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

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SHORT COURSE OF SYSTEMIC PATHOLOGY
Part 3

Recommended by the educational council of Sumy State University for education of foreign students of the 3-rd course of medical institute

Sumy
Publishing of Sumy State University

2007

ББК 52.818.1я73
Р93

Рекомендовано до друку вченою радою
Сумського державного університету
(протокол № 8 від 15.03. 2007р.)

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РоманюкА.М., Карпенко Л.І.
В93 Короткий курс системної патоморфології:
Навчальний посібник: У5 ч. – Суми: Вид-во
СумДУ, 2007.- Ч.3. – 137с.

Посібник містить короткий виклад теоретично матеріалу основних тем системної патоморфології, п відповідає програмі, затвердженій МОЗ України і ЦМК з вищ медичної освіти. У посібнику представлені цифрові мікро- макрофотознімки, викладений їх опис та наведені приклад тестових і ситуаційних завдань до кожного заняття.

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

ББК 52.818.1я73

Content module 5

Diseases of Blood System

Concrete aims:

-To define the acute and chronic anaemia.

-To interpret the etiology, clinicopathologic characteristic, diagnostics of anaemia as a result of blood loss; anaemia as a result of increased hemoclasia and anaemia concerned with hematosis disturbance.

- To interpret the etiology, clinicopathologic characteristic, diagnostics of thrombocytopenia and thrombocytopathy.

-To interpret the etiology, clinicopathologic characteristic, diagnostics of coagulopathies.

-To analyse the etiology, up-to-date classification and general clinicopathologic characteristic of leucoses.

-To analyse the cytogenetic and cytochemical methods of differentiation of cell variants of leucoses.

-To interpret the kinds, up-to-date methods of diagnostics, the stages of development, clinicopathologic characteristics, complications, medical pathomorphism, age peculiarities, causes of death of the acute and chronic leucosis.

-To interpret the kinds, up-to-date methods of diagnostics, the stages of development, clinicopathologic characteristics, complications, causes of death of myeloproliferative diseases.

-To interpret the kinds, up-to-date methods of diagnostics, the stages of development, clinicopathologic characteristic, complications, causes of death of plasmatic cells tumours.

- To interpret the up-to-date methods of diagnostics, clinicopathologic manifestations of tumour diseases of lymph nodes (Hodgkin's and non-Hodgkin's lymphomas).

Theme 21 Anaemias. Thrombocytopenias and Thrombocytopathies. Coagulopathies.
Theme 22 Hemoblastosises. The diseases of Lymphoreticular System organs.

Subject Actuality: blood diseases in the structure of population morbidity occur very often. They can be primary, which testify the pathology of hematopoietic organs, or secondary, which testify the diseases of other organs. The secondary diseases are more common. In the modern hemopathology of anaemia, thrombocytopenia, thrombocytopathy and coagulopathy the hemoblastosises are highly rated among other blood diseases. The knowledge of the subject is necessary for mastering haematology problems at the clinical chairs.
Aim: to study the etiology, the mechanisms of development, clinicopathologic manifestations, classification, consequence of blood and marrow diseases in the organism.
Task: 1. To know etiology, histogenesis, anaemias morphogenesis, thrombocytopenias, thrombocytopathies, coagulopathies, blood tumours.
2. To learn how to identify the blood diseases by macro- and microscopical features.
3. To be able to diagnose clinical and morphologic manifestations of the diseases of lymphoreticular system organs.
4. To know the histogenetic classification of hemoblastosises.

Theme 21 Anaemias. Thrombocytopenias and Thrombocytopathies. Coagulopathies.
The main questions for the individual training:
-The role of the marrow biopsy in the blood diseases diagnostics.
-Anaemias: definition and classification.

-The acute and chronic anaemias as a result of blood loss (posthemorrhagic): etiology, clinicopathologic characteristic, diagnostics.
-The anaemias as a result of increased hemoclasia (hemolytic): inherited, acquired, autoimmune, isoimmune, of mixed genesis. Pathogenesis, diagnostics, clinicopathologic characteristic, causes of death.
- The anaemias connected with the hematosis disturbance: megaloblastic, pernicious (Biermer's, Biermer-Ehrlich anaemia; B12- and folic deficient), iron deficient, hypoplastic (hyporegeneratory) and aplastic. The etiology, pathogenesis and morphogenesis, clinicopathologic characteristics and the methods of diagnostics, complications, the causes of death. The diseases and states, which are accompanied by anaemias.
-Thrombocyte diseases. Thrombocytopenias and Thrombocytopathies: definition, classification, the causes of development, diagnostics, clinicopathologic characteristic. Qualitative anomalies of platelets: classification, manifestations, the causes of development.
-Coagulopathies: classification, etiology, pathogenesis, clinicopathologic characteristics.

Theme 22 Leucoses (Hemoblastosises). Diseases of Lymphoreticular System organs. Lymphomas.

The main questions for individual training:

-Leucoses – the primary tumour affections of the marrow, the definition. The etiology of leucoses, chromosomal and antigenic transformations. Classification, general clinicopathologic characteristic. Cytogenetic and cytochemical methods of differentiation of cell variants of leucoses.
-The acute leucosis: its kinds, modern diagnostic methods, the stages of development, clinicopathologic characteristics, complications, medical pathomorphism, age peculiarities, causes of death.

