitivity (types II, III and IV) immune system dysfunction – T-lymphocytes and antiidiotype antibodies suppressive activity decrease. Autoimmune diseases could be *organ non-specific* (Hashimoto's thyroiditis, inculineresistant diabetes, disseminated sclerosis, encephalomyelitis, polyneuritis, aspermatogenesis, etc.) and *organ specific* or systemic diseases (systemic lupus erythematosus, atrophic arthritis, dermatomyositis and others). Organ specific

autoimmune diseases develop in connection with immunologic separated organs immune barriers damage (thyroid gland, cerebrum, nerves, testicles, adrenal glands, eyes). Antibodies and sensibilized lymphocytes are formed for unchanged antigens of these organs, morphologic changes develop, characteristic for delayed-type hypersensitivity reaction: tissue is subject to infiltration with lymphocytes, parenchyma dies, conjunctive tissue expands. Lymphoid system failure to control immune homeostasis of organism is characteristic for autoimmune diseases. Most of autoimmune diseases have family inclination (systemic lupus erythematosus, Hashimoto's thyroiditis and others) or are connected with specific HLA antibodies.

Autoimmune diseases of intermediate type are also differentiated: myasthenia gravis, diabetes mellitus of the 1st type, thyrotoxicosis, Goodpasture's syndrome, Sjogren's sicca syndrome, etc. Besides that the following diseases with autoimmune disorders are differentiated: autoantigens appearance at them occurs as the result of tissues and organs antigen features change, tissue proteins denaturation: burns, irradiation, traumas, chronic inflammations, viral infections.

Immunologic deficiency is manifested with immunodeficiency state progress, which could be primary in the result of underdevelopment (hypoplasia, aplasia) of central or peripheral organs of immunogenesis – congenital or heritable immunodeficiencies and secondary (acquired) – occur under sicknesses and other exogenous influences. *Primary (congenital) immune deficiencies* are manifested with cells humoral immunity deficiency or combined immunodeficiency. The most investigated are the following types of congenital immune deficiencies: severe combined immunodeficiency, hypoplasia of thymus (DayJorge syndrome), congenital agamoglobulinemia (Brutton's disease), isolated IgA deficit, complement deficit, Nezelof-type thymic dysplasia, immune deficiencies connected with heritable diseases (Wiskott-Aldrich

syndrome, ataxy- telangiectasia Lui-Barre), etc. Clinicopathological manifestations of primary immune deficiencies often are presence of thymus congenital anomalies, spleen, lymphatic nodes underdevelopment. Aplasia, hypoplasia of thymus is accompanied with cellular immunity deficiency or combined immunodeficiency. At aplasia (agenesia) thymus is absent completely, at hypoplasia it is of smaller size, division into cortex and medullary substance is abnormal, lymphocytes quantity is sharply reduced. In spleen follicles size is noticeably reduced, light centers and plasma cells are absent. In lymphatic nodes follicles and cortex layer (B-dependent zones) are absent, only pericortex layer (T-dependent zone) is kept. The course of patients' death is infection diseases (purulent infections, tuberculosis, sepsis, etc.) progress and organism inability to struggle against microorganisms.

Secondary (acquired)immunodeficiences are met rather often at various diseases or drug therapy. Acquired immunodeficineces progress could be caused by infection diseases, leucosis, malignant lymphomas (lymphogranulomatosis), thymomas, sarcoidosis. *Yatrogenic immune deficiencies* often occur after radiation therapy, administration of corticosteroids, immunosuppressants, antilymphocytic serum, thymectomy, thoracic duct, drainage. At various organs and tissues transplantation graft-versus-host reaction often develops. At that graft antigens induce specific antibodies creation and sensibilized erythrocytes production, infiltrating graft and causing its destruction and rejection by the way of direct cytotoxic action or by the way of lymphoquins secretion. Graft immunity manifestations are similar to delayed-type hypersensitivity reaction. In these cases immunosuppressive agents ought to be used. An example of yatrogenic immune reactions could be reactions of " graft-versus-host". These statuses occur in case introduction into recipient's suffering from immunodeficiency body big amount of HLA-incompatible and

viable lymphocytes, for example at bone marrow transplantation or intestine transplantation, or at lymphocytes transfusion together with blood. Diseases is manifested with skin rash, diarrhea, liver impairment, anemia, neutropenia.

Acquired immune deficiency syndrome (AIDS)

Among secondary immune deficiencies the most important one in all the countries at the moment is *acquired immune deficiency syndrome (AIDS)*. This is chronic, rarely – acute disease with prevailing injury of immunogenesis organs and blood cells, the final stage of which is complete oppression of immune system. *Etiology* - T- lymphotropic virus of human immunodeficiency (HIV). In the recent years this virus was defined as HIV - 2 (African AIDS virus), in Japan HIV-3 was also revealed. Because of infinite inclination to mutation, there are various viral strains. Virus contains two RNA molecules – virus genome and reversible transcriptase. On the capsule surface there are two glycoproteins providing virus binding with cells which on their surface carry СД4+ antigen. These cells include as follows: Т-СД4+ lymphocytes (helpers), В-lymphocytes, which have СД4+ receptors, monocytes, macrophages, microglia, dendritic cells, endotheliocytes.

Epidemiology. AIDS expansion is of pandemic character. Approximately every 8-10 months amount of those ill with AIDS doubles, half of them die in 3 years period. Most of them are found in USA, West European countries, Africa. In certain regions of Central Africa up to 60 % of adults are infected. In Ukraine by 01.04.1998 thirty six thousand of HIV-infected were registered. The source of infection is sick person - virus carrier. The highest concentration of virus is found in blood, sperm, cerebrospinal fluid, it is lower in saliva, tears, in cervical and vaginal secretions of sick people. *Three ways of infecting* were proved: sexual, parenteral (by the way of virus

introduction with blood preparations or with contaminated instruments utilization), transplacental and with mother's milk. According to the data of American Center of Sickness Rate Control risk of medical employees infection in case contaminated syringe needle prick or in case cut equals to 4,7:1000.

Pathogenesis. In human blood virus hitches cells with СД4+, penetrates inside with receptor and builds in cell's genetic code. By the way of reversible transcriptase virus codes production of particles similar to it until cell dies. Than it occupies new cells with СД4+ receptors. In СД4+ lymphocytes-helpers HIV could stay in latent state for indefinitely long time. Cells with immunodeficiency virus on their surface stimulate immune response by the way of HIV-antibodies and cytotoxical lymphocytes production which cause both damaged and undamaged T-lymphocytes-helpers' cytolysis. All that cause cellular and humoral immunity decrease which in the final of disease ends with complete loss of delayed-type hypersensitivity for various antigens.

In AIDS clinical course four periods are differentiated: incubation period (asymptomatic carrier), lymphadenopathyc syndrome (LAS), pre-AIDS (syndrome, associated with AIDS), acquired immune deficiency syndrome (AIDS).

Incubation period could last from 6 months up to 12 years and longer. As a rule there are no symptoms manifested at this stage. Anti-HIV – antibodies are found in blood. Various factors reducing organism resistance could provoke clinical symptoms. Approximately in 20 % cases acute signs of primary AIDS infection appear in 3-6 weeks from the moment of contamination. Major signs of disease beginning is high and long-term fever (38-39 C) with lymphatic nodes injury, more often it is neck lymphatic nodes enlargement, skin rash appearance and mononucleosis syndrome. Signs frequency:

fever 92%, myalgia – 83 %, skin rash – 50 %, mononucleosis and plasmacytosis in blood formula – 70 %.

Period of persistent generalized lymphadenopathy is characterized with persistent enlargement of various groups of lymphatic nodes. Morphologically lymphatic nodes follicles increase is revealed. Period duration is 3-5 years.

Pre-AIDS (syndrome associated with AIDS) progresses on the ground of moderate immunodeficiency and is characterized with body weight decrease up to 20 %, development of fever, diarrhea, progressive lymphadenopathy, recurring acute viral respiratory infections.

Period of acquired immune deficiency syndrome (AIDS) is accompanied with considerable loss of body weight, up to cachexia, sharp immunity depression causing opportunistic infections and malignant tumors (lymphoma, Kaposi's sarcoma) progress. AIDS manifestations are really various but they are grouped in three main syndromes – lymphatic nodes injury, lesions caused by opportunistic infections, malignant tumors progress.

Changes in lymphatic nodes schematically are manifested in three stages.

Stage of follicular hyperplasia is characterized with follicles size increase with large light centers. Peripheral lymphocytic crown surrounding follicles is narrow or completely absent, medullary tension bars are hard to determine. *Stage of diffuse hyperplasia similar to angioimmuneblast lymphadenopathy* is characterized with lymphatic nodes usual structure loss. Histologically vessels prevail in lymphatic node, the amount of cells is small, their composition is polymorphous: round of irregular shape lymphocytes, plasmacytes, immunoblasts, eosinophils, tissue basophils. Follicles atrophied, little. Sometimes follicle centers' hyalinosis is found. *Stage of lymphoid emaciation.* Lymphatic nodes are represented with stroma only. Sinuses are dilates,

filled with mononucleate cells. Lymphatic nodes and diminished, sclerosed, amount of lymphoid elements is not big, plasmacytes and immunoblasts are found. Similar changes are observed in spleen, thymus gland, lymphoid apparatus of bowel.

Injuries caused by opportunistic infections are various in their localization and nature: bacterial, fungi, parasitogenic, viral. Opportunistic are called infections caused by conditionally-pathogenic causative agents contamination with which healthy people does not accompanied with pathologic changes. At AIDS opportunistic infections are characterized with recurrent course, process generalization. Treatment is ineffective. Interstitial pneumonia, esophagitis, gastroenterocolitis, encephalitis, meningitis, abscess, sepsis.

Malignant tumors at AIDS are mostly of two types: Kaposi's sarcoma, malignant lymphomas among elderly people. At AIDS there are often early manifestation of disease. Besides cutis mucus tunics, lymphatic nodes are subject to injury, sometimes multiple visceral lesions are observed. Microscopically Kaposi's sarcoma is represented with numerous neoplasms, thin walled vessels localized in random way. Malignant lymphomas injure central nervous system, lymphatic nodes, digestive tract, upper air passages, bone marrow.

AIDS always ends mortally caused by purulent infections, sepsis, tuberculosis or malignant growth progress.

Amyloidosis

Amyloidosis is characterized with abnormal fibrillar protein (F-component) accumulation in tissues which is connected with blood plasma glucoproteins (P – component) with characteristic physics-chemical features. This composite substance is called amyloid-glycoprotein, that is protein with carbohydrates admixture and subject to iodine and sulphuric acid is colored in blue (Virhov's reaction). Amyloid consists of albumines, fibrin, complement, blood plasma globulins, lipids, lipoproteins, calcium salts, acid glycosamineglycanes of main substance - chondroitin sulfate and heparitin sulfate. Fibrillar and globular proteins of amyloid are closely connected with polysaccharides.

Amyloidosis morphogenesis, in accordance with V.V.Serov, goes through a number of stages:

1-stage transformation of reticuloendothelial system cells, plasmacytes and lymphocytes into amyloidoblasts,

2-stage amyloidoblasts' synthesis of amiloid's fibrillar component,

3-stage fibrils aggregation with amyloid framework formation,

4-stage amyloid fibrils combination with plasma components (proteins, glucoproteins, lipids, immune complexes, etc.) and glycosamineglycanes of main substance.

By biochemical structure the following is differentiated:

- AA – amyloidosis (protein is not associated with immunoglobulins) – is observed at secondary amyloidosis and certain forms of hereditary (Maccle-Wells' disease);

- AL - amyloidosis (protein associated with immunoglobulins) – is observed at primary (idiopathic) amyloidosis and secondary one, connected with multiple (plasma cell) myeloma and other monoclonal B-cellular malignant lymphomas (Valdenstrem's disease, heavy-chain

Franklin's disease), this form is of generalized character and is accompanied with heart, vessels, lungs injuries;

- AF – amyloidosis (prealbumin prevails in protein formation) is of hereditary origin and is observed at family amyloidosis with nervous tissue injury;

- ASC – amyloidosis (prealbumin is precursor) is observed among elderly people and is of generalized character.

By its spread amyloidosis could be:

Generalized: primary, secondary, hereditary, senile;

- localized amyloidosis includes tumor like, separate forms of hereditary amyloidosis, cardial, insular, cerebral amyloidosis of elderly people, APUD-amyloidosis, etc. *Localized amyloidosis* is characterized with nodular shape amyloid masses appearance, which are seen microscopically in one organ: lungs, larynx, skin, urinal bladder, tongue. Lymphocytic or plasmacytic infiltration is often observed surrounding amyloid masses being a provement of their immune origin. *Endocryne amyloidosis* is characterized with amiloid masses appearance in endocrine tumors: medullary carcinoma pancreatic islets' tumors, pheochromocytoma, poorly differentiated gastric carcinoma; in islet of Langerhans at II[nd] type diabetes mellitus. *Senile amyloid* is manifested in two variants: - amyloid depositing in the heart (in ventricles or auricle) and lungs, spleen, pancreatic gland of elderly people; - senile cerebral amyloidosis, when amyloid deposits in blood vessel walls and plaques of cerebral cells at Alzheimer's dementia.

By etiology: - primary (idiopathic); - secondary (acquired reactive);

- hereditary (genetic); - senile.

The most often *secondary (acquired) amyloidosis* is observed. It occurs as complication of sicknesses accompanied by tissues decay: chronic abscesses, osteomyelitis, pulmonary tuberculosis, extensive burns, multiple bronchiectasis, chroni

pneumonias, tumors disintegration. Tissues decay products are absorbed in blood, hyper- and disproteinemia develops. During this process first of all discharge organs (kidneys) are littered, second – organs depositing blood (spleen, liver) and third turn – other organs (heart, skeleton muscles, adrenal glands, etc.). This causes intoxication and autoimmunization. In kidney amyloid accumulates in mesangium, capillary walls. *Macroscopically* kidneys enlarge, harden. Organ is pale on section, looks like wax or lard - "lardaceous kidney". In spleen amyloid appears first as homogenous mass around vessels - "sago" spleen, later on in all the pulp – "lardaceous spleen". In heart, skeleton muscles amyloid deposits mostly downstream vessels. *Microscopically* in case hematoxylin and eosin coloration amyloid is represented with amorphous eosinophilic masses, and in case colored with Congo-red (specific coloration of amyloid) amyloid is colored in brick-red color. *Consequence* is unfavorable, the process is irreversible, function of tissue or organ sharply decreases or completely stops, for example, renal insufficiency at renal amyloidosis.

II Algorithm of the practical part of class

To learn and be able to describe macrospecimens in oral form

Amyloidosis of the kidney is characterized by appearance of anomalous fibrilar albumen and formation of composed glycoproteid amyloid in intermediate tissue. Immune disorders in an organism, as a result of which cells begin to synthesize pathological albumen, play considerable role in pathogenesis of development of the noted changes. According to causes and pathogenic mechanisms amyloidosis is divided into: idiopathic (primary), inherited, acquired (secondary), senile and local. This macropreparation illustrates secondary amyloidosis. Kidney is enlarged in size, dense consistency. The surface of

cut has waxen, greasy (lardaceous) colour. Cortical layer is yellow – white colour, thickened. Medullar is pink, with spots. Such kidney has the name "large grey kidney". It is met at chronic purulent processes: chronic abscesses of lung, bronchoectatic disease, osteomyelitis, fibrinousli – cavernous tuberculosis and also in rheumatic diseases, tumour.

2 *Amiloidosis of the spleen.* "Lardaceous" or "sago" spleen is thickened in both cases, howewer in "Lardeceous" spleen amyloid is located in red pulp, giving lardaceous kind to tissue of organ, and in "sago" in follicles, reminding the corn of sago. Specify the reasons of origin of small pathological changes in organ. In what diseases does such pathology appear?

3 *Lupus nephritis.* Kidney is enlarged, pied, with areas of haemorrhage, dense consistency due to excrescence of connective tissue and substitution of parenchimatous structures by it. On cut parenchyma is dim, cortical layer is with tint of grey, medullar layer is cyanotic such changes in liver are expression of reaction of hypersensitiveness of the III type.

4 *Croupous (lobar) pneumonia.* Macropreparation is cut of lung, on which light – grey, smallgranulated dim colour (is conditioned by a presence of plenty of exudates in clearance of alveoli). Parenchyma is seen . it is an example of hyperreaction of parenchyma of lung on invasion of pathogen. Part of lung has crimson colour, and is a bit more dense and more heavy than uninjured areas. The surface of cut has a brownish-red colour and draining as a result of massive infiltration o parenchyma of lungs by the cellular elements of blood with predominance of lymphocytes

5 *Large motley kidney.* It is seen on preparation that kidney i enlarged almost in 1,5 times. It is pied on the surface due t presence of greyish – yellow colour areas (dystrophic an necrobiotic changes in parenchyma) and crimson spot – lik and entire areas of haemorrhages and plethora of vessels glomeruli. Indicated changes are expressed greater on a cu

specially in cortical layer. Such changes in kidney are haracteristic for suboccute glomerulonephritis and are onsidered as expression of reaction of hypersensitiveness of ıe II type.

Hashimoto thyroiditis. lobe of thyroid gland, enlarged in 2,5 mes, with hilly surfaces is represented on preparation. Tissue pied on a cut, with presence of greyish – pink colour areas, ıcculent pink colour homogeneous structures. Changes in and are considered as expression of organspecific ıtoimmune disease.

Chronic gastritis. Mucousa of stomach is represented on reparation. Smoothing of folds of mucous which is most ıown in fundal part of stomach is marked. Similar changes in ucoûsa of stomach are observed in autoimmune diseases.

Rheumatic endocarditis. Heart with changed endocard is presented on preparation. On the surface of mitral valve position of thrombic masses is seen, that is conditioned by damage of endothelial lining and dystrophic changes in the er of valve, its connective tissue structures. Such changes in art in rheumatic endocarditis are conditioned by velopment of autoimmune disease of immunocimplex type.

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

Amyloidosis of the kidney. Preparation is stained with congo ed. In glomeruli, and also in epithelium of tubules deposition amyloid masses is observed. Clearness of capillary omeruli is decreased. There are homogenous eosinophylic sses (cylinders) in clearance of tubules, that testifies to the creasing of function of kidney. There is surplus excrescence connective tissue in stroma. Designate: 1-amyloid masses in omeruli, 2-cylinder in clearance of tubules, 3-excrescence of nnective tissue.

2 *Amyloidosis of the spleen.* Preparation is stained with congo – red, haemotoxilin – eosin. Amyloid deposits both in lymphatic follicles ("sago" spleen) and in all pulp ("grey" "lardaceous" spleen). At what diseases may this process develop? Designate: 1-amyloid masses in lymphatic follicles, 2-amyloid masses in pulp of spleen, 3-unchanged follicles.

3 *Autoimmune Hasimoto thyroiditis.* Preparation is stained with haemotoxilin – eosin. Parenchyma of thyroid is represented by the follicles of different sizes, which are filled with the colloid of a different density. Stroma and parenchyma are infiltrated by lymphoid elements, plasmatic cells and reticular cells. At the same time activated lymphocytes, are seen which destroy parenchyma of gland prevails in infiltrates. Designate: 1-colloid of different density in follicles, 2-lymphatic follicles in parenchyma of gland, 3-unchanged follicles.

4 *Suboccute glomerulonephritis.* Preparation is stained with haemotoxilin – eosin. Kidney glomeruli are sharply enlarged in connection with proliferation of cells of endothelium of capillaries of mesangium. Shhumlanskiy – Boumens' capsule in one cases is extended and filled with exudates, in other is vice versa narrowed. In the walls of capillaries there is fibrinoid necrosis. Parenchyma of organ is infiltrated by lymphocytes. Designate: 1-enlarged kidney glomeruli, 2-lymphocytic infiltration in parenchyma, 3-fibrinoid necrosis of capillaries.

5 *Chronic bronchitis with immune component.* Preparation is stained with haemotoxilin – eosin. Parenchyma of lungs is in condition of sharply reduced pneumatization due to excrescence of connective tissue, walls of alveoli are sharply thickened due to cellular infiltration and deposition of fibrinous exudates. There are numerous lymphocytic infiltrates as lymphomas in stroma of lungs, in interalveolar septa. Similar cellular infiltrates are seen in clearance of alveoli. Designate: 1-fibrinous exudates in clearance of alveoli, 2-lymphocytic

infiltrates in parenchyma of lungs, 3-excrescences of connective tissue.

6 *Accidental involutions of thymus*. Preparation is stained with haemotoxilin eosin. Lobules of thymus are diminished in size and hasn't clear boundaries. Disappearance of division of organ on cortical and medullar layer is marked. At the same time amount of lymphocytes is sharply reduced in cortical layer. Considerable excrescence of connective tissue in place of atrophied parenchyma appears at the same time. Designate: 1-atrophy of parenchyma, 2-lymphocytic infiltrates, 3-excrescences of connective tissue.