-The chronic leucosis: classification, diagnostic methods, the stages of development, clinicopathologic characteristics, causes of death.
-Myeloproliferative diseases: chronic myelosis, polycythemia, myelofibrosis. Modern diagnostic methods, clinicopathologic characteristics, complications, consequences, causes of death.
-Plasmatic cells tumours. The main characteristics, the methods of diagnostics. Classification: multiple (plasma cell) myeloma (myelomatosis, plasmocytoma, Kahler's disease), Valdenstrem's macroglobulinemia, Franklin's disease of heavy chains. The etiology, pathogenesis, morphologic characteristic, clinic manifestations, prognosis, causes of death. Modern methods of diagnostics.
-Tumour affection of thymus.
-Tumour diseases of lymph nodes. The general characteristic, clinic manifestations, localization, prognosis.
-Hodgkin's disease (lymphogranulomatosis): clinical stages, pathohistological types, morphologic characteristic and the methods of diagnostics, clinic manifestations, prognosis, causes of death.
-Non-Hodgkin's lymphomas. General characteristic, localization, prognosis, typology and classification. Immunohistochemical markers, cell types of non-Hodgkin's lymphomas.
-T- and B-lymphocyte tumours: kinds, morphologic characteristics, immune marker variants, cytogenetic and molecular-genetic markers, clinic manifestations, prognosis, causes of death.

Lesson equipment:

Macropreparation: disturbed tubal pregnancy, chronic stomach ulcer, cardiac (pericardial) tamponade, aortic intima circular rupture and separating aortic aneurysm, atrophic gastritis, fatty heart (cor adiposum), fatty hepatosis, ordinary

(simple, general) adiposity, spleen changes under hemolytic anemia as to the "General hemosiderosis" macropreparation, subepicardial hemorrhages, necrotic tonsillitis (angina) at the time of acute leukemia, lymph nodes at the time of lymphatic leukemia, splenomegaly (hypersplenism) at the time of myeloid leukemia, lymph nodes at the time of lymphogranulomatosis (Hodgkin's disease), liver, spleen at the time of the chronic myeloid leukemia, kidney, spleen under the lymphogranulomatosis (porphyric spleen), rib and skull plasmacytoma (multiple [plasma cell] myeloma), renal amyloidosis.

Micropreparation: fatty heart (cor adiposum) (painted with hematoxylin and eosin, Sudan III), liver under the chronic anaemia "Fatty (adipose) degeneration of Liver" (painted with hematoxylin and eosin, Sudan III), fatty myocardosis (painted with hematoxylin and eosin), liver hemosiderosis (Perl's reaction), extramedullary hematosis of heart (painted with hematoxylin and eosin), liver, spleen at the time of the chronic myeloid leukemia (painted with hematoxylin and eosin), liver at the time of the chronic lymphoid leukemia (painted with hematoxylin and eosin), leukemic infiltration of kidney and myocardium (painted with hematoxylin and eosin), lymph node, spleen at the time of the lymphogranulomatosis (painted with hematoxylin and eosin), renal amyloidosis (painted with hematoxylin and eosin).

Tables and slides which are present in the chair archive: normal erythroblast, blast cell at the time of leukemia, myelogenetic cell, hematosis system.

I Preauditorium individual training for the practical lesson

Theoretic Material Summary

Anaemia is a blood disease of erythrocytes quantity or their hemoglobin saturation per unit blood volume. At the same time in the peripheral blood there can appear erythrocytes of

different sizes (poikilocytosis, poikilocythemia), different shapes (anisocytosis), different levels of colouring (hyperchromatism and hypochromatism), erythrocytes with inclusions (Joli's corpuscles, Kabo's rings), nuclear erythrocytes (erythroblasts, normoblasts, megaloblasts).

To define the peculiarities of anaemia morphogenesis and other blood diseases the sternal puncture of marrow biopsy is widely used. In breast bone (sternum) punctate it is possible to diagnose the marrow regeneration level at the time of the anaemia as well as the type of erythropoiesis (erythroblastic, normoblastic, megaloblastic).

Classification of anaemias. According to the etiology and pathogenesis there are three groups of anaemias: posthemorrhagic anemia (as a result of blood loss), anaemia as a result of hematosis disturbance, and hemolytic anaemia (as a result of increased erythrocytes destruction). According to the clinical course anaemias can be acute and chronic.

Posthemorrhagic anemia develops as a result of massive hemorrhage of the stomach or bowels vessels at the time of the ulcer or tumouric affection, of uterine tube rupture at the time of the extrauterine pregnancy, of aortic rupture, of lung vessels fret at the time of tuberculosis, etc. Because of the big vessels bleeding the *acute posthemorrhagic anemia* comes and the death occurs faster than morphologic manifestations of anaemia appear. Because of the prolonged bleeding of small vessels the *chronic posthemorrhagic anemia* develops and its manifestation can be the bleach skin, mucous tunics, and internal. Red marrow of flat bones, epiphysial plates hyperplasies and turns to intence, succulent. Yellow marrow metaplasies to red, the centres of extramedullary hematosis in the spleen, thymus, lymph nodes and other tissues appear. As a result of hypoxia (oxygen starvation) in the internal dystrophic changes, small hemorrhages in mucous and serous tunics can develop.