7 *Active viral hepatitis*. Preparation is stained with haemotoxilin – eosin. Hepatic lobules are enlarged in sizes and do not have clear boundaries in favour of big number of leucocytes, which diffusely, and by places centrally with formation of lymphoid follicles infiltrate parenchyma of organ. At the same time dystrophic and necrobiotic changes in parenchimatous structures of liver, dilatation of portal tracts are observed. *Designate*: 1-dystrophic changes in hepatocytes, 2-lymphocytic infiltrates.

Lupus nephritis. Preparation is stained with haemotoxilin – eosin. Kidney glomeruli in favour of necrosis of vascular interlacements have sharply basophilic staining. Thickness of basal membranes of capillaries is considerably increased due to precipitation of immune complexes thrombotic formations appear in clearance of separate capillaries. In cells nuclei have sharply basophilic staining in favour of their picnosis. Shumlanskiy – Boumens` capsule is extended and filled with exudates in one cases and in the other is vice versa narrowed. There is fibrinoid necrosis in walls of capillaries. Parenchyma of organ is infiltrated by lymphocytes. Designate: 1-1) basophilic kidney glomeruli, 2- lymphocytic infiltrates in parenchyma, 3- fibrinoid necrosis of capillaries.

9 Decompensated tonsillitis. Preparation is stained with haemotoxilin – eosin. Tissue of tonsil is sharply changed in favour of impoverishment of lymphoid structures and almost complete atrophy of follicles. At the same time mixed cellular inflammatory infiltration of parenchyma, excrescence of connective tissue takes place. Designate: 1-atrophied lymphoid follicles, 2-inflammatory infiltrates, 3-excrescences of connective tissue.

Situation tasks

1 In two weeks after acute follicular tonsillitis patient suffered from junctions pain, swelling, general fatigability, temperature increase up to 37^0C . Diagnosis was made: rheumatism. Explain the sense of clinical symptoms, name mechanism of immune reactions development. Give characteristic to morphologic signs of pathologic process in the case.

2 Patient who worked at chemical plant for a long time at contact with acetone expiratory asthmatic fits occur with viscous sputum discharge. Make the diagnosis. What reactions can cause attack progress? Name components of these reactions.

3 Thyroid gland enlargement was found in patient, subjectively she undertakes difficulties when swallowing, feels squeezing in the neck portion, weakness. It is known from anamnesis, that 5 years ago she stand inflammatory process in thyroid gland. Thyroid gland was surgically removed, under histologic investigation parenchyma hyperplasia, lymphocytic infiltration with follicles formation, sclerotic changes were found. What pathomorphologic process took place in this case, what is the mechanism of its development?

4 Patient suffered from lungs tuberculosis for 15 years. In extremeties he has edemas, protein in urine, protein in plasma was whirl decreased. Patient died of uremia. What process developed in kidneys? Give explanation above said changes.

Answers to situation tasks

In this case immune reactions occurred caused by ensitization and organ specific autoimmune process progress, ne reason of which most likely was B-hemolytic reptococcus.

Bronchial asthma, chemical allergen starts IgE, reagine actions develop, tissue basophiles produce hystamin and ther mediators, causing bronchiospasm and mucus tunic nflammation.

Autoimmune thyroiditis and lymphadenoid goiter. lorphologic features of delayed type hypersensitivity reaction.

Amyloidos developed in kidneys. Above said changes dicate renal function deterioration, protein metabolism failure d renal insufficiency progress.

Test tasks

Girl of 2 years old ill with bronchopneumonia died of sepsis. morphologic investigation multiple failures of facial skull nes development failures, thymus absence. munoglobulins quantity in blood is within the norm. Name in cause of child's death.

Chronic intoxication syndrome. **B.** Combined mmunodeficiency syndrome.

Syndrome of cellular immunodeficiency insufficiency.

Secondary immunodeficiency syndrome. **E.** Acute mphatic leukemia.

Patient A., 15 years old, was ill with bronchial asthma. uring influenzal infection asthmatic status developed with hal consequence. At morphologic investigation the llowing was revealed: spasm, bronchioles wall edema with dent infiltration with lymphocytes, eosinophils, labrocytes granulation. What mechanism of hypersensitivity is the ound of this case?

A. Autoimmune. **B.** Inflammatory. **C.** Immune complex. **D.** Immune caused cellular cytolysis. **E.** Reagin reaction of hypersensitivity.

3 After renal transplantation patient was subjected to puncture renal biopsy. At hystologic investigation stroma diffuse infiltration with lymphocytes, plasmacytes, lymphoblasts, plasmablasts were observed, as well as necrotic arteritis. What pathologic process developed in graft?

A. Pyelonephritis. B. Glomerulonephritis. C. Tubulenecrosis. D. Ischemic injury of kidney. E. Immune graft rejection.

4 In patient with immunopathologic disorders adrenal glands cortex insufficiency developed. At histologic investigation lymphocytic infiltratuion of gland was found as well as parenchyma substitution with conjunctive tissue, Addison's disease was diagnosed. What is disease genesis?

A. Inflammatory. B. Tumor. C. Dyshormonal. D. Autoimmune. E. Metabolic.

Answers to test tasks in theme

1. C. 2. E. 3. E. 4. D.

Illustrations to theme

Figure 1 – Allergic edema of larynx. Regular croup. Mucus tunic of larynx is sharply edematic. Lumen is slot-type narrowed. Name diseases at which regular croup can develop.

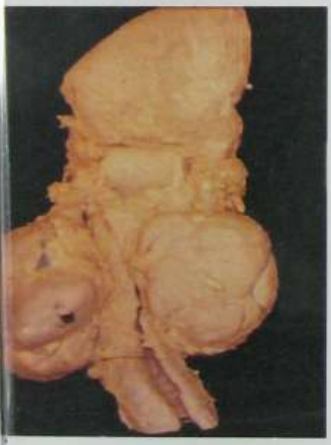


Figure 2 – Nodose goiter. Histologically - Hashimoto's thyroiditis. Thyroid gland is increased. Its surface is coarse-gibbous.

Figure 3 – Renal amyloidosis. Kidney is enlarged, of hard consistence. Section surface is of tallowy color. Cortical layer is of yellow-white color, incrassate. This kidney is named "large tallow kidney". At what diseases renal amyloidosis develops ?

Figure 4 – Croupous pneumonia. Macrospecimen represents lung slice at which it is seen that parenchyma is of light grey, fine-grained, dim color caused by big quantity of exudate presence in alveoli lumen. This is an example of lung parenchyma hyperreaction for causative agent hitting.

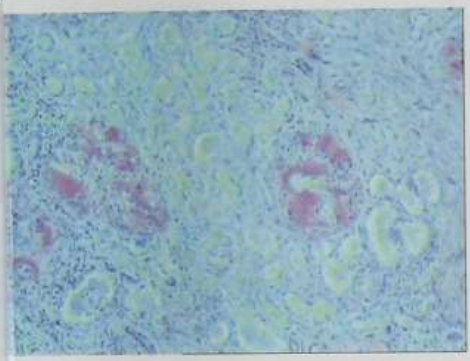


Figure 5 – Renal amyloidosis. Specimen is colored with iodine-grune. Amyloid masses depositing is observed in glomerules. Capillary glomerules acuteness is decreased. There are homogenous

nasses (cylinders) in renal tubules' lumens.

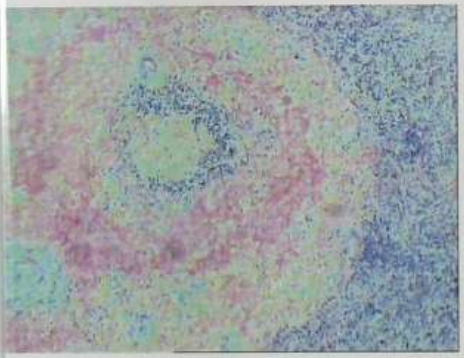


Figure 6 – Spleen amyloidosis. Specimen is colored with gentian violet. Amyloid is deposited like it does in lymphatic follicles – "sago" spleen. At what diseases this process can progress?

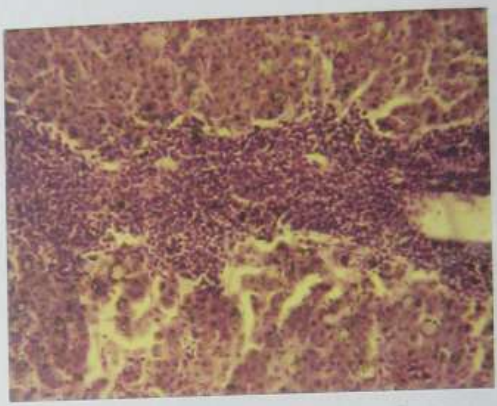


Figure 7 – Viral hepatitis. Specimen is colored with hematoxylin-eosin. Liver plates are enlarged and are not well-defined because of considerable quantity of lymphocytes which diffusely and in certain places foci with lymphoid follicles formation infiltrate organ parenchyma.

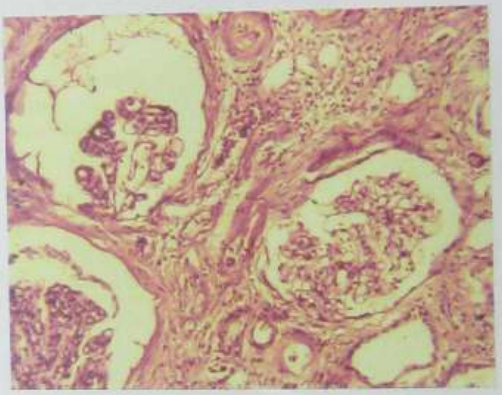


Figure 8 – Lupous nephritis. Specimen is colored with hematoxylin-eosin. Renal glomerules are of sharply basophilic coloration caused by vascular plexus necrosis. Capillaries' basal membranes thickness is increased considerably on the account of immune complexes depositing. Thrombotic formations are observed in separate capillaries' lumen. Nuclei in cells are of sharply basophilic coloration on account of their pyknosis. Shumlyanskyy-Bowman capsule in some cases is dilated and filled with exudates, in the other cases – it is narrowed. Capillary walls are subject to fibrinoid necrosis. Organ parenchyma is infiltrated with lymphocytes.

Concept module 3

Regeneration, adaptation and compensation processes

Specific objects of module:

To make conclusions regarding organs' physiologic adaptation structural basis

To analyze types of adaptive changes.

To explain stage character of compensation.

To analyze causes, mechanisms, types, stages, clinicopathologic characteristic of hyperplasia.

To analyze atrophy causes, mechanisms, types.

To analyze organs' morphologic changes and consequences under atrophy.

To analyze morphologic changes under metaplasia and dysplasia.

To explain dysadaptation mechanisms.

To explain regenerative process morphogenesis.

To explain the role of munoral and cellular factors in reparation process.

To analyze the types of regeneration, complete (restitution) and incomplete (substitution) regeneration morphologic characteristic.

Practical class 11

Theme 13 Regeneration, adaptation and compensation processes

Theme topicality: Various pathologic processes cause sues injury and their function deterioration, but basic dition of organism existence is its internal environment tively constant content keeping. To substitute (compensate) ect and normalize function the work of uninjured served) portions of this organs and other organs is anced, assisting organism to adapt new living conditions.

In the other words compensative and adaptive processes continuously take place under various pathologies and they are directed to correct internals' structure and function under numerous diseases.

The object is to learn compensative and adaptive processes taking place in organism etiology, mechanisms of development, morphologic manifestations, consequences.

Specific aims:

1) To know diversity of compensative and adaptive processes and their significance in organism homeostasis.
2) By macro- and microscopic features to learn to identify various compensative and adaptive processes.
3) To master diagnosis of clinical and morphologic features of regeneration, organization, metaplasia, hypertrophy, atrophy, dysplasia.

Basic matters for self-training

Structural basis of organs' physiologic adaptation. Types of adaptive changes. Hyperplasia: definition, causes, mechanisms, types, stages, clinicopathologic characteristics. Physiologic and pathologic hyperplasia. Atrophy: definition, causes, mechanisms, types, clinicopathologic characteristics. Brown atrophy of liver, myocardium, skeleton muscles. Metaplasia: definition, types. Metaplasia in epithelial and mesenchymal tissues, morphologic characteristics, clinical significance, role in carcinogenesis. Dysplasia: stages, morphologic characteristics of dysplasia stages, clinical significance, role in carcinogenesis.

Hypertrophy: definition, causes, mechanisms, types, clinicopathologic characteristics. Morpho-functional feature of myocardial hypertrophy.

Stage character of compensation processes progress in pathologic conditions.

Pathologic anatomy of organism dysadaptation: morphologic features of stress-syndrome, features of immune-endocrine and neuro-endocrine adaptation failures. Compensation.

Idea of specialized cells' physiologic self-recovery regularities. Regeneration: definition, essence and biologic sense, connection with inflammation, consequences. Equal recovery of structural elements. Cells reparative regeneration: molecular basis and reparation characteristics of damaged nucleus, mitochondrial DNA and micro bodies. Cellular and intracellular forms of regeneration. Morphology of injured organs tissues' reparation and remodulation: reparative angiogenesis and territorial matrix reproduction, injured organ architectonics reproduction. Morphologic characteristic of organs' reparative remodulation under incomplete reparation of organ, wound repair characteristics.

Regenerative process morphogenesis: proliferation and differentiation phases. Types of regeneration: physiologic, reparative, pathologic. Their morphologic characteristics: complete (restitution) and incomplete (substitution) regeneration. Role of humoral and cellular factors in reparation process.

Granulation tissue: stages, morphologic characteristics. Regeneration of separate types of tissues and organs. Types of wounds healing. Wounds healing kinetics.

Dysregeneration: molecular basis and morphologic characteristics of injured tissues' hyperregeneration and hyporegeneration.

I Pre-auditorium self-training for practical class

In the vital activity process organism continuously adapts to changing living conditions. We differentiate

physiologic adaptation – cells respond to normal stimulation with hormones or other endogenous biologically active substances and *pathologic adaptation* – adaptation of cells or tissues to external or internal environment pathogen components influence. Adaptation is manifested with hyperplasia, hypertrophy, organization, atrophy, metaplasia, dysplasia.

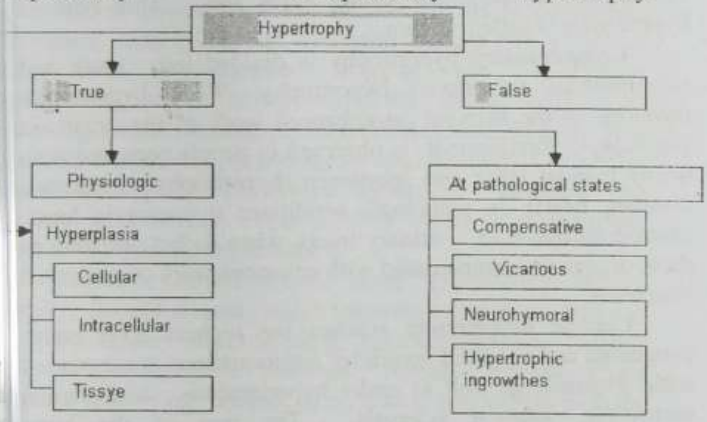
Hyperplasia

Hyperplasia is organ or tissue size increase due to cells amount increase. Hyperplasia could be physiologic and pathologic. Besides that reactive or defensive, neurohumoral or hormonal hyperplasia and substitutive compensatory hyperplasia in case blood loss are differentiated. Reactive or defensive hyperplasia often takes place in immunocompetent organs: thymus, spleen, lymph system, red bone marrow, tonsils under antigen stimulation, septic conditions, anemias, etc. Hormonal hyperplasia could be physiologic (mammary gland hyperplasia during lactation) as well as pathologic: hyperplasia of prostate gland, endometrium, fibrocystic mastopathy, thyroid gland hyperplasia under hormonal disorders in organism. Pathologic hyperplasia occurs under the influence of viral infection – epithelium hyperplasia in verruga, etc.

Hypertrophy

***Hypertrophy* (from Latin hyper – excessive, trophe – nutrition) is cell, tissue or organ volume increase on account of cells reproduction or increase of their quantity and intracellular ultrastructures size.** True and pseudohypertrophy is differentiated. First one is characterized with volume increase on the account of functional (parenchymatous) structures, the other one – on the account of

upport tissues – conjunctive or adipose. Hypertrophy is tegrally connected with hyperplasia (from Latin plaseo – eate), which is manifested in cells reproduction by the way of itosis (cell hyperplasia), tissues excrescence (tissue perplasia) and ultrastrauctures excrescence (intracellular perplasia). Adaptive processes include neurohumoral pertrophy (hyperplasia) and hypertrophy excrescences, mpensatory – compensatory hypertrophy.



Neurohumoral hypertrophy (hyperplasia) occurs on the kground of endocrine glands dysfunction. Its physiologic e is uterus hypertrophy and macromastia under pregnancy. pathologic conditions it is observed endometrium glands perplasia, mastopathy under ovarian dysfunction, mammary nd excretory ducts hyperplasia in males (gynecomastia) er testicles atrophy, enlargement of organs and prominent s of skeleton (acromegalia) under chromophobe adenoma dults.

Role of ***hypetrophic excrescences*** in adaptive processes is insignificant. They are observed under chronic inflammations of mucus tunics with polyps formation, under lymph flow disorders in low extremities and lymphostasis causing conjunctive tissue excrescence (elephantiasis). Adipose and conjunctive tissues can fill the space occupied by organ or tissue causing their atrophy. An example could be cranial bones thickening under cerebral atrophy, adipose tissue excrescence in atrophied kidney hilus area. This type of hypertrophy is called vacant.

Compensatory hypertrophy is divided into work and substitutional (vicarious) hypertrophy. Work hypertrophy develops as the respond on enhanced work of the organ. In physiologic conditions it is observed in people occupied with heavy manual labor and sportsmen (hypertrophy of skeleton muscles, heart). In pathologic conditions it occurs in heart, gastrointestinal tract, urinary tracts, when defect existing in these organs are compensated with enhanced work of preserved structures.

Cardiac hypertrophy reaches the highest level under congenital and acquired ventricles malformations accompanied with stenosis, as well as under hypertensions, aorta lumen narrowing, vascular sclerosis. The part of the heart undertaking functional load is subject to hypertrophy in the first turn. In these cases heart weight reaches 1 kg. Structural manifestation of compensation is heart length increase as well as its cavity dilation determined as active, compensatory, *tonogenous*. However in case prime cause persists ventricular cavity reduces with time passing by. Hypertrophy of cavitary organ (heart, bowel, urinary bladder) under which its lumen decreases is called *concentric*. It testifies intensive compensation. Left ventricle thickness in these cases can reach 2 cm, and right – 1 cm. Microscopically in such a case it is observed considerable thickening of cardic hystiocytes and

ir nucleus enlargement. Hyperplasia of stroma's fibrous uctures, intramural vessels, nerve apparatus components ponsible for enhanced function' neurohumoral support, is siderable behind the tempo of cardic hystiocytes' racellular ultrastructures hyperplasia. Thus contributing in mpensation phase is fictitious, in its bud it is already has the tures of decompensation. In case prime cause is not oved, unbalance occurs between increased demands of pertrophied myocardium and the level of its blood supply, ervation, energy supply, exchange area of newly formed astructures' membranes. Adipose and albuminous enerations occurs in hypertrophied cardiac hystiocytes kening cardiac beating activity. In the result of tonus lose cardiac hystiocytes passive *myogenous* dilation of ventricles ities takes place. Concentric hypertrophy converts into *ntric* with cavitary organ dilation, which is morphologic ure of cardiac decompensation.

Gastric or bowel muscle layer hypertrophy occurs, rally, upward stenosis which impedes evacuation. This can place under ulcers healing, tumors presence. Urinal der hypertrophy is observed under prostate gland oma, narrowing urethra, as well as in connection with the r impediments of bladder emptying. Functional fficiency of above named organs occurs under myocytes degeneration and manifests in their cavities tion.

Vicarious (substitutional) hypertrophy compensates the tion of one of the dead or surgically removed paired ns (lungs, kidneys, adrenal glands). By its pathological nce it is close to regenerative hypertrophy. Significant role ts occurrence plays the complex of reflex and hymoral iences, the same with compensatory hypertrophy.

Atrophy

Atrophy is lifetime change of organs', tissues' and cells' volume, accompanied with their functions weakening or their functions termination. Physiologic and pathologic atrophies are differentiated.

Physiologic **atrophy** is observed during the whole lifetime of human being. Upon the birth umbilicial arteries, arterial (Botallo's) duct atrophy and obliterate, aged people face with genital glands atrophy, old people – with bones and intervertebral cartilages atrophy.

Pathologic atrophy is observed in any age and can be caused by various reasons - insufficient feeding, endocrine glands dysfunction, central and peripheral nervous system lesions, intoxications. Pathologic atrophy is reversible process. In case the cause is removed under condition that atrophy didn't reach high level, organ structure and function can be completely rehabilitated. Pathologic atrophy can be general and local.

Cachexia or emaciation is divided into the following types: alimentary cachexia emaciation under cancerous cachexia, emaciation under cerebral cachexia, emaciation under other diseases. Concept of "emaciation" and "cachexia" are not identical. Cachexia in primary stages can be free from emaciation and be manifested with progressive degenerative changes of the organs, for example, with osteoporosis.

Alimentary emaciation occurs during starvation. Gradually fat stock decreases, skeleton muscles atrophy. Atrophied adipose (fatty) tissue becomes ochre-yellow color due to lipochrome pigment accumulation. Fatty tissue of atrium and fatty marrow impregnate with serous fluid and become dropsical (serouse atrophy of fatty tissue). Pigment melanin accumulates in the skin of starving, so it colors in grey-brown color. Heart, liver and other organs decrease in size. Pigment lipofuscin, (wear-and-tear pigment) accumulates

cardic hystiocytes, hepatocytes and myocytes of skeleton uscles, as the resuly of which organs become of brown color *rown atrophy of organs*).

Emaciation under cancerous cachexia is aracteristic for cancerous growth of any localization. The ost fast it develops in patients ill with cancer of esophagus, stric carcinoma or intestine cancer caused by digestion sorders.

Emaciation under cerebral and hypophysial immonds' and Schigens' diseases) cachexia occurs due to pothalamus' or hypophysis' injury with inflammatory cess or tumor.

Emaciation under the other diseases takes place in case g term chronic infections (tuberculosis, dysentery, chronic sis). It is caused by severe disorder of metabolism.

Under general emaciation subcutaneous fatty tissue is ent, eyes are hollow, skin is dry, abdomen is scaphoid. rvation edemas sometimes take place.

Local atrophy occurs by various reasons. The owing types of it are differentiated: dysfunctional, caused nadequate blood supply, compression, honeurotic, caused by physical and chemical agents uence.

Dysfunctional atrophy or atrophy caused by inactivity urs because of organ function decrease: muscles atrophy er bones fracture, optic nerve atrophy after eye ectomy. ophy development in patients with ruptures could be slow n in case massage and physical exercises are applied.

Atrophy caused by inadequate blood supply occurs ed by narrowing of arteries feeding organ. Exsanguination s to hypoxia in the result of which parenchimatous ents' functions fall and cells size reduces Hypoxia ulates fibroblasts proliferation (reproduction), so sclerosis lops under inadequate blood supply. Patients with

atherosclerosis suffer from this process in myocardium, kidneys, cerebrum, legs.

Atrophy from compression occurs in organs subject to compression by tumor or aneurysm (local evagination of aorta). Even the bones of spinal column and breast bone atrophy because of their compression by aneurysm. Under urinary tracts obstruction with calculus urine stretches renal pelvis and cups (hydronephrosis) causing kidney parenchyma atrophy. In case liquor outflow hindrance ventricles of brain dilate (hydrocephalus) and cerebrum atrophy.

Trophoneurotic atrophy is caused by failure of organ connection with central nervous system under peripheral nerves traumatic, tumor or inflammatory injury. Skeleton muscles' atrophy often develops by this scenario.

Atrophy caused by physical and chemical agents influence occurs, for example, in marrow and genital glands under radiation influence. Radioiodine causes thyroid gland atrophy. After long term treatment with adrenocorticotropic hormone or glucocorticoids adrenal glands cortex' atrophy develops.

Organs reduce in size under atrophy. Their surface in most cases is smooth (smooth atrophy), in kidneys – granular (granular atrophy). Under hydronephrosis and hydrocephalus organs are enlarged due to liquid accumulating in them and their parenchyma is atrophied.

Metaplasia

Metaplasia is adaptive pathologic process characterized with substitution of one differentiated tissue with the other in the limits of one histiotype: mesenchymal or epithelial.

This phenomenon does not take place in muscular and nervous tissue. The most wide spread example of metaplasia is one layer prismatic epithelium substitution with multilayer flat

ithelium, observed under bronchi mucous tunic flammation, gastric epithelium substitution with intestinal ithelium – intestinal metaplasia, or gastric mucus tunic terolization. A-hypovitaminosis and others could be the uses of metaplasia. Conjunctive tissue metaplasia is served with cartilage or bone formation in cicatrix, aorta all under atherosclerosis. Metaplasia occurs in connection ith previous non-differentiated tissues' proliferation – direct metaplasia. Metaplsia is grounded on the change of netic program of differentiation on column cells level. etaplasia could be the background for malignant growth velopment.

Dysplasia

Dysplasia is major failures of proliferation and thelium differentiation with cellular atypia development d histoarchitectonics change: loss of polarity, loss of thelium histo- and organo- specificity.

Basic membrane is not injured under dysplasia. The st often dysplasia develops under inflammatory and enerative processes. Depending on proliferation stage and dition of cellular and tissue atypia three stage of displasia differentiated: I – minor (small), II – moderate (middle), III severe (major). Minor and moderate dysplasia are of ersible character. Cellular and tissue changes under severe plasia are rare subject to reversible process and are treated precancerous process. Sometimes locally they are hard to differentiated from carcinoma.

Regeneration

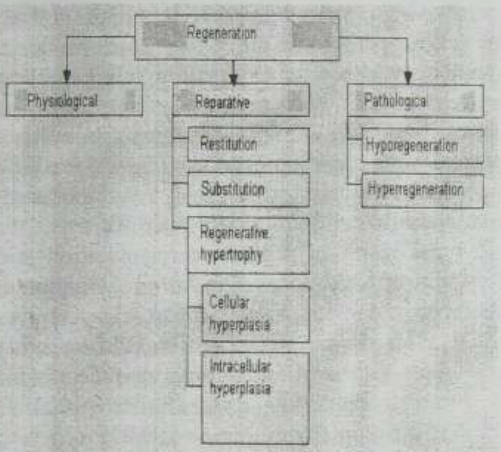
Regeneration (from Latin regeneratio – restoration) is process of living matter self-recovery in injured area.

Regeneration takes place on molecular, subcellular, ular, tissue and organ levels and reflects the principle of

living functions autoregulation. It is grounded on cellular and intracellular hyperplastic processes. Cellular reproduction is characteristic for cellular form of regeneration, ultrastructures and their components quantity increase (hyperplasia) and their enlargement (hyperplasia) are characteristic for intracellular form. The last form is peculiar for all organs' cells and is universal.

Two phases are differentiated in regeneration morphogenesis – proliferation and differentiation. In the term of the first phase reproduction of non-differentiated (cambial, column) cells or pre-cells are observed. During the second phase young cells mature and specialize.

Regenerative process is regulated with humoral, immune, nervous and functional mechanisms. Humoral mechanisms are realized in cells and tissues at intracellular and tissue regulators participation, and out of them – at participation of hormones, poetines, mediators, growth factors as well as keylones (substances depressing cells division). Immune mechanisms are connected with "regenerative information" transfer by leukocytes, nervous – with trophic function of nervous system, and functional – with adequate demands of organs and tissues.



Three *types of regeneration* are differentiated: ıysiologic, reparative and pathologic.

Physiologic regeneration

Physiologic regeneration is done in the course of the hole life and reflects endless process of substances' sintegration and synthesis. It is characterized with tracellular renewal of molecules and ultrastructures as well as ıtire cells, fiber structures and major substance of conjunctive ssue. Intracellular regeneration is the only form of content ıd function renewal of central nervous system's cardiac stiocytes and neurocytes. Combination of intracellular ıewal with cells mitosis is observed in liver, kidneys, ncreas. Continuous change of epidermis, digestive tract ucus tunic epithelium, synovial membranes, marrow, blood ements are done on the account of cells division.

Reparative regeneration

Reparative regeneration is organ defect substitution under various pathologic processes. It is grounded on the same mechanisms which refer to physiologic regeneration, moreover injury reparation in each organ is going on the same way as in conditions of physiologic recovery, but more intensive. Intracellular regeneration becomes major form of degenerative changed tissues cells' structure rehabilitation, as well as cellular and intracellular – under their necrosis.

Final result of reparative regeneration is expressed in restitution or substitution. *Restitution* (complete regeneration) is characterized with tissue defect substitution with tissue identical to dead one. It is attributable to those organs and tissues where regeneration is going on exceptionally in cellular form (marrow, epidermis, mucus tunics epithelium).

Substitution (incomplete regeneration) is characteristic for the organs healing of which goes on mostly or exceptionally by intracellular reparation (heart, central nervous system). For example, in myocardium necrosis focuses are substituted with conjunctive tissue, in cerebrum dead neurocytes – with glial cicatrix. Function renewal is provided with nucleus and cytoplasm ultrastructures enlargement in preserved cells which hypertrophy. Incomplete regeneration variation is "distance regeneration". As an example of it could be named qualitative reconstruction various portions of gastrointestinal tract, compensating exocrinous, function of pancreas head or uninjured cerebral hemisphere reconstruction in case the other hemisphere injury.

Pathologic regeneration

Pathologic regeneration is the type of reparative regeneration going on in conditions of local and general regulatory mechanisms failure, and is characterized with regenerative process distortion, violation of proliferation phase

hange into differentiation phase. Deficiency of proteins or itamins, nervous regulation failure, hormonal disorders, nmune system depression could seriously influence healing peed and quality. In that way long term nonhealing crus ulcers t patients with chronic cardiac insufficiency could be xplained as well as persistent wounds under diabetes mellitus. n example of pathologic regeneration can be conjunctive ssue hyperproduction with keloid formation under radiation thermal trauma.

Regeneration of separate organs and tissues

Blood can regenerate by physiologic, reparative and thologic regeneration type. An example of blood reparative generation under anemia can serve extramedullary matosis. Pathologic blood regeneration is observed under liation, leucosis. Small size ***vessels*** regenerates satisfactory d big vessels regenerate by substitution type – cicatrix mation on the place of mid and external layer portions ury. ***Conjunctive tissue regeneration*** starts from young senchymal cells proliferation and vascularization with ***mulation tissue*** formation, that is young conjunctive tissue ch with cells: non-differentiated lymphocytine cells of njunctive tissue, leukocytes, plasmocytes, labrocytes, roblasts; loop-like thin wall vessels. Granulation tissue turing is ended with rough fibered cicatrix tissue rmation, sometimes even keloid. ***Osteous tissue*** generation after uncomplicated rupture of bone goes by the y of primary bony union, which have the following stages: mary conjunctive tissue callus, primary bony callus, final ny callus. Under regenerative process failure secondary ny union occurs in bone through prior osteocartilaginous llus. ***Cartilage tissue*** regeneration goes as incomplete eneration with scar tissue growth. ***Muscle tissue*** eneration depends on its type. Unstriped muscles

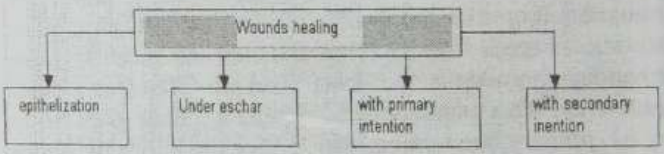
regenerate completely under minor defects. Transversely striated muscles regenerate only in case sarcolemma is preserved. Cardiac muscle regeneration goes by the way of cicatrix formation. ***Epithelium*** regenerates by the way of new cells reproduction, in other words by restitution type. *Nervous tissue* regeneration goes ambiguous. Cerebrum and spinal marrow cells regenerate by substitution, that is glia growth and cicatrix formation.

Organization

Organization is protective-adaptive process directed to separate and substitute with granulation tissue focus of necrosis, hemorrhage or exudates as well as thrombi, foreign objects and parasites.

Its essence comes to conjunctive tissue formation under defects healing in wounds and ulcers, substitution with conjunctive tissue areas of necrosis or thrombotic masses (properly organization) and their encapsulation.

By I.V.Davydovsky the following forms of *wounds healing* are differentiated: epithelium defect immediate closing, healing under eschar, primary intention of wound, secondary intention or healing by granulation.



Epithelium defect immediate closing provides cells rowth on wound sides and its skinning over with cells layer ithout mitotic cells division. Such simple form of healing is eculiar to surface injuries of cornea, mucus tunics, vessels ıtima.

Healing under eschar is also characteristic for minor ıjuries of epidermis. For example, under surface excoriation mph and blood excude fast drying and converting into crust schar). Epidermis regenerate under crust which in the result rejection process drops away on the 3^{rd} -7^{th} day.

Healing of wounds involved not only skin but lower tuated tissues goes by the way of primary or secondary tention. Principal difference in them is in the manner of ound cleansing. Primary cleansing is characteristic for ***aling with primary intention.*** Under phagocytes' oteolytic ferments influence partial lysis of grumes and sue detritus takes place and wound content is removed in very first date after injury together with exudate. On the -3^{rd} day granulation tissue appears which ripens on the 10^{th}-th day. In the clinic the sides of big wounds connect with ures and support with dressings. In case distance between sides equals even 10 mm, in few days this distance will minish то zero due to tissue edema and fibrin clot reduction ıich sticks wound edges. In those cases when wound sides parated due to suppurative inflammation, primary intention is possible and healing is done through ***secondary intention.*** is characterized with wound release of detritus and foreign jects by "outsuppuration". On the boarder with necrotic sue fast appears the features of demarcation suppurulent flammation, and its melting comes. Necrotic masses ection takes place during the first 5-6 days (secondary ansing of the wound) and granulation tissue starts to develop wounds edges. Under wounds healing by primary or condary intention granulation tissue maturing is

accompanied with epithelium regeneration. However under secondary intention healing on the place of wound cicatrix forms anyway.

Inflammatory process always precedes ulcers healing. Granulation tissue grows into necrosis area which matures into rough fiber and often subjects to hyalinosis. The latter causes cavitary organ deformation and stenosis. Epithelial layer stratifies conjunctive tissue.

Really organization of necrotic masses starts from reactive exudates inflammation in surrounding tissues and necrosis areas lysis. Exudative reaction transfers into productive with mesenchymal cells proliferation. Granularion tissue ingrows from periphery and gradually transforms into cicatrix. This type of organization is peculiar to myocardial infarction healing, as well as kidneys and spleen. Thrombus organization starts from 2^{nd}-3^{rd} day of its origination, goes parallel with aseptic autolysis and is finalized with thrombotic masses substitution with conjunctive tissue, canals formation and vascularization. Organization of hemorrhage or exudates in intermediate tissue also ends with cicatrization and in serous cavities – with their obliteration or joints formation. Fibrinogenous exudates organization in alveoli under croupous pneumonia results in carnification.

II Algorithm of the practical part of class

To learn and be able to describe orally macrospecimens of the Chair macro museum.

1 Nodular regeneration of liver at cirrhosis. Surface of organ is small nodular. On cut parenchyma is parted by white fibrous crosspieces into separate lobules. On this back ground there are large regenerator nodes of parenchyma of liver, greyish-yellow which don't have an ordinary lobular structure. A liver acquires such kind at postnecrotic cirrhosis. That is, in areas of massive

ecrosis of substitution of it by connective tissue. Parenchyma liver and well kept hepatocytes forms nodes of regeneration they are less then 1cm in size, such cirrhosis is named small odular, if they rich 5 cm – great nodular

Cicatrize (scar) stenosis of intestine. Part of intestine on a it, which reminds "sand-glasses", is seen on acropreparation. Above and under narrowing folds of mucosa e located horizontally. In the place of most narrowing folders e absent, wall is deformed, clearance of intestine in that place almost twice less. It is consequence of cicatrization of ulcer intestine with formation of scar. Such process is often the ason of intestinal impassability.

Commissural pericarditis. Thickened epicardium joint with ricardium by comissures is seen on a slit. Such process is a ult of organization of serousli-fibrinous exudates. metimes connective tissue is limed, that considerably ede work of heart. Such heart is named "armour"

Hypertrophy of heart. For comparison normal size heart and ngside enlarged in 2-3 times in favour of enlarging of right ıtricle are represented in preparation. Hypertrophy of diomyocytes in favour of hyperplasia of intracellular uctures lies in basis of hypertrophy of myocardium, ultaneously hyperplasia of stromal carcass takes place. The ses are: congenital and acquired heart disease, chronic specific diseases of lungs, chronic forms of secondary erculosis and others like that.

Concentric hypertrophy of heart. Thickened to 2,5 cm wall of ventricle and interventricle partition are seen on horizontal of heart, clearance of ventricle is enlarged a little. In norm kness of left ventricle of adult is 1,2 cm. Such hypertrophy named tonogenous or compensative. Thus, it provides mpensates) necessary functional level of general circulation blood at heart diseases.

6 Eccentric hypertrophy of heart. Enlarged in two times clearance of ventricle is seen on a horizontal cut of heart. If not remove cause, which predetermines process of hypertrophy, dystrophic changes in hypertrophied cardiomyocytes and sclerotic in stroma, which also weaken contractive activity of myocardium, appears. Thus cardiac decompensation develops at which muscle is unable to execute intensive work. At decompensation of hypertrophied myocardium transversal, passive or myogenous extend (dilatation) of ventricles takes place.

7 Hydronephrosis kidney is enlarged and looks like thin-walled sack which is filled with a liquid. Develops as a result of hampered outflow of urine, the cause of which can be presence of stone with obturation of ureters, tumour of urinary bladder, adenoma of prostate. Urine, accumulating, stretches clearance of pelvis major and minor calyces, squeezes tissue of kidney, that result in atrophy of parenchyma of kidney caused pressure.

8 Postinfarctional scar (paunch) in myocardium. Deep inside of cut myocardium greyish-white scars which substitute damaged cardiomyocites on considerable area of transverse section are seen. Give explanation for this process.

9 Emphysema of lungs. Lung is extracted from the organism of man, which died on height of attack of bronchial asthma. Lung is of pale grey colour, large lobular structure as a result of swelling of acinuses. There is squeezing in pulmonary tissue in place of location of heart. Edges of lungs are rounded. It is seen on section, that the front edges of lungs cover a heart, mediastinum, lies on each other. By touch lungs are flabby, surface is smooth, brilliant. After pressuring with a finger there is a pit. At a cut-crepitating sound. Such emphysema develops as a result of violation of bronchial permeability when valve-like mechanisms act. If lungs shrink at dissection of thorax, it testifies to sharp emphysema. At chronic emphysema, lungs

es not shrink after dissection of thorax. Consequently, on eparation panacinar emphysema is represented.

Splenomegalia. Spleen is enlarged in sizes and mass in 2-3 nes, capsule is strained. In what diseases hypertrophy of leen takes place?

Hydrocephalia. In ventricles of brain there is great quantity liquid. Ventricles are enlarged. Parenchyma of cerebrum is nned. What pathological process developed in tissue of rebrum? Explain mechanisms of development.

Brown atrophy of myocardium. Heart which is diminished size is represented in preparation. On the surface of ricardium and muscle deposition of brown pigment – ofuscin. Specify in what diseases similar changes in heart e place.

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

Carnification of lung. Preparation is stained with matoxilin-eosin. Pulmonary tissue is seen in preparation, ut what presence of bronchial tubes, alveoli, coal dust ifies about. Inflammatory exudates in clearance of alveoli is minated by connective tissue. Also growing in granulated ue from the side of thickened walls of alveoli takes place. newhere the structure of lung is fully lost.

Designate: 1-alveoli, filled by connective tissue, 2-vessels, 3-bronchi.

ranulative tissue. Staining with haematoxilin-eosin. Many illaries are filled with blood, and also many cells: roblasts (oblong shape) eosinophilles, lymphocytes trophillic leucocytes, which are located between the layers mmature collagen fibers. Designate: 1-fibroblasts, eutrophylles, 3-collagen fibers.

landulous hyperplasia of mucousa of uterus. Staining with matoxilin – eosin. Thickening of endometrium, plenty of

glands of winding form are marked, some glands are cystously extended. Stroma is infiltrated by lympho – leucocytic elements. What does this pathological process testify? Designate: 1-glands of winding form, 2-cellular infiltrates, 3-unchanged glands.

4 *Atrophy of kidney at hydronephrosis*. Staining after the Van – Gizons' method. At study of preparation with naked eye considerable atrophy of parenchyma of kidney is seen (convex surface is capsule, opposite, concave is pelvis). Thickness of parenchyma 0,2 – 0,3cm in place of 12cm in norm. At microscopic examination there are evidently sharply extended tubules filled with concentrated urine ("thyroid kidney"), that testifies hampered outflow of urine. Parenchyma is almost absent, sclerosed, glomeruli are also sclerosed, small inflammatory infiltrates are seen in addition, that testifies pyelonephritis. Designate: 1-extended tubules, 2-sclerosed glomeruli, 3-cellular infiltrates.