Anaemia as a result of hematosis disturbance develops under the deficiency of iron, B-12 vitamin, folic acid. To this type hypo- and aplastic anaemias are numbered. Asiderotic (iron-deficiency) anemia is always hypochromic and develops under the poor arrival of iron into the organism with food. Such anaemias are common among children, and also under intense need of iron while pregnancy, female juvenile or climacteric chlorosis. This anaemia can appear under the stomach, bowels diseases, especially after their resection. *B-12 and folicdeficient anaemias* (megaloblastic hyperchromatism, pernicious (Biermer's, Biermer-Ehrlich) anemia) are characterized by erythrogenesis destruction and appear under food B-12 vitamin disturbance in the stomach, which is observed at the time of its diseases, when gastromucoprotein secretion prolapse is met. Such changes can be of hereditary origin or autoimmune genesis. At the time of the lymphogranulomatosis, polyposis, syphilis, corrosive (necrotic, (toxico)chemical) gastritis, malignant growths of stomach, after the ulcer of the stomach, bowels resections perniciouslike anaemias can appear. The cause of such anaemia can be exogenous deficiency of B-12 vitamin or folic acid of children fed on goat's milk. As a results of this the hematosis is realized by the megaloblastic type and the blood destruction exceeds the hematosis. The pathomorphologic manifestations of this anaemia are as following: liver, spleen, kidney hemosiderosis, fatty degeneration of parenchymatous organs, general obesity, bleach lemon-tinged skin, small hemorrhages in mucous, serous tunics and skin. In gastrointestinal tract there are atrophic and sclerotic changes, the marrow turns to raspberry-red with the predominance of erythroblasts, normoblasts, and megacaryoblasts. In lateral and posterior (dorsal) columns of spinal cord there is funicular myelosis, in the brain there are the centres of encephalomalacia and ischemia. *Hypoplastic and aplastic anaemias* can be endogenous or inherited (familial

aplastic anaemia of Fankoni and Erlich's hypoplastic anaemia), and exogenous or acquired (radiation, toxic, medicamentosis anaemias).

Hemolytic anaemia is characterized by the increased erythrocytes destruction which can be intravascular and extravascular. Intravascular anaemia appears when hemolytic poisons get into the organism, at the time of the bad burns (toxic anaemia), at the time of malaria, sepsis and other infections (infectious anaemia), at the time of blood transfusion of incompatible blood group or Rhesus factor (posttransfusion anaemia), at the time of immune pathologic processes (immune, isoimmune and autoimmune anaemias (hemolytic disease of newborns, chronic lympholeucosis, marrow carcinomatosis, systemic lupus erythematosus, medicamentosis immune hemolysis, thermal hemoglobinuria and other). Extravascular (intracellular) anaemia is mostly of inherited origin and is divided into erythrocytopathy, erythrocytoenzymopathy and hemoglobinopathy. To the hemolytic anaemias of such origin as erythrocytes membrane structural defect are ranked such diseases as microspherocytosis, inherited ovalocytosis, etc. Erythrocytoenzymopathic hemolytic anaemia appears because of enzyme deficiency of pentose-phosphate cycle - glucose 6-phosphate dehydrogenase and pyruvate kinase. This anaemia grows progressively worse at the time of viral infections, usage of some medicaments. Hemoglobinopathic hemolytic anaemia develops at the time of disturbance of haemoglobin synthesis – a and b-thalassemia or at the time of appearance of anomalous haemoglobin – S,C,D,E. Falcated cellular anaemia can include hemoglobinopathies.

Morphologic manifestations of hemolytic anaemias are very specific: general hemosiderosis, hemolytic jaundice in serious cases with hemoglobinuric nephrosis, splenomegaly at

the time of inherited hemolytic anaemias, the presence of centres of extramedullar hematosis.

Thrombocyte diseases. Diseases which manifest themselves in reduced erythrocytes quantity in peripheral blood as a result of their increased destruction or deficient creation are called *thrombocytopenias*. They can be inherited or acquired. Inherited thrombocytopenias are divided into immune and non-immune. Immune thrombocytopenia appears while incompatibility of blood in any system, at the time of the disturbance of antigenic thrombocytes structure (heteroimmune), at the time of production of antybodies against their own thrombocytes (autoimmune). Non-immune thrombocytopenia appears in case of mechanic injuries of thrombocytes, oppression marrow cells proliferation because of toxic agents, radiation, metastases of malignant growths, hemoblastosis, B-12 or folic acid deficiency, disseminated intravascular coagulation (DIC), etc. Morphologic manifestations of thrombocytopenia are the presence of hemorrhagic syndrome on the skin, mucous tunics, and parenchyma of internals.

Thrombocytopathies are diseases at the time of which morphologic, functional, biochemical thrombocytes inferiority is observed, which causes the hemorrhagic syndrome development in the vessels of microcircular canal. Thrombocytopathies can be inherited or acquired. They are characterized by the disturbance of the formation of hemostatic thrombocyte plug including adhesion, secretion, and aggregation. *Inherited* variants of pathology mostly accompany the other inherited defects. In their essense there is autosomal recessive disturbance of membrane glycoprotein synthesis and thrombocytes secretion. As an example we can observe Glantsman-Negeli disease with absent thrombocytes aggregation, the disturbance of binding with fibrinogen and prolonged bleedings. The other example is Bernar-Sulie

disease with large thrombocytes and lowering of their adhesion. *Acquired* thrombocytopathies appear at the time of many diseases: hemoblastosis, B-12 deficiency anaemia, cirrhosis, tumouric liver diseases, uraemia, radiation sickness, scorbutus (scurvy), massive hemotransfusion, DIC syndrome, hormonal disturbance, medicamentosis and toxic affections of organism, etc. Thrombocytopathies can course with more or less apparent thrombocytopenia.

Coagulopathies is a group of diseases connected with the disturbance of blood coagulation system. Stable deficiency of any coagulation factor causes hemorrhagic syndrome in organism: prolonged bleeding, spontaneous petechia, large posttraumatic haematomas, hemorrhages into gastrointestinal tract, joints, etc.

Coagulation disturbances can be inherited and acquired. *Acquired coagulopathies* appear under K vitamin deficiency, when the factors of coagulation: II, VII, IX, X and C protein are oppressed. Such conditions are common at the time of the liver diseases since here almost all coagulation factors are synthesized; at the time of DIC syndrome. DIC syndrome is a coagulopathy with the activation of coagulation which leads to the formation of microthrombs in the microcircular canal. As a result of thrombophilia the deficiency of thrombocytes appears, the coagulation factors and the secondary activation fibrinolysis mechanisms, which increases the hemorrhagic diathesis.

Inherited coagulopathies appear as a deficiency of one coagulation factor. They are often met in family marriages (rulers dynasties in Europe, Russia). It is an A-haemophilia at the time of factor III deficiency, and B-haemophilia at the time of factor IX deficiency. For the most coagulopathies autosomal transfer is typical. Hemostasis disturbance is evident through such coagulation changes: prolonged bleeding and prothrombine time (duration in seconds of formation of blood

plasma clot with the presence of thromboplastin and calcareous salt), thromboplastin time (formation period of thromboplastin-factor III of thrombocytes which helps to transform prothrombin into thrombin).

Leucoses

Leucoses are systematic tumouric diseases of hematopoietic tissue (blood-forming tissue) which are characterized by the progressive overgrowth of tumouric cells-leukemia cells. First tumouric cells increase in hematopoietic organs (marrow, lymph nodes, spleen) and then hematogenously spread in whole organism with the infiltration of some organs; and also appear in peripheral blood. Progressive overgrowth of leukemia cells leads to anaemia, hemorrhagic syndrome, dystrophic changes in parenchymal (parenchymatous) organs, immunity oppression, ulcero-necrotic and septic complications. Leucoses *etiology* can not be always identified since it is a polyethiologic disease. The cause can be genetic and inherited factors, chromosomal anomaly, and all factors which can cause cellular mutation hematopoietic system. To the mutation genes belong: viruses (retrovirus HTLV-I,II, Epstein-Barr DNA-virus), ionizing radiation, chemical compounds (benzpyrene, pesticides, herbicides, benzene ring compounds, etc). Leucoses *classification* is based on the morphologic and cytochemical peculiarities of marrow tumouric cells. The acute and chronic leucoses there divided according to the level of differentiation of tumouric blood cells and their development (non-malignant or malignant). Acute leucoses are characterized by the proliferation of non-differentiated or differentiated, blastic cells and have malignant development. Chronic leucoses are characterized by the proliferation of differentiated leukemic cells and relative non-malignant development. As to the quantity of leucocytes and leukocyte cells there are the following variants of leucosis: leukemic (dozens and hundreds of thousands of cells per 1mcl

(microliter) of blood), subleukemic (not more than 15-25 thousands cells), leukopenic (lowering of leucocytes quantity but with their presence), aleukemic (no leucoses in peripheral blood).

Acute leucoses as to morphologic and cytochemical peculiarities of leucocytes are divided into lymphoblastic and myeloblastic leucoses or lymphoblastic and non-lymphoblastic. As to contemporary knowledge of hematosis among the acute leucoses there are non-differentiated, myeloblastic with blasts maturation, promyelocytic, myelomonocytic, monocytic, monoblastic, erythroleucosis, megakaryoblastic variants which develop from spinal cell or cell precursories of class II-IV. Among the lymphoblastic leucoses according to immunal and cytogenetic characteristics 3 morphologic forms: are distinguishedL1, L2, L3.

Clinicopathologic characteristic. The first manifestation of the acute leucosis is the presence of blastic cells in punctuation of breast bone marrow as a result of what it changes its painting and consistence (red, succulent, sometimes with grey shade under non-differentiated form; pyoidic at the time of myeloblastic form; raspberry-red at the time of lympholeucosis). In the peripheral blood the leukemic (leucemicus) hiatus develops. It is a great number of blastic cells, too little of mature, and the total absence transferring cell forms. There is a substitution of marrow with the new blastic leukemic cells. Gradually leukemic infiltration appears in the spleen, liver, lymph nodes, kidneys, meninx (brain tunic) (neuroleukemia at the time of lymphoblastic leucosis), mucous tunics of gastrointestinal tract, lungs (leukemic pneumonitis at the time of myeloleucosis) and other organs. There develops anaemia, thrombocytopenia, and hemorrhagic syndrome on skin, mucous tunics, serous tunic, internals, cerebrum, necrotic tonsillitis (angina), septic complications, and dystrophic changes in parenchymatous organs.