5 *Brown atrophy of liver*. Structure of organ is not considerably changed. Scopes of lobules are contoured, definitely. Diminishment of sizes of hepatocytes is observed mainly in the central departments of lobules, located near central vein. Hepatocytes loose their regular polygonal form there, their nuclei diminish in size and as a result of thickening of chromatin seems more dark. In favour of diminishment of hepatocytes vessels in centre of lobules seems extended. Goldish – brown granules of lipofuscin appears in cytoplasm. In direction to periphery of lobules hepatocytes acquire normal size and pigment in cytoplasm appears rarely. Designate: 1-granules of lipofuscin, 2-atrophied hepatocytes, 3-extended veins.

6 *Massive area cardiosclerosis*. Preparation is stained after Van Gizons' method. Parenchyma (cardiomyocytes) is stained in light – green colour, stroma in pink or pale - red. Massive areas of excrescence of connective tissue are seen between

rdiomyocytes and in place of perished muscle fibers. So, ffusive and massive area rough postinfarctive cardiosclerosis, hich developed on a background of diffuse cardiosclerosis, at is characteristic for chronic ischemic heart disease, take ace. Designate: 1-massive area cardiosclerosis, 2-stenosed ssel, 3-diffuse excrescence of connective tissue.

Situation tasks

Urinary retention increases in patient ill with adenoma of state. What is the cause?

Patient was subject to pulmonectomy because of cancer of g. What changes will develop in preserved lung?

n some time after scratch no sign of it has left. What racter of healing took place in this case?

Patient undergone myocardial infarction of heart left tricle front wall. After treatment and rehabilitation he was charged from hospital in satisfactory condition, got back his fessional activity. In two years he died in traffic accident n cerebral hemorrhage. What macroscopic changes of the rt could be found on autopsy in the front wall of left tricle? What microscopic changes could be found at this in liac hystiocytes?

Child of 10 years old was subject to appendectomy. toperative period passed without complications. Patient was charged from the hospital in satisfactory condition. wever in some time in the place of postoperative cicatrix lening of bluish-red color occurred. Biopsy showed junctive tissue growth with big quantity of collagen fibers. lesion periphery there are infiltrates of lymphoid and matic cells, neogenic fibroblasts. What process we are aking of? On account of what tissue cicatrix develops?

Answers to situation tasks

1 Urinary retention increases because of mid part of prostate gland hypertrophy compresses urinary tract (urethra). Besides that compensatory hypertrophy of urinary bladder wall is ended with decompensation – wall becomes thinner, lumen dilates.

2 Preserved lung takes the function of extracted, enlarges in size - vicarious (substitutional) hypertrophy.

3 Covering epithelium is of high regenerative ability. Under complete reparative regeneration (restitution) injured skin structure completely renews. Character of healing is called epithelization.

4 In the heart is was found conjunctive tissue growth in the left ventricle front wall where myocardial infarction took place. Hypertrophy is found in non-injured cardiac hystiocytes.

5 Keloid occurred on the place of operating incision as the result of wound healing with secondary intention. Cicatrix was formed on the account of granulation tissue intensive growth.

Test tasks

1 After hip and shin skin burn in popliteal area semi-transparent white-red deforming cicatrix of cartilage consistence was formed which distinctly restricts movements in knee joint. Microscopically cicatrix is built of thickened homogenous collagen fibers and individual fibrocytes. Indicate cicatrix name.

A. Hyalinosis. **B.** Fibrinoid swelling. **C.** Mucoid swelling.
D. Keliod. **E.** Metaplasia.

2 In - patient died of pneumoconiosis right cardical ventricle cavity dilarion was revelaed. Hystologically hypertrophy of cardiac hystiocytes was found. Name the most likely pathology.

A. Concentric hypertrophy. **B.** Eccentric hypertrophy.
C. Work hypertrophy. **D.** Neurotic hypertrophy.
E. Hypertrophic excrescence.

3. Patient was diagnosed with renal pelvis calculus. He died of myocardial infarction. Section shows thinning of kidney medullar and cortex layers. Indicate the most likely kidney pathology.
A. Neurogenic atrophy. **B.** Atrophy of inactivity. **C.** Atrophy of compression. **D.** Concentric hypertrophy. **E.** Eccentric hypertrophy.
4. Hemorrhagic stroke and left side hemiparalysis developed in patient with hypertension. In some time movements partially recovered. What leaded to that?
A. Complete regeneration of cerebrum cells. **B.** Hyperplasia of preserved neighbor ganglionic cells. **C.** Hypertrophy of preserved neighbor ganglionic cells. **D.** Peripheral nerves regeneration. **E.** Skeleton nerves regeneration.

Answers to test tasks.

1.D. 2. B. 3. C. 4. C.

Illustration to theme

Figure. 1 – Adhesive pericarditis. It is seen on longitudinal section that epicardium is thickened and is connected with pericardium, by commissures. This process is the result of serofibrinous or fibrinous exudates organization. Sometimes conjunctive tissue calcified which considerable impedes heart work. This heart is called "stone heart".

Figure 2 – Concentric hypertrophy of heart. On horizontal section of the heart it is seen thickened wall of the left ventricle and interventricular septum, ventricle lumen is concentrically narrowed.

Figure 3 – Eccentric hypertrophy of the heart. Enlarged lumen of right ventricle is seen on the heart horizontal section.

Figure 4 – Postinfarction cicatrix of myocardium. In the stratum of cut myocardium grey-white cicatrix focuses are seen, substituting injured cardiac hystiocyte on substantial area of transverse section. Give an explanation of this process.

Figure 5 – Pulmonary emphysema. Lung is of pale-grey color, large blisters structure as the result of acinuses' inflammation.

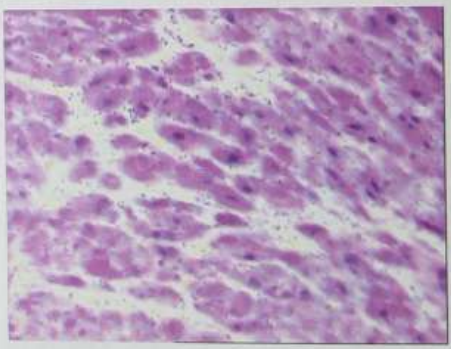


Figure 6 – Myocardial hypertrophy. Specimen is colored with hematoxylin and eosin. Cardiac hystiocytes' sarcoplasma is enlarged in volume. Nucleus are enlarged, hyperchromic, their contours are saw-edged. Excessive development of stroma.

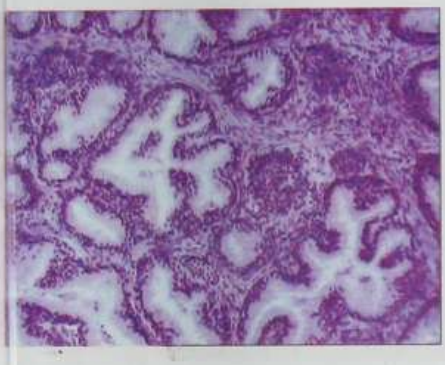


Figure 7 – Prostate gland hyperplasia. Specimen is colored with hematoxylin and eosin. Hyperplasia of glands is observed. Their contours are stellate. Stroma is excessively developed, infiltrated with lymphocytes.

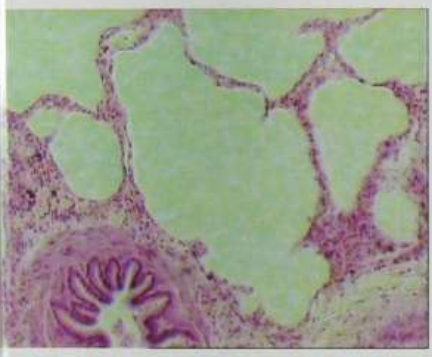


Figure 8 – Pulmonary emphysema. Specimen is colored with hematoxylin and eosin. Bronchiole is in spasm condition. Alveoli lumen is enlarged. Alveolar septums are thinned, straightened.

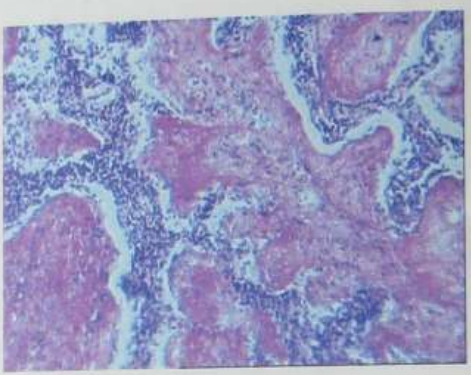


Figure 9 – Lung carnification. Specimen is colored with hematoxylin and eosin. Inflammatory exudate invades with conjunctive tissue in alveoli lumen. Also granulation tissue growing-in from alveoli thickened walls side takes place.

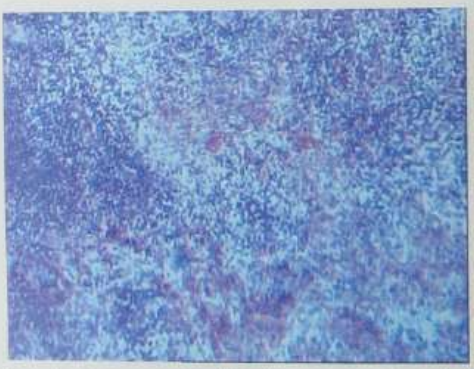


Figure 10 – Granulation tissue. Specimen is colored with hematoxylin and eosin. A lot of capillaries overfilled with blood can be seen in specimen as well as a number of cells: fibroblast /elongated shape/, eosinophils, lymphocytes, neutrophilic leucocytes, situated between immature collagen fibers' layers.

Figure 11 – Cicatrix. Specimen is colored by Van Gizon method. Tissue is represented with fibrous conjunctive tissue. Vessels are sclerosed.

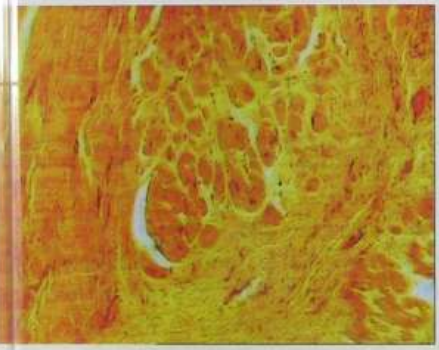


Figure 12 – Big space-occupying cardiosclerosis. Specimen is colored by Van Gizon method. Big focuses of conjunctive tissue excrescence could be seen between cardiac hystiocytes and on the places of dead muscle fibers.

Concept module 4 Tumors
Lectures – 4 hours
Practical classes – 10 hours
Student's self-work – 11 hours
Form of student's individual self-work – thesis or library-research papers

Specific objects:

- *To interpret up-to-date ideas of malignant and non-malignant growth etiology (carcinogenesis) and pathogenesis.*
- *To interpret pretumor (precancerous) conditions and changes, their essence and morphology.*
- *To interpret general morphological and clinical features of malignant and non-malignant growth.*
- *To interpret malignant cell features, types of tumors growth.*
- *To interpret tumors' morphogenesis and hystogenesis.*
- *To explain metastasis mechanisms (metastatic cascade) and ways.*
- *To make conclusions regarding antitumor immunity peculiarities.*
- *To explain the most important clinicopathologic presentations of tumor growth.*

Practical class 12

Theme 14 Tumors, general data. Malignant cell features. Molecular fundamentals of carcinogenesis. Antitumor immunity. Non-malignant (benign) and malignant growth. Tumors morphogenesis and hystogenesis.

Importance of the topic: Oncologic processes are pathological states, which are associated with disturbances of structure and function in organisms and may lead to death. The term

eoplasia" means new growth; the new growth produced is lled "neoplasm" or "tumor". However, all "new growth" is t neoplasms since examples of new growth of tissues and lls also exist in the processes of embriogenesis, regeneration repair, hyperplasia and hormonal stimulation. Neoplastic lls loose control and regulation of replication and form an normal mass of tissue. Research of the etiology, chanisms, morphology, secondary appearance of the tumors important task in the practical medicine because it may help diagnose and treat these diseases. In clinical practice the owledge of the oncomorphology is necessary for the mparison of the clinical dates with the result of the biopsy search and postoperative materials, and also for the clinic-tomical analysis of the autopsy.

pose: Receive the notion about the essence of tumors and principle of their classification. Learn the etiology, rphogenesis, growth; morphological features of epithelial iors and estimate the outcomes (complications) and ermine their significance for organism.

cific aims: 1. Explain the role of the oncologic processes in anism.

2. Know the definition of neoplasia and terminology.

3. Know the histogenic classification of tumors and the rphological classification based on differentiation of the mor cells.

4. Know the terminology of tumors.

5. Tell apart the benign and malignant tumors.

Basic matters for self-work

Introduction to oncomorphology. Role of biopsy gnosis in oncology.

mors etiology and pathogenesis. Modern theories of erogenesis. Tumor growth risk factors. Aging of human g. Geographic zones and environmental factors influence.

Heredity: heredial tumor syndromes, family forms of neoplasia, syndrome of DNA reparation disorder. Tumor growth risk factors. Pretumor (precancerous) conditions and changes, their essence and morphology.

Molecular grounds of carcinogenesis. Cellular oncogenes, oncogenes' protein products. Proto-oncogenes: range, characteristics, detection in human tumors. Growth factors, growth factor receptors, nucleus regulating proteins participating in signals transduction role in oncogenesis. Mechanisms of oncogenes activation. Mutations. Chromosome translocations. Genes amplification. Genes – oncosupressors. Molecular grounds of carcinogenesis. Stages of carcinogenesis. Changes of karyotype in tumors (translocations, deletions, telomeres shortening, DNA ploidy change).

Carcinogenous agents and their interaction with cells. The most important groups of chemical carcinogenes. Radiation carcinogenesis. Viral carcinogenesis. Mechanisms, clinicopathologic implications.

Antitumor immunity. Tumors antigenes. Immune supervision. Antitumor effector mechanisms (cellular and humoral).

Tumor growth biology. Tumors morphogenesis. Malignant cells growth kinetics. Tumor angiogenesis. Tumors progress and heterogeneity. Features of cell population in tumor focus. Invasive growth mechanisms. Metastais (dissemination of tumor): types, regularities, mechanisms. Metastatic cascade.

Tumors. Definition. Scope and principles of classification. Malignant and non-malignant growths: variety, comparative charactristics. Tumors histogenesis (cytogenesis) and differentiation. Basic features of tumor. Tumor structure peculiarities, tumor parenchyma and stroma. Types of tumor

owth: expansive, infiltrating and apposition, exophytic and dophytic.

The most importamt clinicopathologic presentations of mor growth. Neoplastic (tumor) process charactristics. Local fluence of tumor. Organism homeostasis failure. Secondary anges in tumor. Metastases and systemic non-metastatic fluences. Malignant cachexia, paraneoplastic syndromes.

1 Pre-auditorium theoretical training

Tumors etiology. Carcinogen agents and their interaction ith cells. **It is ascertained fact that tumors can be caused h physical, chemical and biological agents which are called cancirogens**

Over 75% of human beings' cancirous diseseas are sed by environmental factors, and in first turn – by nical compounds. First experimental proofs of chemical pounds' carcinogenicity, were Yamagiva's and Ishikava's arches (1915). They induced rabbit's ear skin cancer by ying there coal-tar pitch for the period of 15 months.

Chemical cancirogens are wide-spreaded in invironment the majority of them are of antropogenous origin. Same we shouldn't exaggerate their role in human being ology as only about 100 compounds and manufacturing esses are acknowledged as carcinogenous for human ngs.

By their chemical structure carcinogens are divided into eral groups. The most important of them are as follows: a) cyclic aromatic hydrocarbons; b) aromatic amine and des; c) nitrosoamines and nitrosoamides.

First group consists of over than 200 substances with e and more benzene rings. Only one of them, namely 3,4-nzpyrene considered to be the one able to cause cancerous ases of human being. The others cause tumors only in

experimental animals. The biggest amount of this group of carcinogens is in tobacco fume, exhaust gases of automobiles, blast furnaces smoke, asphalt, waste of chemical plants, dried and overdone food.

Substance of polycyclic structure shows mostly local carcinogenous influence. In case during experiment they are applied on skin cancer occurs, in case they are applied under skin – sarcoma occurs. Polycyclic aromatic hydrocarbons are excreted by various organs of organism, so tumors of these organs occur – kidneys, skin, mammary glands.

The second group of carcinogens are mostly azo dyes, for which two or more azo groups presence is charactristic (mono-azobenzene, 2- naphthylamine, benzidine). These substances are used to color natural and synthetic fibers, in printing industry, cosmetics, color photography, to synthesize medicines, insecticides. Cancirogeneous action of amines and amides becomes apparent when they are introduced in digestive tract, subcutaneous or in case they are applied on skin. Tumors appears in organs far from the place of application, the most often in liver, urinal bladder, bowels, kidneys.

Nitrocompounds (nitrosoamines and nitrosoamides) are characterized with alkyl radical presence. They are utilized as antioxidants, pesticides, paints solvents, semi-products under paints, medicines and polymers synthesis. Their cancinogenity for human being is nor proved but experimental data causes oncologic alertness. Possibility of nitrocompounds synthesis of nitrites, nitrates, nitric oxide in human being's intestinal tract is proved. Nitrites are widely used as conserved agents for foodstuff.

Practically all chemical substances are not carcinogenic as they are. They acquire these features after coming into organism and are subject to metabolic transformations. Here is the origing of idea of final carcinogens which are able to

teract with cells macromolecules – DNA, RNA, proteins. king into consideration role of DNA in heredity information nsfer the most attention is focused to carcinogens' binding actly with this acid. A number of products were found nich made possible to decode fine mechanisms of final rcinogens interaction with DNA. They mostly methylate anine and affect purine bases complementary character – stead of normal combination guanine - cytosine ramethylated guanine – hymine is created. So, carcinogens use point mutations in certain DNA positions. In case these tations refer to transforming genes, i.e. oncogenes a chain of ents starts causing malignization.

Radiation carcinogenesis. Physical carcinogens includes izing radiation and to a lesser extend – ultraviolet rays. izing radiation acts indirectly, through highly active free icals distorting DNA structure. Ultraviolet rays prevent its aration.

Viral carcinogenesis. There are various biologic agents e to cause malignant growth. The biggest group consists of uses. Indisputable proofs were acquired regarding viral gin of many animal tumors – hens' Rous sarcoma, rabbits' ope fibroma and papilloma, mice mammary glands cancer rus is transferred through milk). The quantity of human ngs' tumors which are indoubtfully caused by viruses is not – Burkitt's lymphoma, rhinopharyngitis cancer, carcinoma uterine cervix.

Viruses causing tumors are called oncogeneous. They divided into two groups depending of genome's molecular icture - RNA-containing and DNA-containing. Major up consists of RNA oncogenous viruses, forming the group retroviruses. Their mutual charactristics is the fact that their nom is of one chain RNA, and that they have ferment RNA-endent DNA-polymerase (invertible transcriptase, vertase). The essence of virus inducted carcinogenesis adds

up to the fact that oncogenous viruses introduce their own genome in infected cell, this genome contains transforming gene – viral oncogene. Its activity product (oncoprotein) starts cell transformation and keeps it in transformed condition.

Retroviruses are the major cause of human's malignant growths, however they point the way to understand basic mechanism underlies this diseases. They became model system by means of which the most modern data was received of fine molecular distortions occuring under cellular transformations.

All above said allows to make major conclusion: tumor starts from DNA damage. This mechanism is obligatory for all tumors irrespectively what carcinogens caused them – chemical, physical or biological. All of them are carcinogens exactly because of the fact that they are able to cause genetic apparatus failures. Chemical agents cause mostly point mutations, ionizing radiation – mostly chromosome mutations and retroviruses introduce to DNA molecule additional genes and oncogenes are among them. In such a way DNA damages could be treated as molecular grounds of all further processes tranforming normal cell into transformed cell. In the other words DNA damage is common denominator to which the action of all known carcinogens is reduced.

Pathogenesis of tumors. Molecular grounds of cancerogenesis. The question arises: what kind of DNA damage is realized into tumor? The answer to that is not at all simple. Based on modern knowledge scientific theory was formulated which is known as oncogene consept. It combines all forms of carcinogenesis (chemical, physical and viral) into one universal mechanism. There are really many causes of cancer, but all of them similar to water through watering-can should pass through one critical channel – DNA and leave trace in it, meaning damage. This damage is specific. It will lead to normal cell transformation into malignant cell

ranformation phenomenon) only in case it localizes not at any ndom DNA portion, but exactly in the portion where genes ntrolling cells growth and differentiation are situated. These nes are called cellular oncogenes or *proto-oncogenes*. ney are usual components of cellular genome and are solutely necessary for cell's vital activity. Cellular oliferation would be impossible without proto-oncogenes.