Children have acute leucoses more often; there can be inherited forms of disease. There are nodular infiltrations in different organs. The most common is T-dependent lymphoblastic leucosis, the less common is myeloblastic leucosis.

Causes of death: septic complications (especially often met at the time of non-differentiated form), ulcero-necrotic complications, hemorrhages (especially dangerous into cerebrum which are often met at the time of promyelocytic leucosis, progressive disease).

Medical pathomorphism: under the influence of therapy at the time of leucoses the hemorrhagic diathesises, necrotic changes in mucous tunic of decreased mouth (oral) cavity; more often the ulcero-necrotic changes are met in tunics of gastrointestinal tract; leukemic pneumonics, leukemic meningitis.

Chronic leucoses are divided into leucoses of myelocytic origin, leucoses of lymphocytic origin, and leucoses of monocytic origin (myelomonocytic leucosis and histiocytosis).

Chronic leucoses of myelocytic origin or *myeloprolipheral diseases* are represented generally by chronic myelosis or chronic myeloid leucosis, chronic erythromyelosis, polycythemia, erythromia, myelofibrosis. Chronic myeloid leucosis has two stages: monoclonal non-malignant and polyclonal malignant. The first stage lasts for several years and is characterized by the progressive increasing of neutrophilous leucocytes with transfer to myelocytes. At the later stage in 3-6 months there develops polyclonism, blastic cell form appear (myeloblasts, erythroblasts, monoblasts and other), blast crisis appears, the quantity of erythrocytes in blood increases to several millions per 1mcl, all manifestations of acute leucosis develop.

Morphology: the marrow is red with grey, succulent, pyoidic; the blood is grey with red; internals are anaemic; the spleen is abruptly increased to 6-8 kg (13,22-17,64 lbs), of grey with brown painting, atrophied follicles, sclerosis and hemosiderosis of pulp, leukemic infiltrates, leukemic thrombi in vessels; the liver is increased to 5-6 kg (11,02-13,22 lbs), of grey with brown painting, leukemic infiltration along the sinusoid, fatty dystrophy of hepatocytes, hemosiderosis; lymph nodes are diffusely very increased, soft, of grey with red painting.

Myelofibrosis is characterized by the presence of myeloid leucosis manifestations and the change of marrow to connective or bone (osseous) tissue. Thus the disease has a prolonged non-malignant course.

Erythromia is met among elderly people and is characterized by the increasing of the mass of erythrocytes, thrombocytes, granulocytes in peripheral blood, increased blood (arterial) pressure, inclination to thrombosis, splenomegaly.

Chronic leucoses of lymphocytic origin are represented by chronic lympholeucosis, skin lymphomatosis (Caesary's disease), and paraproteinemic leucosis. Chronic lympholeucosis develops among elderly people, appears from B-lymphocytes, but with abrupt lowering of immunoglobulin formation, the development of autoimmune reactions, the increased quantity of leucocytes in peripheral blood to 100 thousands per 1 mcl, leukemic infiltrates are present in all organs.

Morphology: the marrow is red; the spleen is increased to 1 kg (2,2 lbs), of red painting, follicles are increased due to leukemic infiltrations; the liver is increased, of grey with brown painting, leukemic infiltration along the portal tract, fatty dystrophy of hepatocytes; lymph nodes are abruptly increased, thick, in the form of bags, can squeeze the

neighbouring organs, of grey with pink painting; kidneys are greatly increased, leukemic infiltration abruptly disturbs parenchymal structure. Infectious complication and hemolytic statuses are typical.

Tumours of plasmatic cells or paraproteinemic leucosis develop from B-lymphocytic system, the precursors of plasmatic cells. These cells synthesize the pathologic proteins, paraproteins. To this group of leucoses belong: myeloma (myelomatosis, plasmocytoma, Kahler's disease), Valdenstrem's macroglobulinemia, Franklin's disease of heavy chains. Myeloma is characterized by the spread of tumouric cells of lymphoplasmocytic line – myelomic cells in marrow with bones destruction. In peripheral blood the pathologic proteins are accumulated (paraproteins), which segregates into urine through the kidneys (Bens-Jones's protein).As to the character of myelomic infiltrates in marrow and bones there divide diffusive, diffusive-nodal, multiple forms of disease. The most affective there are the flat bones (skull and ribs), vertebras, more seldom tubal with the development of bone tissue destruction. In the bones osteolysis and osteoporosis develop. Myelomic infiltration is also observed in the internals: spleen, liver, kidneys, lungs, lymph nodes. Complications: paraproteinemic nephrosis, myelomicly wrinkled kidneys, renal amyloidosis (amyloidosis nephrosis), inflammatory changes as pneumonia, pyelonephritis. The other forms of paraproteinemic leucosis are seldom accompanied with bones destructions.

Tumour diseases of lymph nodes or lymphomas. To this group belong: lymphosarcoma, mycosis fungoides, Caesary's disease, reticulosarcoma, Hodgkin's disease (lymphogranulomatosis). There are Hodgkin's and non-Hodgkin's lymphomas. They can be B- and T-cellular. Lymphomas or lymphocytomas are ectomarrow tumours which consist of different lymphocytes or of lymphocytes and

prolymphocytes. They appear in lymph nodes or lymphoid tissue of the other internals. They are characterized by the local growth and non-malignant course. The first manifestation of lymphomas are increased peripheral lymph nodes, they become thicker, mobile, non-painful. Later there appear the manifestations of intoxication, general weakness, weight loss, night sweat, which is the manifestation of the tumouric process. Transformation into lymphosarcoma is rarely met and after the long time.

Lymphosarcoma is a malignant lymphoma of mediastinal, extraperitoneal, inguinal lymph nodes, and lymph tissue of gastrointestinal tract. The nodes increase with the necrotic and hemorrhagic areas. Process generalization courses lymphaticly and hematogenously. To this group belong: Burkitt's lymphoma (Burkitt's tumor) - endemic disease of African children when facial skeleton bones are damaged. The cause is the herpetiformis virus.

Mycosis fungoides is a non-malignant T-cellular skin lymphoma.

Hodgkin's disease (lymphogranulomatosis) is a chronic recurrent lymphoma with the affection of cervical, mediastinal, extraperitoneal, inguinal lymph nodes. There are isolated (local) and spread (generalized) forms. The spleen is often affected (necrosis niduses of white with yellow painting, sclerosis, lymphocytic infiltration), that's why it turns to variegated and porphyric look. In lymph nodes there appear prolypheration of leucocytes, histiocytes, reticular cells, eosinophils, plasmatic cells, neutrophilic leucocytes, necrosis and sclerosis niduses, atypical mononuclear small and big Hodgkin's cells, polynuclear giant Rid-Berezovsky-Stemberg's cells. There are four clinicopathologic forms of disease: predominance of lymph tissue (lymphohistiocytic) variant – I-II stages of disease, its localized form, nodular sclerosis is met at the time of non-malignant course of disease, mixed-cellular

variant appears at the time of disease spread and corresponds to the II-III stages, the oppression of lymph tissue variant is typical for the generalized form and has a malignant course, sometimes called Hodgkin's sarcoma.

II Algorithm of the practical part of the lesson

Study and be ready for the verbal description of the macropreparations:

1 Defective tubal pregnancy. Fallopian tube is gasketed, perforated hole in the wall, grume in the lumen. The same grume is seen in the abdominal cavity. The embryo is seen in it. The disturbance of the wall of fallopian tube is caused by the corrosion of villous (shaggy) chorion (haemorrhagia per diabrosion). Intra-abdominal hemorrhage (hemoperitoneum) and acute posthemorrhagic anemia develops.

2 Chronic stomach ulcer. Ulcer edges are gasketed due to the connective tissue spread in the shape of a roll. Ulcer bottom partially or in the whole area has dark brown painting. Pathologic process corrodes vessels wall and hemorrhage appears (haemorrhagia per diabrosion). Haemoglobin at the time of hydrochloric acid affection turns to muriatic haematin of dark brown painting which paints the ulcer bottom and walls. Prolonged stomach hemorrhages at the time of the ulcerous disease are complicated with chronic posthemorrhagic anaemia.

3 Cardiac (pericardial) tamponade. In the cavity the blood is seen. On the heart top there is a spread subepicardial myocardial infarction at the organization stage – the tissue has light yellow painting. In the lateral wall of the left ventricle at the basis there is an area of triangular shape of dark red painting. This is the recurrent myocardial infarction with myomalacia. The myomalacia area is filled with blood, via this area the blood from the left ventricle cavity arrived to the cardial cavity and the tamponade appeared. The death came as

a result of abrupt pressure change in the cardial ventricle hole, and it stops in the systole phase. At the same time hemopericardium can stay undisturbed.

4 Aortic intima circular rupture and separating aortic aneurysm. Ascending aortic part is widen, the linear transversal aortic intima rupture is seen. In the left ventricle endocardium and in aortic intima there are pale red big macules of vague outlines – the Minakov's macules which are caused by the low pressure in the left ventricle chamber as a result of aortic rupture. Minakov's macules appear as a vacant hyperemia which is similar to medical jars hyperemia. As a result of the pressure in the left ventricle lowering while diastole the negative pressure appears, the blood is sucked from the auricle that's why the hemorrhages in endocardium appear.

5 Atrophic gastritis. Stomach tunic is smooth, no wrinkles – the total diffusive tunic atrophy came. In accessory cells of fundus (fundic) glands of stomach tunic the gastromucoprotein (Kustle's internal factor) is produces. Gastromucoprotein has a transportation function; it combines with B-12 vitamin as a result the protein-vitaminous complex appears which is absorbed by stomach and small intestine mucous tunics. Under atrophic gastritis there is less of gastromucoprotein or it is absent at all. But B-12 vitamin is not absorbed without it which leads to Addison-Biermer anaemia

6 Fatty heart (cor adiposum). The heart is increased in its size. Under the pericardium mostly of the right part of heart there is an increased fat. Fatty heart as the other organs at the time of such disease is developed under anaemias and is caused by hypoxia. Nutrients which arrive into organism with food in the case of the lack of oxygen do not coagulate; it means they are not completely used as an energetic and plastic material, but are saved as neutral fat. The heart increases due to the stretching of its chambers, because fat spreads into the myocardium with the course of perimysium and endomysium.

cardiomycytes nutrition gets worse, they atrophy because of the pressure and are changed by fatty tissue. Ability of myocardium beat lowers – the heart chambers stretch, the heart increases mostly in transversal size.