It is considered that under minor damages normal nction of cellular oncogenes as auxesis could be keept in inciple, but it stops to subordinate controlling influences of e cell itself. Normal controlled process of growth and turing is lost and is interchanged with an endless process of llular divisions under which cells do not have time to ferentiate meaning to mature to condition when they are e to fulfill approprite specialized physiologic functions. It nes out that cell from its creation beginning hides the outs of its own death in the form of cellular oncogenes.

Right now nobody denies that normal cellular oncogenes ler specific conditions could activate and cause malignant wth. Several ways of their activation are differentiated. e of them is viral transduction, in other words cellular cogenes passage through viral genome. It is proved that roviruses damage DNA by the way of introduction to it so led viral oncogenes. It was found that they are of cellular gin. They are proto-oncogenes which on the certain stage of olution were deported from infected cell nucleus by viruses l included into self-genome. Starting from that moment they ame viral oncogenes. Right now over 20 of them are wn. All of them have cellular counteracts in various omosomes.

Viral oncogens coming into cell for the second time aves uncontrolled. The point is that they structurally differs their cellular ancestry. Retroviruses, as a rule, capture ular gene incomplete, without repressor genes, so similar

viral oncogene keeps ability to stimulate cells growth and differentiation but loses regulator (operator) genes and becomes uncontrolled. It causes unlimited non-corresponding organism's needs cells division. Cellular oncogene itself also is subject to structural changes at its capture by retrovirus. This makes difficult regulative influences on it by resprssor genes as well as by epigenome cellular regulators. Thus, viral transduction deprives cellular oncogenes their primary positive function of growth stimulators and simultaneously releases their hidden transformation abilities. Growth and proliferation genes starts to function as cancer genes.

Cellular oncogenes activation can occur in the result of chromosomal translocations. It was noted that under certain forms of tumors chromosome discontinuities take place exectly in those portions where cellular oncogenes are situated.

It was clarified that certain tumors, for example, Burkitt's lymphoma occurs when any foreign (viral) genetic material inserts into DNA molecule close to proto-oncogene, even if this material doesn't include oncogene. Viral DNA built-in close to cellular oncogene activates it up to cancer level of expression. This mechanism is called insertion.

As a rule, cellular oncogenes are represented in DNA in one copy but it was proved that copies quantity can increase in the result of DNA replication abnormality. This phenomenon is called *amplification* (augmenting). Cellular oncogenes copies amount increase causes enhanced division of cells. This mechanism acts in human neuroblastoma and carcinoma of large intestine creation.

Anyway, point mutations independently of their cause are considered to be major mechanism of proto-oncogene transformation into active cancer oncogene. It is proved that that's enough to change in human urine bladder cancer only one base – guanine for the other one - thymine as inactive proto-oncogene becomes transfomating. Totality of scientific

leas of mutations' decisive force in tumor etiology forms the rounds of mutation consept of cancerogenesis.

Epigenome concept adds up to the fact that the grounds f normal cell transformation into malignant one are not enetic apparatus' structures changes, but persistent failures in enous activity regulation. The genes which should be pressed are disinhibited and those which should be active e clocked. Cell loses its specificity, becomes insensitive to gulative influences of the whole organism.

Stages of cancerogenesis. Tumors occurrence and rogress is multistage process. There are three main stages – snformation (initiation), promotion and progression. Proto-ncogene activation finishes first stage – stage of initiation. ain feature acquired by the cell in the result of proto-ncogene transformation into oncogene is immortalization, eaning its potential ability to endless division, to immortality. owever active oncogene presence is only potential ssibilitity for expression. Cell with active oncogene could y for years in latent (delitescence) state, doesn't expressing elf in any way. Immortalized cell needs additional influences ing it out of latent state and give a stimulus to endless vision.

Tumor growth risk factors. These provocative factors uld be additional doses of chemical or physical ncerogenes, retroviral superinfection as well as various ents which do not cause tumors as they are, but are able to e immortalized cells out of latent state. Here starts old idea super multicauses of tumor growth however in reality solute majority of the factors attributed etiologic role should considered among promotional conditions causing pression of latent, potentially cancerous, cells. Factors ivating pre-cancerous cells are called *promoters*. Under their fluence trasnformed cells go into new stage of development –

promotion stage for which cellular oncogenes expresssion is charactristic.

Provided that the fact of oncogenes participation in oncogenesis is not under the doubt at the moment, mechanism of their action is still a mystery. It was ascertained that oncogenes code specific proteins (oncoproteins), most of them having tyrosinase activity. Further on it was found that oncoproteins which cause uncontrolled growth of malignant cells are similar to usual growth factors – thrombocyte growth factor, epidermal growth factor, insulin-like growth factors. Under the normal conditions growth factors comes into cell from outside providing cell dependability from organism. Malignant cells differs with the fact that they produce growth factors by themselves. A part of them is aimed to support their own proliferation (autocrine secretion), and the other one – for other type cells (paracrine secreation).

Progression is the final phase of tumor progress. Under this term persistent, irreversible qualitative changes of tumor to malignization are understood. For example hormone-dependent neoplasms became hormone-dependent, tumor reacted medicines stoped to react them. Progression is the last and the most long lasting stage of tumor progress lasting up to organism death.

The most important clinicopathologic implications of tumor growth. Interrelations between tumor and organism. Tumor negative influence on organism depends on its type (non-malignant or malignant), localization, speed of growth and directions of metastasis. Tumor directly injures organ in which it progresses disturbing its structure and functions. Surrounding organs are subject to atrophy and deformation, lumens of cavity organs narrows. Due to chronic intoxication with decay products and insufficient feeding cachesia develops. Hematosis depression, excessive hemolysis and chronic hemorrhage cause anemia.

In case tumor consists of hormone-active cells deseases ccur connected with corresponding hormone hyperproduction paraneoplastic syndromes of endocrinopathy, neurological pects (dementia, neuropathy), skin implications, matologic implications (hyper coagulability of blood, emia, thrombocytopenia, polycythemia). heocromacytoma (cancer of adrenal glands cerebral layer, oducing adrenalin) causes arterial hypertention progress, sulinoma (tumor of islet of Langerhans β-cells) causes poglycemia, gastrinoma (pancreatic tumor producing gastrin astric secretion stimulator) causes stomach ulcer.

Tumors structure. There are various tumors by their cro- and microscopic structure. Their appearance can nind mushroom, cauliflower, node or intumescence. In tion tumors are mostly of white, grey and red color. The lowing is often found in them: hemorrhages, necrosis and ts cavity of which is filled with mucus or bloody mass. me tumors are of brown color, for example, melanoma.

Tumor size depends mostly of its origin, location and wth period. In some cases they can reach giant sizes roid tumors) in the other cases they can be seen only ough magnifying glass or microscope (microcarcinomas). mors localized close to vitally important centers as a rule are rather small size.

Tumor consistency is defined first of all by the type of going tissue and ratio between stroma and parenchyma. mors of bone (osseous) tissue, cartilage tissue and fiber njunctive tissue are of dense consistence. Malignant growth epithelium in which stroma is underdeveloped are flaccid d by their consistence they are similar to new-born child's in (cancer-brainer).

Stroma and parenchyma are seen microscopically in each nor. Parenchyma is its specific part which is represented by lignant cells and determines tumor place in hystologic

classification. Even in tumors originating from mesenchyma cells producing intercellular substances (collagen fibers, basic substance of cartilage or bone tissue) are also should be treated as parenchyma. Stroma is mechanical-trophic framework including conjunctive tissue, blood and lymph vessels and nerves.

Most of tumors look like organ by their structure, i.e. have parenchyma and completely represented stroma. Such tumors are called *organoid*. In undifferentiated tumors parenchyma prevails and stroma is underdeveloped. They are called *histioid*. Blood circulation insufficiency causing necrosis easily occurs in them. At the same time there are tumors poor with parenchymatous elements and rich with stromal, for example gastric fibrocarcinoma or sceirrhous. These tumors cause complications due to stroma's corrugation. They deform organ or narrow its lumen.

Tumor corresponding structure of the organ it is localized in is called *homologous*, and the one which structure differs from this organ structure is defined as *heterologous*. In case tumor is developed from the cells of organ in which it occurred – this is *homotopy* tumor. In cases it occurs from the cells of embryonal displacement (heterotopia), it is called *heterotopic*, for example tumor of bone marrow in uterus.

Tumor (new growth, neoplasm, blastoma) is typical pathologic process in the form of excrescence of tissue subject to genetic apparatus change, characterized with potential infinity of its uncontrolled growth as well as structural elements' atypicity.

Biology of tumor growth. Universal and mandatory feature of all the tumors – both non-malignant and malignant – is their ability to endless growth. This is fundamental feature of any tumor. Uncontrolled excessive proliferation of malignant cells doesn't mean at all that they divide faster than homologous cells of healthy tissue. Vice versa, certain healthy

issues grow much more faster than the most malignant rowth, for example, embryonal cells, regenerating liver. In uch a way, malignant cells proliferation differs from normal ells proliferation not with cells division and growth speed, but n the character of division and growth.

Infinity of malignant cells growth is based on the fact nat they are unable to exhaust division resource. It is found nat genetic program limiting its divisions quantity is integrated nto each cell. As a result of genetic somatic mutation nalignant cell losses this restrictive program and starts to ivide "endless", escaping aging up to the death of host rganism. In case these cells are carried from living organism the other one of the same species, they will settle down and gain will divide up to the death of recipient organism. In case ese cells are carried to nutrient medium, there they will also ivide endless times, in the other words they become ndependent of Heiflic's rule. This ability of malignant cells to dless division is dominantly propagated to further cells neration.

Malignant cells life could be kept artificially. There are o methods to provide that: transplantation – tumor oculation from one animal to the other one of the same ecies and explantation – malignant cells cultivation on utrient medium. Tumor kept for a long time with ansplantation or explantation method is called tumor strain. rst transplantation strain was made in 1905 (Ehrlich's rcinoma in mice), first explantation - in 1950 (Hela's cells – rcinoma of uterine cervix).

Malignant cell has one more feature – uncontrolled owth. On the level of the whole organism tumor growth is ntrolled with nervous and endocrine systems, and on the cal level – with mitogens and keylones. Malignant cell gets t of this hand, that is shows autonomy, independence of owth. It's clear that this autonomy is not absolute but in this

or that way is characteristic for all tumors. In case tumor partially keeps ability to come under control influence of hormones, it is called hormone-dependent tumor and in case it completely loses this ability - hormone-independent tumor. Autonomy doesn't mean that tumor lost any connection with organism. This connection changed. They can be characterized as relations between host organism and parasite tissue.

Third peculiar feature of malignant cells is *anaplasia*, which means their persistent dedifferentiation, loss of ability to form specific tissue structures or produce specific substances characteristic for normal cells. In the other words its return to embrional state, structural-chemical organisation simplification.

Tumor occurs from single parent cell subject to genous mutation. Malignant cells differs in several parameters from their common normal ancestor. This difference relates to cell's and its organoids' structure, metabolism, specific features and functions. Therefore morphologic, biochemical, physical-chemical, immunologic and functional anaplasia is differentiated.

The essence of *morphological anaplasia* comes to tissue, cellular and subcellular atypicity occurrence. Polymorphism is inherent to malignant cells – they acquire smaller as well as bigger size and shape which is not peculiar for normal cells. Interrelation between nucleus and cytoplasm is shifted in favor of nucleus due to its enlargement. Multinuclear cells, nucleus hyperchromatosis are observed caused by nucleic acids accumulation in them, nucleolus amount increase and their migration into cytoplasm, of subcellular structures mitochondrions are subject to most prominent changes. Their quantity and size are decreased, membranes became thinner, cristas also become thinner and disappear. At tissue level structures' created by malignant cells

ize and shape changes are observed. This referes for example o glandular follicles in adenocarcinomas and focuses of ssification in osteosarcomas. Sometimes tumor completely osses morphologic features indicating its origin from the ertain differentiated tissue.

Biochemical anaplasia is peculiar of malignant cells' etabolism caused by theirs genetic apparatus change. arcinogens are able not only to distort mitosis process and art endless division mechanisms, but also to supress or brake the other genes. As the result of that malignant cells zymatic range changes. Intracellular enzyme insufficiency curs - some enzymes are inhibited but the other ones tivate or start to synthesize absolutely new substances which dn't exist in normal cells.

It is found that all tumors, subject to progression start to ok like each other by their enzymes set independently of at cells they come from. Unification of tumors izoenzymal ge independently of their histogenesis is very characteristic nifestation of malignization.

It is known that every tissue synthesize enzymes specific it, where every enzyme is represented with strictly specific of isoenzymes. This specific feature is lost in tumors. So lled monotonization or isoenzymic simplification is veloped – amount of isoenzymes reduces and their set comes approximately the same for tumor of any origin. enzyme reconstruction goes in the direction of those zymes increase which are peculiar for embrional tissues.

The most peculiar biochemical features of malignant lls relate to proteins and carbohydrates metabolism. Proteins nthesis prevails their decomposition. To build own proteins mor captures aminoacides of the other organs ("tumor - trap nitrogen").

Carbohydrates metabolism and power of malignant cells significantly differ from the norm. In aerobic conditions normal cell provides itself with energy mostly at the expense of more advantageous glucose aplittance in Crabbs' cycle, and in anaerobic conditions – it is forced to change to glycolysis. In case amount of oxygen is sufficient, glycolysis is opressed with breathing (Paster's effect).

Malignant cell also provides its demands in energy on account of glycolysis and breathing, but correlative meaning of these processes is different. Peculiarities of tumors power supply are as follows: a) activation of anaerobic glycolysis and enzymes providing it - pyruvatekinase, hexokinase, fructokinase; b) presence of aerobic glycolisis for which normal cells are not able (exceptions – leukocytes, spermatozoon, eye retina cells); c) breath opression with glycolisis (Crabtree effect), to say exact – with powerfult system of glycolytic enzymes, which intercept substrates – inorganic phosphorus, coenzymes.

Among physical-chemical features of malignant cells the following should be emphasized: acidosis in the result of lactic acid accumulation, intracellular aquation, potassium ions accumulation, electroconductivity increase, colloids density reduction, membrane negative change increase, their surface tension decrease.

Antitumor immunity. Under *immune anaplasia* changes of malignant cell's antigene features is understood. These changes is the result of protein metabolism rebuilding. It is known that each tissue synthesize a set of antigenes specific for it. This set is changed in tumor. *Tumor antigenes*. Antigene simplification and antigene complication are differentiated. Antigene simplification is characterized with antigenes synthesized by malignant cell numerous times decrease.

Antigene complication is manifested with antigene divergence and antigene reversion. Antigene divergence

neans that malignant cells start to synthesize antigenes which re not characteristic for healthy cells, but these antigenes are sually synthesized by the other cells. For example hepatic mor can synthesize antigenes of spleen or kidneys. Tumor's ynthesis of embrional antigenes is called antigene reversion. enal carcinoma of human being synthesizes α- fetoprotein, hich serves as the test for its diagnosis. In the course of mor's malignization it strats to synthesize antigenes haracteristic for moire and more earlier stages of intrauterine volution.

Organism is not defenseless towards carcinogenes and ansformed (mutant) cells. It has strong defensive mechanisms roviding prevention of tumors occurrence or slow down their rogress. Here relates a system of carcinogenic compounds utralization and their evacuation through kidneys, digestive ict and skin. Organism clears of mutant cells due to immune rveillance function, peculiar to T-lymphocytes. System of donucleases exists providing damages oncogenes renewal d stopping synthesis of oncoproteins coded by them. Tumor owth is also influenced with hormones – insulin, adrenalin, pic hormones of hypophysis, gormones of thyroid gland and xual glands. This influence is ambiguous and depends on its mbination with the other mechanisms of antineoplastic fense.

Functional anaplasia is manifested with loss or stortion of function fulfilled by cell. In thyroid gland alignant cells' thyroid hormones synthesis can reduce or crease up to myxedema or thyrotoxicosis occurrence. lirubin conjugation is stopped in hepatoma (liver cell rcinoma). In some cases tumors start to synthesize the oducts not peculiar to them. For exmpale pulmonary and onchi tumors can synthesis hormonoform substances.

Secondary changes in tumor. Secondary metabolism orders can develop in tumors, like sliming, hyalinosis,

adiposity, calcification. Blood circulation functional insufficiency is characteristic for malignant growth as parenchyma always grows faster than stroma. Besides that, blood vessels are often thrombosed causing progress of necrosis on background of which ulcers, hemorrages, perforations occur.

Non-malignant growth and malignant growth. Tumors are not equivalent from the clinical point of view. Depending on the stage of differentiation, speed and character of growth, inclination to metastasis and recurrence, secondary changes in tumors, their influence on organism, they are distributed into non-malignant, malignant and the ones with local destructive growth.

Non-malignant or mature tumors are built of cells from structure of which it is always could be determined from what tissue they grow. In case they do not locate near vital important centers they are manifested with local changes and their influence on organism is minor. But these tumors can transform into malignant ones – malignizate.

Malignant (immature) tumors are built of low-differentiated or nondifferentiated cells which lose structural similarity to cells they originate from. Apart from non-malignant tumors they give metastasis, recur, manifest themselves with local changes and influence on the whole organism non-transforming into differentiated forms.

Tumors with local destructive growth occupy intermediate position between non-malignant and malignant. They have the features of infiltrating growth, but do not metastasis. These are hemangioma, desmoid tumor.

Basic differential features of non-malignant and malignant growth

Characteristic of non-malignant and malignant growth	
Non-malignant growth	Malignant growth
lave minor deviations from arent tissue	Expressed atypism: tissue and cellular
xpansive growth	Infiltrative growth
row slowly	Grow fast
each big size	Rear rich big size
are are subject to ulceration	Often are subject to ulceration
o not give metastasis	Metastasis
ecurrence is not characteristic	Recur often
inor influence on patient's neral condition	Have major influence on the whole organism subject to ulceration

Tumors' growth and spread in organism. Depending on ferentiation level the following forms of tumor growth are ferentiated: expansive, opposition and infiltrative vasive). First form is peculiar for non-malignant growth, and cond and third – for malignant ones.

Tumor which grows *expansively* increases as a node, oving aside surrounding tissues. Cells surrounding it atrophy d stroma is subject to collapse causing pseudocapsule rmation and sharpness of tumor boarder.

Opposition growth is intermediate between expansive d infiltrative. Tumor grows from multiple spots of growth – cal proliferates forming "tumor field". Tumor transformation alignization) is done consequentially from the center to ripheria and is finished with malignization focuses fusion o single node.

Infiltrative growth is characterized with tumor elements spreading into the least resistance directions and ingrown surrounding tissues destructing them. Tumor boarder in this case is indistinct, worn down.

In respect to organ's cavity *endophytic* and *exophytic* growth are differentiated. Pre-invasive or intraepithelial neoplasia is observed as specific form. Hystologically epithelium displasia of epithelium, atypism are found, its normal distribution into layers disappears, but basal membrane is not injured.

Tumors which grow expansively do not spread out of organ's boarder. In case infiltrative growth tumor spreads not only inside the organ but also out of it. Continuous contact tumor spread and metastasis are differentiated.

Continuous spread is tumor ingrowth into neighbour tissues. Under infiltrative growth malignant cells can reach serous tunic where reactive inflammation occurs and excudate organization is ended with commissure formation with neighbour organs. Through commissures tumor ingrow these organs (for example gastric carcinoma grows into liver or pancreas). In case cavity organs coalescence, fistulas formation is possible due to continuous spread and necrosis. Coloenteric fistula, for example, is observed in case gallbladder carcinoma.

Metastasis (dissimination) is malignant cells transfer from primary focus into distant parts with their further settle down and secondary focuses creation. Several ways of tumor dissemination exists: hematogenic, lymphogenic, perineural, implant, mixed.

Hematogenic metastases occur when malignant growth's cells come into blood circulation system and moves by venous or arterial blood stream. Spreading through veins is the most often way of metastasis. In this case two possible directions exist: first is through vena cava system when malignant cells from primary focus (uterum, kidney, skeleton bones) are

ansferred into lungs, and the second one - through portal ein, when gastric, intestine carcinoma, tumor of pancreas etastasis in liver. Sometimes paradoxical and retrograde etastases are possible. Arterial way of metastasis relates, in e first turn, primary focus localized in lungs. At it metastasis to cerebrum, bone marrow, liver and other organs are ssible. Hematogenic way of metastasis is most peculiar to rcomas.

Lymphogenic metastasis is malignant cells transfer into gional, and further on – into distant lymph nodes. Later on alignant cells come into blood circulation system through oracal lymphatic vessel.

Perineural metastases could be better characterized as an ample of endless spread. Cells are disseminated through rineurium fissures.