7 Fatty hepatosis. In the cut the liver has yellow painting while the whole stretch, little increased, the capsule is smooth. Fatty dystrophic liver appears at the time of chronic anaemias as a result of hypoxia. At the time of hypoxia the hyperlipemia appears because of the nutrients which are not completely realized as a plastic and energetic material thus more blood arrives to liver with arterial blood. Also in the case of the oxygen deficiency hepatocytes are not able to split completely the fat which arrives to liver from intestine via portal vein. Liver function lowers on this.

8 Ordinary (simple, general) adiposity. In the macropreparation subcutaneous fat of the front abdominal wall of 10-12 cm (3,93-4,72 inches) thickness is represented. This adiposity is probable at the time of chronic anaemias as a result of nutrients which are not completely used as plastic and energetic material with saving of fats in depot.

9 Subepicordial hemorrhages. On the front heart surface by the course of the terminal branch of coronary vessels the subepicardial diapedetic hemorrhages are seen – the dark brown macules of vague outlines. Increased vessels penetrability is caused by hypoxia, thrombocytopenia which break as a result of compensatory high spread of myeloid or lymphoid hematopoietic shoots with the corresponding oppression of other (erythrocytic, thrombocytic, megakaryocytic). The brown painting is explained by the local hemosiderosis.

10 *Spleen at the time of hemolytic anemia as to the "General hemosiderosis" macropreparation.* In the macropreparation twice increased spleen is represented. From the surface and the cut organ has a dark fulvous painting as a result of saving of

excessive hemosiderine under intensive erythrolysis. The spleen has thick consistence as a result of connective tissue spread.

11 Necrotic tonsillitis (angina) at the time of *the acute leukemia.* On the macropreparation irregular-shaped tonsils are increased in which the areas of grey painting are seen with the ulcering and necrotic changes, hemorrhage niduses, swelling of the surrounding tissues.

12 Liver at the time of *the chronic myeloid leukemia.* The organ is abruptly increased, the surface is smooth, on the cut the tissue is homogeneous of yellow with grey painting.

13 Splenomegaly. It is represented by several preparations. The organ is abruptly increased, capsule is overstretched, thinned. Splenomegaly is common for leucoses, great increasing of spleen is typical for chronic myeloid leucosis. Spleen increasing is caused by extramedullar hematosis in organism. Stretching and thinning of capsule can be complicated by pathologic capsule and pulp rupture even because of the trivial trauma, for example, while rough palpation.

14 Spleen at the time of the chronic myeloid leukemia. Spleen increasing is caused by extramedullar hematosis. The pulp has dark brown painting caused by general hemosiderosis. At the time of the myeloleucosis the compensatory high spread of myeloid or lymphoid hematopoietic shoots is possible with the corresponding oppression of other. In peripheral blood the unripe appears, which is quickly destroyed. Free haemoglobin is absorbed by endothelial and reticular cells of reticular-endothelial system (RES) (spleen, liver, marrow, lymph nodes, substernal glands). In the macrophage cytoplasm haemoglobin turns to hemosiderine which gives brown painting to organs.

15 Lympholeucosis (mesenterial nodes). On the macropreparation the large intestine and abruptly increased mesenterial lymphnodes of bag shape are represented. Diameter of some nodes reaches 10 cm (3,94 inches). The

nodal pulp is homogeneous, of white painting. The nodes are increased due to extramedullar hematosis. The bag of abruptly increased mesenterial lymphnodes can press the vessels, nerves, which clinically manifest the tumour.

16 Visceral lymphogranulomatosis. On the liver cut numerous tumouric spots of round shape in diameter of 0,2-1 cm (to 0,39 inches) are seen. These spots usually have clear shapes. Microscopically they are represented by hyperplasmic lymph tissue with areas of necrosis and sclerosis that is the morphologic features of lymphogranulomatosis. At the same time parenchyma is destroyed by tumouric spots and its function lowers.

17 Porphyric spleen at the time of lymphogranulomatosis. On the spleen cut on the dark red background of normal pulp there numerous areas of white painting of different configuration of clear shape are seen. White spots are the areas of pulp necrosis which are common at the time of lymphogranulomatosis. In its picture in the cut such spleen looks like marble porphyry - white specks on the red background.

18 Rib plasmocytoma. It is represented by two preparations with the same changes –rib structure is completely disturbed, bone tissue is totally absent. With naked eye it seen that rib has a soft consistence and it is possible to cut it with a knife. Bone tissue is disturbed by solitary plasmocytoma at the time of myeloid leukemia.

19 Skull plasmacytoma. It is represented by two preparations. The internal surface of skull bones is covered with spots: on the light grey background there are light brown spots of unclear shape, also there are white spots of different sizes. Such picture remains the geographical map. Relief of internal surface is uneven. The bone thickening is present it means curving of mostly light brown areas into skull cavity. Thickening of a skull on the cut is also seen. While look on skull cavity in the light (at the window), the heterogeneous of bone is seen –

lumen areas. After maceration (or after boiling of bone) the areas of bone tissue destruction are seen – the internal lamina is totally destroyed or almost totally in some places on the destruction edges bone tissue is destroyed, thickened.