Implantation metastasis is called tumor extension ough serous cavities or natural channels. When serous tunic invaded with malignant cells, they can come off and seminate in serous cavity. In case conditions are favorable, y settle down and new focuses occur – implantation tastases. Macroscopically these metastases look like white ques or humps. At that hemorrhagic inflammation occurs. plantation metastases should be differentiated from mphogenous metastases (carcinoma of pleura, peritoneum) hen similar humps are formed downstream lymphatic vessels. uite rare *intracanalicular* extension occurs. For example, alignant cells of bronchi, esophagus, pharynx oimplant into ucus tunic of little bronchi, ventricle, bowels and cause new mors occurrence. Implantation metastases also include binoculated metastasis (malignant cells transfer with rgeon's hands and surgical tools) and contact metastasis ansfer from one organ to the other one, for example from brum to labium).

Metastase cells have parent tumor structure and function. Intensity of metastasis depends on the stage of tumor differentiation and immunologic reactivity of organism. There is no correlation between tumor size and metastasis intensity. Malignant growth is able to metastasis from the moment of its occurrence. Metastases size often exceed parent tumor's size. Most of cells die when transferred to the other place, so metastases could stay latent for a long time.

Recurrent tumor is repeated occurrence of the same tumor by its features in the place of removed or treated tumor. Both non-malignant and malignant tumors recur, the latter - more often.

In clinical picture the following is differentiated: *pretumor* conditions (diseases at which the risk of tumor progress is increased) and precursors of cancer (histologic ";abnormalities" of tissues). They are classified in the following types: a) pathologic regeneration an example of which can be chronic bronchitis with epithelium metaplasia, mucus tunics' leukoplakia, chronic atrophic gastritis, chronic stomach ulcer, subacute skin ulcer; b) chronic proliferative inflammation, first of all polyps of ventricle and large intestine; c) dishormonal diseases – proliferative mastopathy, glandular hyperplasia of endometrium, endocervicitis, prostatic hypertrophy; d) tissues development abnormalities – teratomas, nevus pigmentosis and birthmarks.

Pretumor processes shouldn't be connected with etiology. Pretumor changes presence do not mean at all that tumor will occur on their ground. So by cancer threat level they are distributed into optional (under which cancer develops rarely) and obligatory (under which cancer develops rather often).

At practical work it is necessary to know from what tissue tumor originates, in other words to make clear its histogenesis. In case tumor is built of differentiated cells keeping similarity to the parent one, its relatively easy to be

one. In case undifferentiated cells prevail, histogenesis nderstanding faces with difficulties, sometimes it even ecomes impossible.

umors classification. Terminology. Modern classification is uilt by histogenetic principle taking into consideration orphologic structure, localization, structure features in rtain organs (organo-specificity), non-malignancy or alignancy. Tumor name ends with 'oma" (mioma, fibroma). alignant epithelium growth are called "cancer", esenchymal – "sarcoma", tumors of embrional tissues – lastoma", of several embryonic leafs - "teratomas". Some nors are called with the name of the author described them – posi's sarcoma (angiosarcoma), Wilms' tumor phroblastoma). International TNM system is used in respect tumor process extention, where T(tumor) – tumor racteristic, N(nodus) – presence of metastases in lymph les, M(metastasis) – presence of distant hematogenous tastases. Seven groups of tumors were differentiated nbining over 200 names:

a) epithelial tumors without specific localization gano-nonspecific);

b) organospecific epithelial tumors;

c) mesenchymal tumors;

d) tumors of melanin creating tissue;

e) tumors of nervous system and cerebral mbranes;

f) tumors of hematopoietic and lymphoid tissue;

g) teratomas .

Practical class 13

Theme 14. Nomenclature of tumors from tissues which take place from a mesenchyma. Morphological features of tumors from tissues which take place from a mesenchyma.

Specific objects of module:

- *To interpret general characteristic of mesenchimal tumors.*
- *To analyze morphologic characteristic of non-malignant growth from mesenchyma.*
- *To analyze morphologic characteristic of malignant growth from mesenchyma and the ways of sarcoma metasasis.*

Importance of the topic:. mesenchymal tumors are widespread ones, which have very important significance. These tumors have different localization in mesenchymal tissue; it may lead to secondary changes. All sarcomas have hematogenous metastasis and can become the cause of death. Research of the etiology, mechanisms of the development, morphology, secondary appearance of the mesenchymal tumors can help timely to diagnose and treat these diseases. In clinical practice the knowledge of the oncomorphology is necessary for the comparison of the clinical dates with the result of the biopsy research and postoperative materials, and also for the clinic-anatomical analysis of the autopsy.

Purpose: Receive the notion about the essence of mesenchymal tumors and the principle of their classification. Learn the pretumorous processes, growth, and morphological features of mesenchymal tumors. Estimate the outcomes (complications) and determine the significance for organism.

Specific aims: 1 Know the terminology of the mesenchymal tumors.

2 Explain the role of this oncologic process in organism.

3 Know the histogenic classification of mesenchymal tumors and the morphological classification, based on differentiation of the tumor cells.
4 Tell apart the benign and malignant mesenchymal tumors.
5 Learn the morphology and functional manifestations of the benign mesenchymal tumors.
6 Learn the morphology and functional manifestations of the malignant mesenchymal tumors.

Basic matters for self-work

General characteristic of mesenchymal tumors. Non-malignant growths from mesenchyma: of conjunctive tissue (fibroma and dermatofibroma), of adipose tissue (lipoma, hibernoma), muscular tissue (leiomyoma, rhabdomyoma, granular cell tumor), clodd and lymph vessels (hemangioma, glomus-angioma, pericytoma, lymphangioma), synovial membrane (synovioma), mesothelial tissue (mesothelioma), osteous and cartilage tissue (osteoma, chondroma). Malignant growths from mesenchyma. Sarcoma, its types. Ways of sarcoma metastasis.

1 Pre-auditorium theoretical training

Mesenchymal tumors are tumors growing from tissues derivative mesenchyma: conjunctive, adipose, muscular, vascular, osteous, cartilage tissues, synovial membranes and serous tunics. These tumors do not have organ specificity and are found not as often as epithelial tumors.

Non-malignant (benign) tumors of conjunctive tissue: fibroma (hard, soft) – is found in skin, ovaries, extremities, grow slowly, expansively; fibrous histiocytoma or dermatofibroma – is found in skin, subcutaneous fat; fibromatosises (desmoid), which have local-destructive infiltrative growth, but do not metastasis, occurs downstream

fascias, angioneurosises. Non-malignant growths of *adipose tissue*: lipoma (fibrolipoma, angiolipoma, myelolipoma), hibernoma – tumor of brown fat. Non-malignant growths of *muscles*: leiomyoma – tumor of smooth muscles, the most often occurs in uterus; rhabdomyoma – tumor of transversal striated muscles, occurs mostly among children; granular cell tumor or Abrikosov's tumor localizes in tongue, skin, esophagus.. Non-malignant tumors of *vessels:* hemangiomas, including capillary angioma, cavernous angioma, glomal angioma (Barre-Masson tumor) – occurs on toes and fingers, non-malignant hemangiopericytoma, lymphangiomas. Tumors of *synovial membrane* are represented with synoviomas, which most of the authors attribute to malignant independently of morphologic structure. Among *mesothelial tissue* tumors the most often fibrous mesothelioma is seen. Osteous tumors include osteoma spongiosum and compact osteoma. Cartilage tissue tumors – chondroma – could be of two types: ecchondromas and enchondromas, as well as non-malignant chondroblastomas. Mesenchymal origin tumors include also giant-cell tumor.

Malignant growths of mesenchymal origin are called sarcomas from Greek word sarcos – meat and are found rarely. On the section tumors are of whitish-grey color, look like fish meat, these tumors metastasis mostly in hematogenous way. Fibrosarcoma occurs of conjunctive tissue, which depending on cataplasia level could be differentiated and poorly differentiated, as well as malignant histiocytoma. Malignant tumors of adipose tissue – liposarcomas and malignant hibernomas grow rather slowly and do not metastasis for a long time. Among liposarcomas the following are recognized: high differentiated, myxoid, round cell polymorphonuclear sarcoma. From muscles malignant leiomyoma, malignant granular cell tumor and malignant rhabdomyoma occurs. Malignant growths from vessels – angiosarcomas develop from endothelium and pericytes – malignant hemangioendotelioma

hemangiopericytoma, lymphangioendotelioma, Kaposi's sarcoma. In joints malignant synoviomas are found, in peritoneum, pleura, pericardium – malignant mesothelioma. In bones osteogenic and osteolytic sarcomas develop as well as Ewing's sarcoma, and in cartilage tissue - chondrosarcomas.

II Algorithm of practical work

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

1 *Lipoma*. Tumour is large, yellow colour, large – lobar structure, contours of tumour are clear. What is the histogenesis of tumour? What is the influence on organism?

2 *Fibroma of skin*. (expansive growth of benign tumour). There is tumour of round form, 4-5 cm in diameter, with the clear contours of grey colour, in hypodermic cellulose. It is seen on a cut, that tissue fibred structures are located chaotically, with frequent turbulences.

3 *Osteosarcoma of thigh*. It is seen on the transversal sawing of thigh that a thigh bone is fully destroyed. Tumor germinates in adjoining muscles, destroying them. Contours of tumour are not clear. What is the histigenesis of tumour? Where will metastases be located?

4 *Fibromyoma of the uterus*. Uterus is enlarged. Node with clear boundaries, greyish – white colour, fibred structure is seen in myometrium. Definite contours testify to expansive growth, tumour is surrounded by a pseudocapsule which is formed from myometrium. To the extent of growth smooth muscle cells atrophy from pressure, and stroma is hardening, forming capsule around tumour. Fibred structures are located chaotically, with frequent turbulences in tumour, unlike their location in surrounding myometrium. It is the first sign of tissue atypicalness. There are considerably more connective

tissue (white areas) in tumour comparative with surrounding myometrium. It is the second sign of tissue atypicalness. So, benign tumour with expansive growth is represented in macropreparation. Histogenesis is cells of smooth muscle and connective tissue of myometrium

5 *Fibrosarcoma of upper extremity.* Excrescence of tumour without definite contours, grey colour with areas of necrosis is seen on the cut of tissues of upper extremity tumour has dense consistency, tissue of tumour is fibred. Fibred structures are located chaotically, with frequent turbulences and necrotic changes.

6 *Cavernous haemangioma of liver.* Numerous cavities of different size and form, which are filled with blood are seen on cut of liver. Blood cavities have clear contours, somewhere continuous blood fields appears

7 *Chondroma of lung.* Greyish – yellow colour tumour with clear boundaries, dense consistency, is seen on a cut in upper part of lung.

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

1 *Cavernous haemangioma of liver.* Formaton, represented by channels (caverns) of irregular form with connective tissue thin partitions between them, is in the liver tissue. Internal surface of caverns is lined by endothelium. There is blood in the clearance. Designate: 1-cavernous vessels, 2-endothelium, 3-hepatocytes.

2 *Fibromioma of skin.* Preparation is stained with haemotoxilin – eosin. Mature tumour of fiber connective tissue appears in any age and at persons of both sex. It has histoid type of structure. Consists of cells of type fibroblats and fibrocytes. Cells located between collagen fibers, which form bunches. Only prolonged, with thick chromatin, nuclei are seen. In deep of fibroma there are less cells those on peripheries. It testifies

to tendency of tumour to become maturel. Designate: 1-collagen fibers, 2-fibroblasts.

3 *Leyomyoma of uterus*. Preparation is stained after van Gizons` method. Connective tissue is stained in red colour, parenchyma (smooth muscular fibers) in light – green. Contours of tumour are definite, tumour is limited by connective tissue capsule, so it is expansive growth. Tissue atypicalness is expressed by chaotic location of fibred structures, their turbulence and surplus excrescence of stroma as compared to surrounding myometium take place. Cellular atypicalness is absent, that smooth muscular cells of tumour are identical to the cells of myometrium. Consequently it is benign tumour. *Designate*: 1-tumour, 2-capsule of tumour, 3-tinchanged myometrium.

4 *Undifferentiated (polymorphic – cellular) sarcoma*. Staining with haemotoxilin – eosin. Pay attention to the presence of cells of different form and size. Nuclei are also of different form and size, as a rule, hyperchromic (dark blue), many of them are of indefinite form, mitosis is frequent. Separate cells contain few nuclei. Atypical cells don't form any tissue structures, are located chaotically or autonomously, that is named decompensation. Pay attention that tumour has no clear boundaries, infiltrates surrounding tissues so, infiltrative growth and cellular atypicalness characteristic to malignant tumours take place in this micropreparation. Designate: 1-cellular atypicalness, 2-infiltrate growth.

5 *Lipoma*. Preparation is stained with haemotoxilin – eosin. It is mature tumour from adipose tissue. Lipocytes have different size, are located chaotically. Designate: 1- polymorphic lipocytes.

Illustrations to the themes

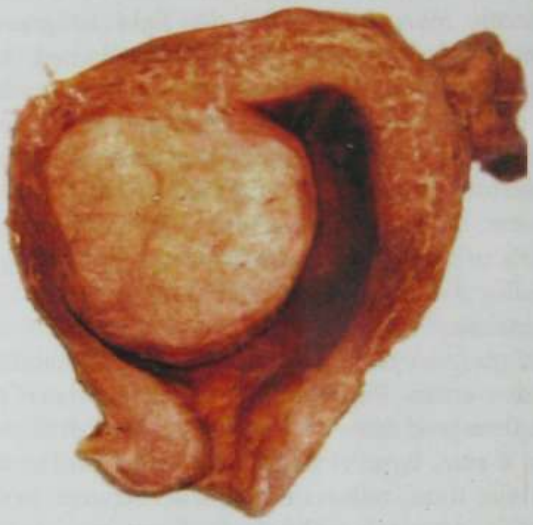


Figure. 1 - Uterine fibroid tumor. Uterine is enlarged. Node with distinct boundary of grey-white color, fibrous structure is seen in myometrium. Sharp limits indicate expansive growth. Tumor is surrounded with pseudocapsule, which occurred of myometrium. As growth is going on unstripped muscles cells atrophy from pressure and stroma hardens creating capsule around the tumor. Fibrous structures are situated in tumor in random way, with frequent vorticities, different from their location in surrounding myometrium – first sign of tissue athymia. There is much more conjunctive tissue (white portions) in tumor comparing with surrounding myometrium – second sign of tissue athymia. So there is non-malignant growth with expansive growth in macrospecimen. Histogenesis – unstripped muscles and conjunctive tissue cells of myometrium.

Figure 2 – Chondroma of lung. Tumor well-defined. Surrounding pulmonary tissue is sclerosed. Tumor hystogenesis is bronchi cartilage.

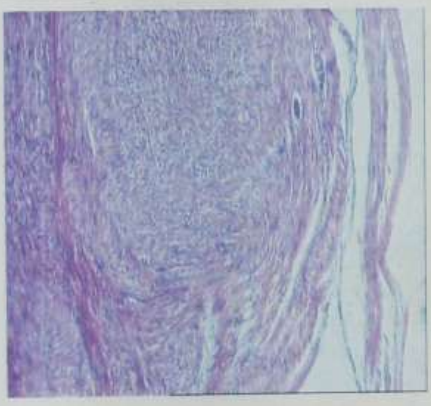


Figure 3 – Uterine fibroid tumor. Specimen is colored with hematoxylin and eosin. Tumor contours are distinct, tumor is limited by conjunctive tissue capsule – expansive growth. Tissue atypia is expressed with fibrous structures random way location and excessive excrescence comparing with surrounding myometrium. There is no cellular atypia.

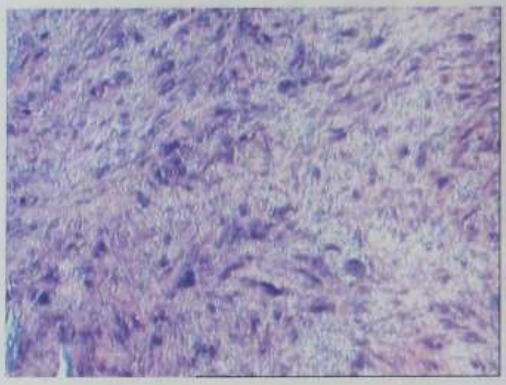


Figure 4 – *olymorphonuclear (epithelioid cell) sarcoma.* Specimen is colored with hematoxylin and eosin. Pay attention that there are cells of various shape and size. Nuclei are also of various shape and size, hyperchromic as a rule (intensive blue), many of them are of undefined shape, often mitosises are seen. Some cells contain a number of nuclei. Atypical cells do not create any tissue structure, they are located in random way or autonomous, which is called decomplexation.

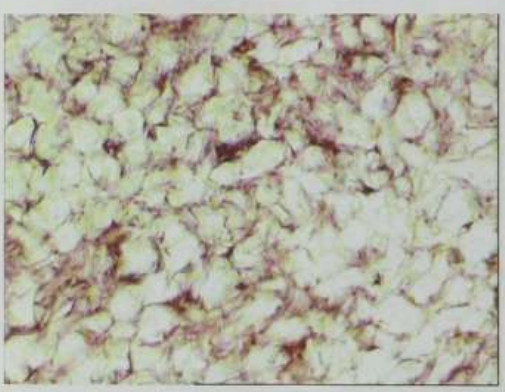


Figure 5 – Lipoma. Specimen is colored with hematoxylin and eosin. Lipocytes are of various sizes. They are located in random way.

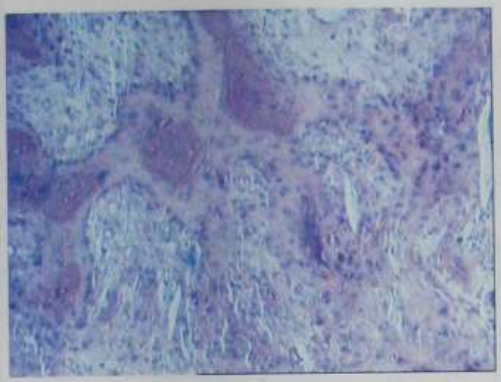


Figure 6 – Osteosarcoma. Specimen is colored with hematoxylin and eosin. Invasion with atypical cells is observed as well as osteous beams destruction.

Practical class 14

Theme 15. Nomenclature and morphological features of nervous tissue tumors. Features of CNS tumors

Theme 16. Nomenclature of tumors derived from melanin-producing tissue. Morphological features of tumors derived from melanin-producing tissue.

Specific objects of module:

To analyse clinicopathologic features of nervous system tumors

- *To interpret features of central nervous system tumors and peculiarities of their metastasis.*
- *To interpret pretumor changes importance at tumors of melanincreating tissue.*
- *To interpret morphologic features of nevuses.*
- *To interpret clinicopathologic forms of melanoma.*

Basic matter for self-work:

Tumors of central nervous system: neuroectodermal (astrocytic, oligodendroglial, ependymal, tumors of choroid epithelium, neuronal, poorly differentiated and embrional), meningovascular. Clinical features and peculiarities of metastasis.

Tumors of vegetative nervous system. Tumors of peripheral nervous system.

Significance of pretumor changes. Nevuses, their variety. Melanoma, its clinicopathologic forms.

1 Pre-auditorium theoretical training

Tumors of neural tissue. Neural tissue tumors have a number of clinical peculiarities: referring to their course practically all of them are malignant independent of their morphological characteristic as they press neighbour portions of cerebrum, their extension goes on in the limits of neural tissue

without distant hematogenous metastases. Nervous system tumors are distributed into neuroectodermal and meningovascular.

Neuroectodermal are divided into astrocytic, oligodendroglial, ependymal tumors of choroid epithelium, neuronal, poorly differentiated and embrional. Astrocytic tumors could be non-malignant (benign) – astrocytoma (fibrillar, protoplasmatic, fibrillar-protoplasmatic) and malignant – astroblastoma, and occur in any part of cerebrum. Oligodendroglial tumors are represented with oligodendrogliomas and oligodendroglioblastomas. Ependymal tumors include ependymomas, ependymoblastomas, chorioidpapillomas and chorioidcarcinomas. Among neuronal tumors the following is differentiated: ganglioneuroma or gangliocytoma, ganglioneuroblastoma, neuroblastoma. Poorly differentiated and embrional tumors include medullary blastoma (the most often is found in cerebellum and among children) and glioblastoma (occurs among adults in white substance, second by frequency, grows fast and causes death).

Meningovascular tumors develop from cerebral membranes and are represented with meningiomas and meningial sarcomas. Meningiomas could be arachnoidendotelial and fibrous. Meningial sarcoma by its histological picture looks like fibrosarcoma.

Tumors of peripheral nervous system, which develop in most cases from nerve sheathes are separated. They include neurinomas (Schwannomas), neurofibromas, neurofibromatosis (von Recklinghausen's disease) and neurogenic sarcomas.

Tumors of melanincreating tissue develop from cells of neuroectodermal origin – melanocytes, which are located in basal layer of epidermis, hair follicles, soft cerebrum membranes, eye retina and cornea. Melanocytes could be a source of tumor-like lesions – nevuses and malignant growthes

– melanomas. *Nevuses* are found in skin of face, extremeties and other parts of the body in the form of dark protruding lesions. They could be of several types: epidermic-dermic (junction) nevus, intradermal nevus, complex (mixed) nevus, epithelioid or spindle-cell (juvenile), blue. *Melanomas* (melanoblastomas) mostly occur among females and are found on skin, pigment choroid, cerebral layer of adrenal glands, cerebral membranes. They grow in the form of a node or with surface extention. Melanoma, as a rule, looks like brown spot with red or black impregnations, bluish-black soft node or plaque. In cells cytoplasm melanin of yellow-brown color is found often, nevertheless sometimes pigmentless melanomas are found. Melanoma gives hematogenous and lymphogenous metastases early. Melanomas development is often connected with high
solar irradiation. Sometimes melanomas occur in the place of pigment formations, Lentigo maligna, dysontogenetic nevus, congenital giant nevus.

II Algorithm of practical work

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

1 *Glioblastoma of cerebrum.* Area of brain structure destruction without clear boundaries, with a plural haemorrhages and necrosis is seen on a cut. Tumour node is absent. What is the degree of maturity of the tumour? What is the influence on organism?

2 *Melanoma of skin.* It is seen on preparation, that there is growth on the surface of skin, up to 3 cm in size, dark colour with areas of necrosis. Tumour has dense consistency, germinates in adjoining tissues of skin.

3 *Astrocytoma* Tumour of 5 cm in diameter, which has clear contours, grey colour, connected with tissue of cerebrum,

covered by brain – membranes, is seen on the surface of hemisphere of cerebrum in area of temple region.
4 *Metastasis of melanoblastoma in liver*. Numerous black colour formations, which somewhere combine together, are seen in parenchyma of liver on a cut. Dark colouring of tumour areas is conditioned by presence of dark pigment – melanin.
5 *Metastasis of melanoblastoma in lymph node*. Lymph node is enlarged to 2-3 cm, tissue of lymph node is black colour.
6 *Melanoma of eye*. Dark colour growing to 0.8 cm in size, with areas of necrosis is seen on a cut of eyeball. Tumour is dense consistency, germinates into contiguous tissues

To learn micropreparations from a theme and be able to draw the essence of pathological process with proper designations
1 *Glioblastoma*. Area, represented by noncerebral tissue is seen the matter of cerebrum. Small cells with hyperchromic roundish nuclei are located in it. Cells are located chaotically, and don't form any structures. Contours of tumour are unclear. There are massive haemorrhages which prevails over its area. What is the tumour histogenesis? Designate: 1-atypical glioblastes, 2-haemorrhages, 3- uninjured (intacted) brain tissue.
2 *Melanoblastoma of skin*. Preparation is stained with haemotixilin – eosin. Tumour is formed of large and polymorphic cells with signs of pathologic mithosises. High amount of black pigment melanin is marked in cytoplasm of atypical cells. Such pigment is observed in structures of stroma of the tumour. Designate: 1- atypical melanocytes, 2-melanin.
3 *Meningioma*. Preparation is stained with haemotoxilin – eosin. Tumour is formed of epithelium – like cells, which lie close to each other, forming nest – like structures. Microconcentric structures, which contain lime (plasmic bodies) and are stained in blue colour, are observed

somewhere. Designate: 1- epithelium – like cells, 2- plasmic bodies.

4 *Neurofibroma.* Preparation is stained with haemotohilin – eosin. Tumour grows from elements of connective tissue, nervous cells, bodies and fibers. Designate: 1-nervous cells, 2-connective tissue fibers

5 *Neurinoma.* Preparation is stained with haemotohilin – eosin. Shvanns` cells forms parallel bunches, which form rhythmic or "palisade" structures Verokai bodies. Boundaries of tumour are unclear. Designate: 1-nuclei of Shvanns` cells.

Illustrations to the themes

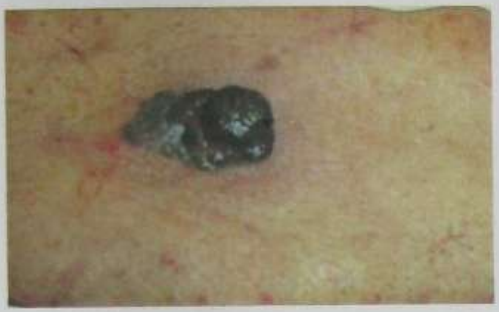


Figure 1 – Skin melanoma. There is an excrescence on skin surface of dark color with necrosis portions. Tumor is of hard consistency, ingrowths surrounding tissue of skin.

Figure 2 – Eye melanoma. Tumor-like node of black color could be seen on section.

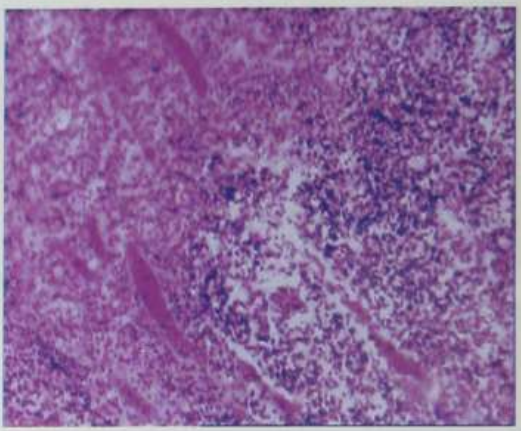


Figure 3 – Glioblastoma. Little cells with hyperchromic nuclei of round shape are situated in the medullary substance. Cells are located in random way, they do not create any structure. Tumor contour is not distinct. There is massive necrosis in tumor.

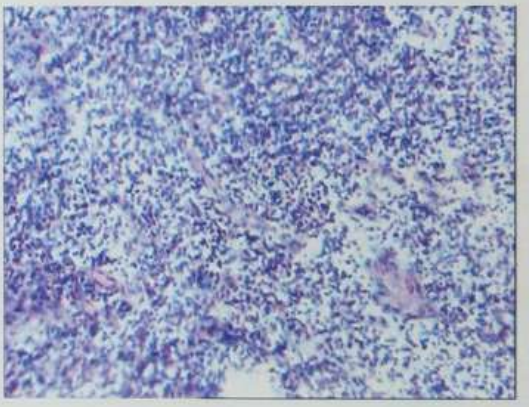


Figure 4 –Oligodendroblastoma. Specimen is colored with hematoxylin and eosin. Tumor is built of large and polymorphic cells with the signs of pathologic mithosises.

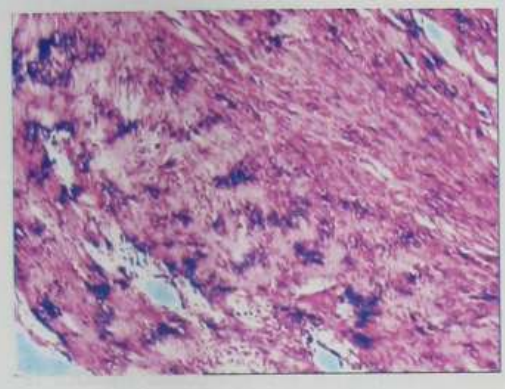


Figure 5 – eurinoma. Specimen is colored with hematoxylin and eosin. Schwann cells are located in the way of parallel bunches. Tumor boarder is not distrinct.

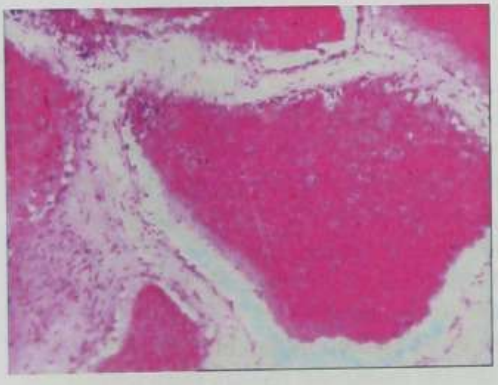


Figure 6 – ernous hemangioma. Specimen is colored with hematoxylin and eosin. Spaces between vessels are thinned. Lumen is filled with erythrocytes.

Practical class 15

Theme 17 Nomenclature and morphological features of tumors derived from epithelium

Specific objects of module:

- *To interpret general characteristic of epithelial tumors.*
- *To analyze morphologic characteristic of non-malignant growth from epithelium.*
- *To analyze morphologic characteristic of malignant growth from epithelium and the ways of cancer metasasis.*

Importance of the topic: research of the epithelial tumors is important task in the practical medicine because it may help to diagnose and treat these diseases. In clinical practice the knowledge of the oncomorphology is necessary for the comparison of the clinical dates with the result of the biopsy research and postoperative materials, and also for the clinicoanatomical analysis of the autopsy.

Purpose: Receive the notion about the essence of tumors and the principle of their classification. Learn etiology, morphogenesis, growth, morphological features of tumors; estimate the outcomes (complications) and determine the significance for organism.

Specific aims: 1 Explain the role of the oncologic processes in different organs: lungs, stomach, cervix, uterus and breast.

2 Know the histogenic classification of epithelial tumors and their morphological classification in lungs, stomach, cervix, uterus and breast.

3. Know the terminology of epithelial tumors.

4. Tell apart the benign and malignant tumors from epithelium.

5 arn the morphology and functional manifestations of the benign tumors from epithelium

6 earn the morphology and functional manifestations of the malignant tumors from epithelium

Basic matters for self-work

Epithelial tumors without specific localization: non-malignant (papilloma, adenoma) and malignant (cancer). Histological variants of cancer. Metastasis peculiarities.

Tumors of excretory (exocrine) and incretory (endocrine) glands and epithelial coatings' tumors.

1 Pre-auditorium theoretical training

Epithelial tumors. Depending on histogenesis we differentiate tumors of covering epithelium (multilayer, flat and transitional) and glandular epithelium. By their course and differentiation epithelial tumors could be non-malignant (benign) and malignant. Depending on organ specificity epithelial tumors are divided into organ specific tumors and tumors without specific localization. *Non-malignant* tumors without charactristic localization of covering epithelium - papillomas are found in skin, larynx, urinal bladder, etc., of glandular epithelium – adenomas are found in all glandular organs. The following morphologic variants of adenomas are differentiated: acinous (alveolar), tubular, trabecular, solid, papilloma cystoadenoma, villous adenoma, fibroadenoma. *Malignant* epithelial tumors are called cancer or carcinoma. The following forms of carcinoma without specific licalization are differentiated: epidermoid cancer, developing from multilayer flat epithelium and is found in corresponding tissues or in mucus tunics where squamous cell metaplasia occurred. Carcinomas could be high-, moderate and poorly differentiated. Cancerous keratin perls presence is characteristic for high differentiated carcinomas. Carcinoma in situ – carcinoma which does not penetrate through basal membranne and does not invade tissue depth is marked out separately. Carcinoma from glandular epithelium is called glandular neoplasm or adenocarcinoma. It occurs in organ with corresponding

epithelium and also could be of three stages of differentiation. Peculiar for poorly differentiated adenocarcinoma is sccirrhous carcinoma, containing big quantity of fibrous stroma squeezing tumor parenchyma. Undifferentiated forms of epithelial malignant growths are represented with small cell carcinoma, carcinoma, signet ring cell carcinoma and meddulary carcinoma. Malignant organ-specific epithelial growths include chorioncarcinoma and trophoblastic tumor, clear-cell carcinoma of kidney, etc.

II lgorithm of practical work

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

1 *Metastases of cancer in liver*. Numerous white colour nodes of different size are seen on cut of liver. Specify primary localization of the tumour.

2 *Ulcer – cancer of stomach*. Ulcer has rounded form, penetrate wall of stomach to the serous layer. The bottom of ulcer is unequal, edges bank – like prodject above the surface of mucousa, dense, callous.

3 *Polyposis of stomach*. Formation of soft consistency, round form with smooth surface, which projects above unchanged folds of mucosa of stomach is seen in preparation. Tumours is on leg with wide basis. Name types of polypuses of stomach.

4 *Saucer – like cancer of stomach*. Bank – like circle thickening of mucousa of stomach is seen. Folds of mucosa are absent. It is seen on the transversal cut, that tumour is some similar to saucer. What is the histogenesis of tumour and its complications?

5 *Diffuse cancer of stomach*. Wall of stomach is thickened in favour of infiltrative growth of tumour. Folds of mucosa are

absent in area of tumour infiltration of stomach wall. Name complications, ways of metastasizing, histogenesis of tumour.

6 *Cancer of stomach. W*all of stomach is thickened, deformed, folds of mucosa are absent. Tumour infiltrates the wall of stomach. Specify form of growth of tumour, is it benign or malignant

7 *Central cancer of lung.* Tumour is of bronchogenous origin – there are polyp – like growings, ulcers in clearance of bronchus. There is homogenous white tissue of considerable thickness around the bronchus. Black areas in tumour are lymphatic nodes with the dust of coal. What is the histogenesis of tumour?

8 *Peripheral cancer of lung* is represented by two macropreparations. In first, there is a tumour of white colour, with clear boundaries, located under pleura. In other, there is a tumour, represented by the large nodes of grey colour, which damage almost all lung.

9 *Cystadenoma of ovary*. Ovaries are enlarged, it is seen on cut that tissue of them is represented by plenty of little cysts tightly located, papillary growings are seen on internal surface.

10 *Papilloma of urinary bladder*. Papillary formation of pink – red colour is seen on preparation. Tumour has soft consistency, thin leg and does not germinate into adjoining tissues of urinary bladder.

11 *Breast's Cancer*. Massive nodular growing of grey colour tissue, without clear boundaries, penetrating into depth of organ and presence of secondary changes in tumour is seen in preparation. Breast has considerably changed form, is deformated. At histological examination of tumour tissue, tissue and cellular atypicalness of epithelial structures are observed. Specify localization of possible metastases of malignant tumour of breast.

12 *Hypernephroidic cancer of kidney*. Tumour nodes, pied on cut (areas of yellowish colour are alternated with the areas of

haemorrhages of different size) are seen in region of upper pole of kidney.

13 *Cancer of body of uterus*. Uterus is enlarged, lower segment is sharply thickened, tissue is white. Contours of tumour are not clear. There are papillar growings, ulcers in mucousa. Absence of capsule (absence of clear boundaries of tumour) testifies to infiltrative growth peculiar to malignant tumours

14 *Teratoma of ovary*. Large cyst is placed in ovary, in cavity of which hair and fat are present, tissues which are not inherent to ovary. Such tumours are named heterotopic. They appears as a result of displacement of tissues in embryo period the name originates from the Greek word "teratos" – miracle. Sometimes teratomas become malignant (teratoblastomas)

15 *Cystadenocarcinoma of ovary*. Ovary is enlarged, it is seen on a cut that tissue of organ is represented by a large cyst, numerous papillary growings on internal surface look like cauliflower.

16 *Papilloma of skin*. It is seen in preparation, that pink colour growing as polypus, up to 6 cm takes place. Tumour has soft consistency, thin leg and does not germinate in adjoining tissue of skin.

17 *Polypus of small intestine*. Mucous layer, on surface of which polyploidy growing up to 3 cm in diameter, is seen in preparation.

18 *Cancer of colon*. Wall of large intestine, deformated in favour of bank – like thickening, which considerably narrows clearance of intestine is presented in preparation.

19 *Carcinomatosis of stomach*. Numerous white colour nodes of different size are seen on the serous layer of stomach.

20 *Cancer of pancreas*. Organ is considerably deformated, in favour of excrescence of grey colour nodes of different size, which are soldered between themselves.

21 *Kruckenbergs` cancer*. Ovaries are enlarged in favour of excrescence of homogenous consistency tumour nodes.

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

1 *Carcinomatosis of lung*. Lymphatic vessels are extended, filled with cells of different size and form, with hyperchromic nuclei with frequent mitosis. "Nests" of such cells, which are intensively stained in dark blue colour are seen in tissue of lungs. Boundaries of those nests are clear, because they are limited by walls of vessels. Designate: 1-tumour cells in lymphatic vessels, 2-tumour cells in lung, 3-alveoli

2 *Metastasis of adenocarcinoma in liver*. Preparation is stained with haemotoxilin – eosin. Area of non-hepatic glandular tissue, which is chaotically located in parenchyma of organ is seen in micropreparation. Cells in that tissue are hyperchromic, form primitive glandular structures. What is the primary localization of tumour? Designate: 1-Hepatocytes, 2-Atypical glands, 3-Cellular atypicalness.

3 *Metastasis of adenocarcinoma in lymphatic node*. Tissue of lymphatic node is represented by lymphocytes, cells with rounded nuclei bordered with narrow strip of cytoplasm. Large epithelial cells with hyperchromic nuclei, frequent mitosis, are seen among lymphocytes. Here and there that cells form primitive glandular structures. Designate: 1-lymphatic follicle, 2-atypical glandular structures.

4 *Papilloma of skin*. Preparation is stained with haemotoxilin – eosin. Tumour grows as papillae. Papillae excrescence of squamous epithelium is microscopically seen. Epithelium is located on basal membrane, has kept polarity. Its thickening takes place. There are signs of tissue atypicalness in tumour: prevalence of epithelial tissue above stroma. Designate: 1-Stratified squamous epithelium, 2-Hypodermic adipose cellulose

5 *Quamous cell cancer of cervix of the uterus without ceratinization*. Preparation is stained with haemotoxilin –

eosin. Bundles of epithelial cells with hyperchromic nuclei are seen in smooth muscle and connective tissue of wall of cervix of the uterus, bundles grow deep in adjoining tissue. Cellular atypicalness and frequent mitosises are marked in epithelial cells. Give description of growth of tumour. Designate: 1-atypical epithelial cells, 2-pathological mitosis, 3-infiltrative growth.

6 *Squamous cell cancer with keratinization.* Bundles of epithelial cells with hyperchromic nuclei, which grow deep in derma and adjoining tissue, are seen in connective tissue of derma. Formations of round form and homogenously – pink colour (cancer pearls) are seen among cells with hyperchromic nuclei. Give description of growth of tumour, essence of tissue and cellular atypicalness. What is the mechanism of formation of cancer pearls? *Designate*: 1-atypical cells, 2-cancer pearls

7 *Fibrous cancer of stomach.* Preparation is stained with haemotoxilin – eosin. Large fields of connective tissue with remains of destroyed muscular layer are presented in preparation. Connective tissue is infiltrated by atypical cells of different form and size with hyperchromic disfigured nuclei and frequent mitosis. Cancer cells are located trabeculary as bundles or big nests. Designate: 1-atypical connective tissue cells, 2-cancer pearls.

8 *Adenocarcinoma of stomach.* Preparation is stained with haemotoxilin – eosin. Glandular formation of tumour have different size and form, cellular elements, here and there located in few levels, are polymorphic. Atypical, pathological mitosis is marked in some cells. Designate: 1-atypical glands, 2-atypical epithelial cells, 3-pathological mitosis.

9 *Adenocarcinoma of body of uterus.* Preparation is stained with haemotoxilin – eosin. Excrescence of atypical glandular structures, in which epithelial cells are characterized by expressed polymorphism, presence of numerous pathological mitosis and infiltrative germination into the wall of uterus is

marked in tissue. In addition there are excrescences of atypical cells in stromal component of tumour. Designate: 1-atypical endothelium, 2-atypical cells in glands, 3-infiltrative growth.

10 *Fibroadenoma of mammary gland.* Preparation is stained with haemotoxilin eosin. Correlation between epithelium and connective tissue in tumour is different. Epithelial part is represented by long and short tubes with thickening on ends, they often are ramified and anastomose between each other. Clearance of them are of irregular form, here and there are cystously extended, other are vise versa narrowed. They are formed by low cylindrical or cuboidal epithelium. In favour of that glandular structures have character of excretory ducts. Structure of tumour reminds unfunctioning breast. Cells are located regularly, are clearly bordered from connective tissue, which has some features: in one cases it is observed around excretory tubes, consists of thin fibers, and has many fibroblasts, clearances of canaliculi are not deformated (pericanalicular fibroadenoma); in other – fibers are located concentrically around tubes, deforming their clearances as a result of projecting into them. (Intracanalicular fibroadenoma). In addition, connective tissue is represented also by bunches of more rough collagenous fibers with small maintenance of cells. That bunches are separated from each other by ramified tubular structures. Designate: 1-deformed glands, 2-cysts , 3-collagenous fibers.

11 *Papillary cystadenoma of ovary.* Preparation is stained with haemotoxilin – eosin. Cystadenoma has glandular structure and is formed of few cavities, lined by one layer epithelium and filled with papillaes, which have different form and length and are located on different distance one from other. Loose connective tissue serves as the bar of papilla, small number of vessels, separate histiocytes are in that bar. Desquamation of integumentary epithelium is observed in some papillaes.

Designate: 1-cystously extended glands, 2-papillary excrescence of epithelium.

12 *Chorionepithelioma.* Preparation is stained with haemotoxilin – eosin. Tumour grows from chorionic epithelium of foetus and also from syncitial elements. It is microscopically seen that stroma and vessels are absent in tumour. The bulk of tumour is made by Langhans' and syncitial cells. First are elements of cytotrophoblast represented by cells with a light cytoplasm, round, poor in chromatin nuclei. Cells of syncitium are located on periphery, they are dark, with hyperchromic nuclei, mitosis is observed rarely. The role of vessels is realized by cavities covered by tumour cells. Designate: 1- cells of syncitium, 2- cells of trophoblast, 3- pathological mitosis, 4- haemorrhage.

Illustrations to theme

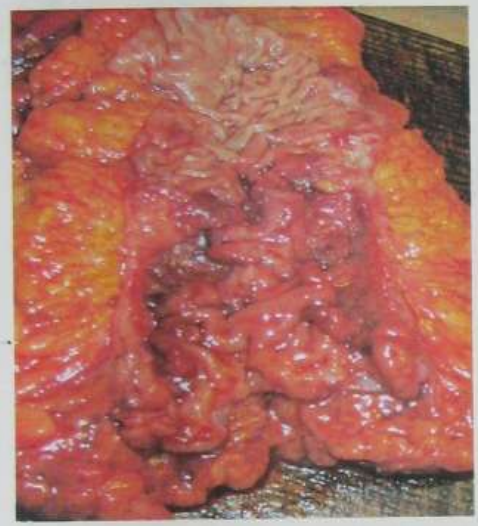


Figure 1 – Large intestine carcinoma. Roll-like bulge of mucus tunic. Name tumor histogenesis, its complications.

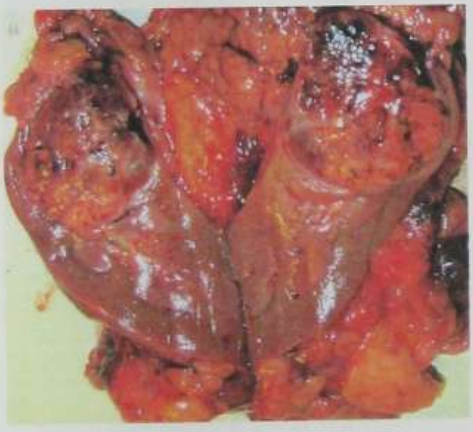


Figure 2 – *Renal cell carcinoma (hypernephroma).* Tumor node is in kidney upper pole. It is stripped on section, yellowish color portions alterate with portions of hemorrhages. Why this tumor is called hypernephroma?

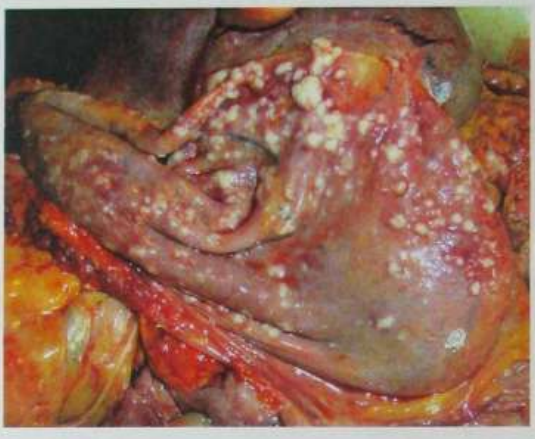


Figure 3 – Gastric carcinomatosis. Multiple nodes of white color and various size are seen on gastric serous tunic.

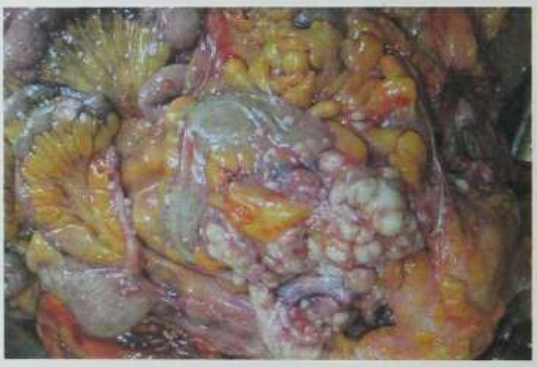


Figure 4 – Pancreas cancer. Organ is represented with white color nodes which are interunited .

Figure 5 – Krukenberg's carcinoma. Ovaries are enlarged. Ovaries on section are homogenous with micro cycts.

Describe Krukenberg's carcinoma genesis.

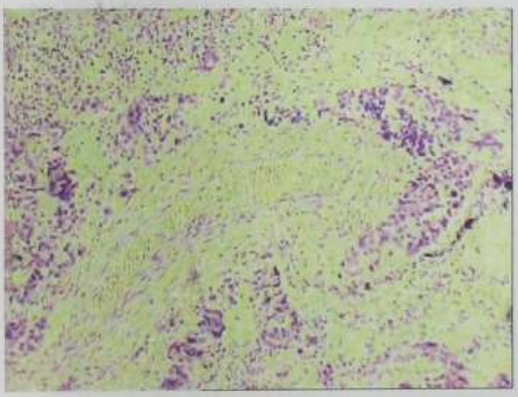


Figure 6 – Lymphangitic carcinomatosis of lung. Lung lymph nodes are dilated, filled with varous size and shape cells with hyperchromic nuclei with frequest mitosis.

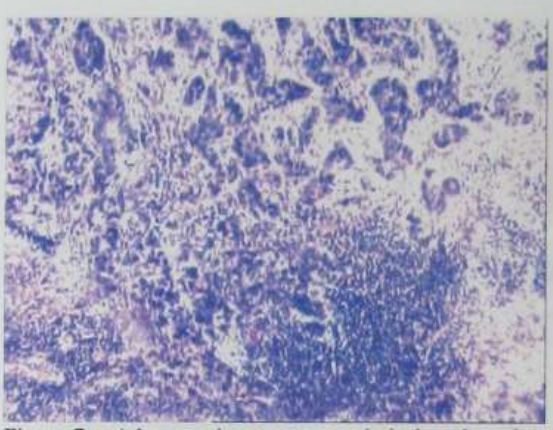


Figure 7 – Adenocarcinoma metastasis in lymph node. Large epithelial cells with hyperchromic nuclei, frequent mitosis are seen. Here and there these cells form primitive grandular structures.

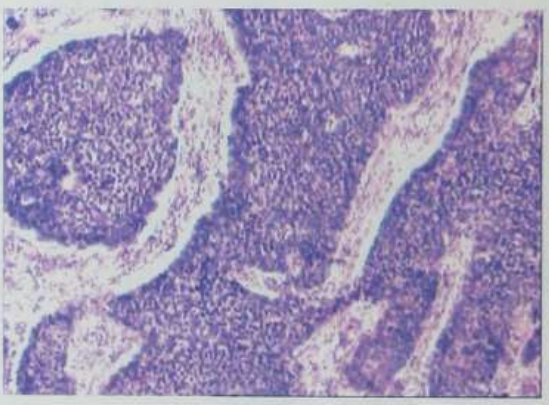


Figure 8 – Squamous cell carcinoma of skin without keratinization. Specimen is colored with hematoxylin and eosin. Tension bars of epithelial cells with hyperchromic nuclei are seen, tension bars ingrow deep into adjacent tissue. Cellular atypia is seen in epithelial cells as well as numerous mitosises. Give characteristic of tumor growth.

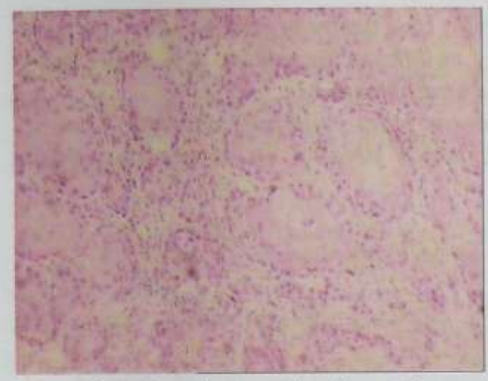


Figure 9 – Squamous cell carcinoma of skin with keratinization. Specimen is colored with hematoxylin and eosin. Tension bars of epithelial cells with hyperchromic nuclei are seen, tension bars ingrow deep into derma and adjacent tissue. Among cells with hyperchromic nuclei round shape formations are seen of homogenous red color – epithelial cancerous perls. Give charactretistic of tumor growth, essence of tissue and cellular atypia. What is the mechanism of epithelial cancerous perls creation.

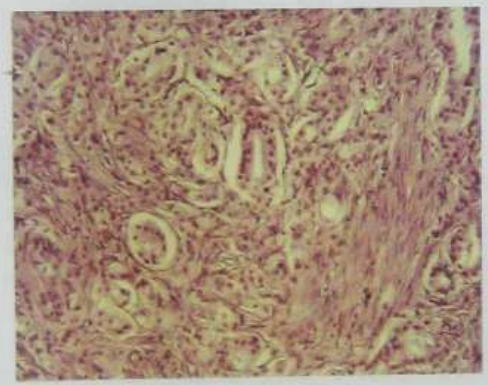


Figure 10 – Gastric adenocarcinoma. Specimen is colored with hematoxylin and eosin. Glandular formations of tumor are of various size and shape, cellular elements in certain places are located in several layers and are remarkable with polymorphism. In some cells pathlogical atypical misosises are seen.

Practical class 16. *Tumors of childhood*

Theme 18 Features of childhood neoplasia. Dysontogenetic tumors. Teratomas and teratoblastomas.

Theme 19 Tumors from cambial embryonic tissues. Tumors of childhood, which develop on as the tumors of adults.

Specific objects:

- *To explain the features of children's tumor in comparison with adults.*
- *To interpret modern classification of tumors of childhood.*
- *To explain the morphological features of dysontogenetic tumors.*
- *To draw conclusions about the morphological features of teratomas and teratoblastomas.*
- *To draw conclusions about the morphological features of tumors derived from embryonic tissues.*
- *To draw conclusions about the morphological features of tumors of childhood, which develop on as the tumors of adults.*

Topicality of theme: tumor growth in child age, dysembryomas, teratomas and teratoblastomas, tumors from cambial embryonal tissues, tumors in infancy which develop on like adult's tumors, which have unique features by morphological as well as by clinical features, that is of major importance for timely diagnosis and adequate treatment of them.

Aim – to learn etiology, mechanisms of development, morphologic manifestation, consequences of tumors in infancy.

Task: 1) To know types of tumors in infancy. 2) To master to differentiate benign and malignant tumor processes in infants by macroscopic and microscopic features. 3) To be able to diagnose clinical and morphological features of tumors in children.

Basic matter for self-work

Features of childhood neoplasia in comparison with adults. Classification of tumors of childhood. Dysontogenetic tumors: hamartomas and hamartoblastomas of vascular origin, hamartomas and hamartoblastomas from skeletal muscles, hamartoblastomas of internal organs. Teratomas and teratoblastomas.

Tumors from cambial embryonic tissues: meduloblastoma, retinoblastoma, neuroblastoma. Tumors of child age, which develop on as the tumors of adults: tumors of CNS, hemapoietic system, soft tissues, bones. Features of course and metastatic spreading.

1 Pre-auditorium theoretical training

Tumors in infants. Peculiarities: they often develop from embryonal tissues as the result of their development and formation disorder – these are dysembryomas or teratoid tumors (teratomas); - benign tumors (angiomas, nevi) occurs more often then malignant, - sarcomas (lymphosarcomas, osteosarcomas) are found more often than cancers which occur mostly in internal organs, endocrine glands; - malignant tumors (embryonal carcinosarcomas, hepatoma) in infants keep expansive growth for quite a long time, don't metastasis for long and even are able to reverse – to transfer into benign tumor – neuroblastoma into ganglioneuroma; - malignant tumors in infants most often are found in children of 3-5 years, which confirms significance of antenatal cancerigenic

influences; - certain benign tumors are inclined to infiltrative growth – angiomas.

Classification: - the first type are dysembryomas, teratoid tumors or teratomas. They could be histoid, organoid, organizmoid and embryonal, which could be homologous – teratomas and heterologous – teratoblastomas. Histoid teratomas are also called hamartomas (angiomas, nevi, embryonal tumors of internal organs) or hamartoblastomas;

- the second type are tumors with embryonal cambial tissues in nervous tissue, sympathetic ganglia, adrenal glands (medulloblastomas, retinoblastomas, neuroblastomas). They are also could be referred to as hamartoblastomas,

- the third type are tumors developing like adults' tumors - these are tumors of mesenchymal origin: haemoblastomas, osteogenetic and tumors of soft tissues.

Dysembryomas: - hamartomas and hamartoblastomas of vascular origin, among which capillary and cavernous hemangiomas on skin (in the form of red-bluish node) are found most often as well as in liver and other organs. Capillary hemangiomas have ability for infiltrative growth, so they can recur after oncotomy. Angiosarcomas and lymphangiomas are found rarely, they can reach big size on the neck with endothelium and capillaries proliferation and infiltrative growth;

- hamartomas and hamartoblastomas of cross-striped muscles – rhabdomyomas, which are found in heart, extremetes muscles as a 10-15 cm node of grey-brown color, rhabdomyoblastomas or embrional rhabdomyosarcoma – malignant tumor which is found in small pelvis organs;

- hamartomas of internal organs: Wilms tumor or embryonal carcinosarcoma (Wilms tumor, adenosarcoma) grow expansively in capsule for long, can reach giant size, reddish-white color with hemorrhages. Histologically in tumor among kidney tissue structures elements of mesenchymal origin are found; hepato blastoma or embryonal hepatoma – malignant

tumor of hepar, on section it looks like numerous white-yellowish nodes of solid fields of embryonal hepatic tissue and structures of mesenchymal origin. Metastasize, complicates with internal hemorrhages.

Teratomas and teratoblastomas: organismoid and organoid teratomas – tumors derivated from three germ layers are found in testis, ovaries, mediastinal, extraperitoneal, base of brain. In girls' ovaries malignant teratoblastomas develop more often and benign teratomas – in testis, throat teratomas grow as polyps, are of benign course, intracranial teratomas more often are of malignant course, they often are hormonally active.

Tumors of cambial embryonal tissues: medulloblastoma is malignant tumor in tentorium, retinoblastoma is malignant tumor from embryonal poorly differentiated cells of retina, neuroblastoma is malignant tumor in sympathetic ganglia, adrenal meddula, fast metastasizes, discharge catecholamine.

Tumors developing like adults' tumors are tumors of nervous system: astrocytomas, hematopoietic system: leucosis, malignant lymphomas; bones' tumors: osteomas, chondromas, osteosarcomas, Ewing's sarcomas.

Situation tasks from concept module 4: *tumors*

1 Under patient's gastroscopy at low curvature it was found tumor-like growth on foot. Removed tumor is soft and elastic, of grey-red color. Histologically glandular structures were found without cellular atypia. Name what tumor patient had. What is prognosis?

2 For the course of three years patient was treated because of hypertension. He was taken to neurologic section with symptomes of apparent cerebral pathology caused death. Section showed hemorrhages into lateral ventricles of cerebrum and tumor of right adrenal gland. Histologically in

tumor tissue, built similar to medullar substance of adren gland tissue atypia signs were found. Explain clinical symptomes. What tumors we are speaking of?

3 In patient's finger nail skin sharply painful small tumor occurred. Histologically tumor is built of slot-like vessels, coated inside with endotelium and is surrounded with big quantity of large cells with normochromal neclei without signs of atypia. From what tissue tumor developed, its name?

4 In hand skin of patient multiple small tumors of hard consistency occurred, painful. Tumors are located linearly downstream the nerves. What are the names of tumor and disease?

5 Patient was taken to clinic with compliants on weakness, weight lose, presence of big quantity of tumor-like nodes in subcutaneous fatty tissue. A month before he accidentally damaged pigment nevus on the back between shoulder blades. Some of nodes are of brown color. Liver is enlarged, its surface is nodular. Death came under increasing signs of cachexia. On section nodes of black-brown color were found in subcutaneous fatty tissue, liver, lungs, lymph vessels. Name tumor? What caused nodes color?

6 In 6 monthes after surgery where non-malignant (benign) tumor of front wall woman came to the doctor complaining occurance of tumor which permamntly enlarges in the place of postoperative scar. What tumor could be suspected?

7 Knee of football player after multiple traumas swelled up, pain occurred. Radiologic examination showed femoral bone lower epiphysis destruction and in lungs – well-defined shadow. What disease could be suspected?

8 Under patient's shoulder skin soft, good moving incapsulated tumor occurred. On section it is of yellow color, represented with adipose tissue. Microscopically – adipose cells of various size. Name tumor, form of growth, is it benign or malignant?

9 Hard node occurred in woman's mammary gland which was united with surrounding tissues, stiff. Nipple is inverted, blood excudes from it. Subclavian and supraclavicular, auxillary lympatic nodes are enlarged. What disease could be suspected? Why lymphatic nodes are enlarged?
10 Patient ill with pulmonary tuberculosis has increased neck and submaxillary lympatic nodes. Histologically in lymphatic node various shape and size cells of epithelium origin were found with hyperchromic mutilated nuclei, pathologic mitosises are present. What disease could be suspected? What caused changes in lymphatic node?
11 Patient was diagnosed with hip sarcoma. Name localization of possible metastasis.
12 Rectal cancer was diagnosed with patient. Name localization of possible metastasis.

Answers on situation tasks

1 Patient was diagnosed with adenomatous polyp. It could regenerate into malignant tumor – adenocarcinoma. Could recur after removal.
2 Patient has benign tumor from medullar layer of adrenal gland - pheochromocytoma, which is able to produce catecholamine, which caused named clinical and morphological changes.
3 Tumor developed from cells paving capillaries. This is glomus-angioma.
4 Patient is ill with neurofibromatosis and Recklinghausen's disease.
5 Patient is ill with melanoma with metastases in the named organs. Nodes color results from melanin accumulation.
6 Desmoid tumor could be suspected with patient.
7 Patient sufferes from malignant osteous tumor – osteosarcoma which gave hematogenous metastases in lungs.

8 Lipoma, growth is expensive, it is benign tumor.
9 The signs of breast cancer take place. Lymphatic nodes are enlarged because of lymphogenous metastasis.
10 Carcinoma of lungs developed against tuberculosis background. Changes in lymphatic nodes are caused by tumor metastases.
11 Sarcomas, as a rule, metastasis hemotogenously. Metastases are most probable in lungs.
12 Cancer metastasis in the first turn lymphogenously. Early metastases are most probable in regional lymphatic nodes.

Test tasks

1 Autopsy of man died from cerebral hemorrhage, in VIII craniocerebral nerve region it was found a tumor of round shape. Incapsulated, of white color on section. Histologically it was built of elonged shape cell with rod-shaped nuclei. In some places nuclei are located parallel, alternating with portions built of fibers. Name the tumor.
A. Paraganglioma. **B.** Neurofibromatosis. **C.** Meningioma.
D. Ganglioneuroma. **E.** Neurinoma.
2 In the skin hard tumor was found, movable, well-limited from surrounding tissues. On section the tumor is of whitish color, is represented with fibrous tissue, microscopically – collagen fibers twisted in random way, small amount of cells. What is the name of tumor?
A. Hard fibroma. **B.** Soft fibroma. **C.** Histiocytoma.
D. Dermatofibroma. **E.** Desmoid.
3 Woman was subjected to sector resection because of tumor-like node with induration in mammary gland. Histologically tumor is represented with glandular slot-like complexes, squeezed with conjunctive tissue prevailing over tumor parenchyma. What is the tumor name?
A. Tubular adenoma. **B.** Fibrous adenoma. **C.** Pericanalicular fibrous adenoma.

D. Intracanalicular fibrous adenoma. **E.** Adenocarcinoma.

4 Patient who smoked for a long time and suffered from chronic bronchitis was diagnosed with tumor of lungs. Tumor was removed. This was round formation up to 3 cm in diameter with poor defined boarder, ingrowing bronchi wall. Histologically in tumor layers of atypical flat epithelium were found among well developed stroma. What is histological name of the tumor?

A. Papilloma. **B.** Squamous cell keratinous carcinoma.

C. Squamous cell nonkeratinous carcinoma.

D. Adenocarcinoma. **E.** Undifferentiated cancer.

5 Under gastroscopy patient was diagnosed with tumor of gasric small curvature hazelnut in size, on the foot. Tumor is of soft-elastic consistence, grey-red color on section, histologically looks like gastric mucus tunic. What tumor is it?

A. Adenoma. **B.** Adenomatous polyp. **C.** Inflammatory polyp.

D. Adenocarcinoma. **E.** Mucous cancer.

6 During gastroscopy mid aection of esophagus tumor cells biopsy was made. Histologically – numerous nests of pithelial cells with phenomenon of polymorphism, with numerous mitosises. In the center of the nests – homogenous masses of keratin. What is histogenetic type of tumor?

A. Fibrocarcinoma. **B.** Solid carcinoma. **C.** Epidermoid cancer.

D. Squamous cell keratinous carcinoma. **E.** Squamous cell nonkeratinous carcinoma.

Answers to test tasks

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

Theme 20. Practical skills. Autopsy. 2 hours

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