20 *Renal amyloidosis.* The kidney is increased, of homogenously white painting, the edges between organ areas are absent. Renal amyloidosis complicates myeloid leukemia. At this time plasmocytes produce a great number of plasmaglobulines which go out via kidneys (Bens-Jones protein) and constipate them. Besides destruction products of bone tissue also of protein nature go out of the organism via kidneys and constipate the renal filter – the walls of glomerule capillaries.

Study the micropreparations of the theme and be ready to show on the picture the main points of the pathologic process with the following descriptions:

1 Fatty heart. Hematoxylin and eosin painting. Between the cardiomyocytes in the perimysium and endomysium the wide edges of fat are seen - the lipocytes membranes, fat is washed out of the cell by the alcohol. **Designate:** 1 – myocardiocytes, 2 – fat.

2 Fatty myocardium dystrophy. Sudan III and osmic acid painting. Sudan III paints the fat into yellow with orange, osmic acid – into black. On the preparations it is seen that fat contained in the cardiomycytes (fatty dystrophy). Pay attention to the nidus of fat saving in some groups of cardiomycytes but not to the diffusive. It is caused by the appearance of hypoxia mostly in the venous end of the capillaries. That is why in the cardiomycytes which are the touches of the venous end of the capillaries because of the oxygen deficiency metabolism is reduced; fat is not totally realized and is saved in the sarcoplasma. Besides hypoxia is complicated by the destruction

of incellular ultrastructures and the free fat and proteins are saved in the sarcoplasma. Nidus of fat saving in cardiomycytes causes stripes of myocardium – the darker undistracted stripes change to lighter where there is more fat – "tiger heart" which is seen from the endocardium side.

Designate: 1 – cardiomycytes, 2 - fatty inclusions.

3 Fatty liver dystrophy. Hematoxylin and eosin painting. In the centre of the pieces the lighter bulbs are seen, the former fatty vacuoles in hepatocytes. Fat was washed while cuts fixations with alcohol and light bulbs stay instead of fat. Fatty dystrophy is more seen in the centres of pieces that's why dystrophy is caused by hypoxia which is common at the time of anaemia. Absorbed in intestine fat at the time of oxygen deficiency in hepatocytes do not completely split and is saved in cell cytoplasm. In the periphery of kernel particles in hepatocytes they are bigger, more intensively coloured in blue with hematoxylin, sometimes bikernal hepatocytes are met which is the manifestation of regeneration.

Designate: 1 – hepatocytes, 2 – fatty inclusions.

4 Liver hemosiderosis. Perls' painting of organ tissue (reaction for Prussian blue). Hemosiderine has blue painting. In endolithocytes, five-finger cells, hepatocytes the not big blue granules are seen which hemosiderine is. This is the manifestation of general hemosiderosis. While intravascular erythrolysis (for example, of megaloblasts at the time of Addison-Biermer anaemia) free haemoglobin is absorbed in blood by endothelial and reticular cells of reticuloendothelial system to which the marrow, spleen, lymph nodes, liver are numbered. In macrophages haemoglobin turns to hemosiderine.

Designate: 1 – hemosiderine.

5 Extramedullar hematosis in heart. Preparation is painted with hematoxylin and eosin. In endocardium nests of cells with hyperchromic round kernels of hemopoietic origin are seen.

This is the extramedullar hematosis nidus which is common for chronic anaemias.

Designate: 1 – cardiomyocytes, 2 – hematosis nidus.

6 Liver under myeloleucosis. Preparation is painted with hematoxylin and eosin. Between the pieces along the portal tracts big cellular infiltrates are seen, cell kernels are hyperchromic. Leukemic cells with hyperchromic kernels are also seen along the sinusoid capillaries in the capillary holes. Thus in this case there is leukemic infiltration of liver at the time of the chronic myeloid leucosis, the hepatocytes beams are grinded off which the atrophy is caused by pressure. Besides the light brown spots are seen which are the bile granules. Cholestasis is caused by hemolytic anaemia which is common at the time of the myeloid leucosis. The light hollows in hepatocytes of different size are also seen which is fatty dystrophy of hepatocytes.

Designate: 1 – liver beams, 2 – leukemic infiltrates.

7 Liver under lympholeucosis. Preparation is painted with hematoxylin and eosin. The numerous big accumulation of lymphoid tissue in portal tracts between the liver pieces are seen. In the pieces only single leukemic cells of lymphocytic type in the sinusoid capillaries are seen. Thus diffusive leukemic infiltration between and in the pieces is common for myeloleucosis; between the pieces – nidal – is common for lympholeucosis. **Designate:** 1 – liver beams, 2 – lymphoid leukemic infiltrates.

8 Spleen under myeloleucosis. Preparation is painted with hematoxylin and eosin. Spleen structure is distroyed, the picture is erased. There are small groups of lymphocytes which are the remainings of lymph follicles; these are the groups of cells with small round of one size kernels and small edging of cytoplasm. Liver pulp is changed to myeloid cells of different ripeness – from myeloblasts to segmental (segmentonuclear) leukocytes. The tightly set leukemic cells are seen in the vessel

holes. There are also the nidal disturbances of hematosis which is vessel plethora and hemorrhages.

Designate: 1 – lymph follicles, 2 – myeloblasts.

9 Leukemic kidney infiltration. Preparation is painted with hematoxylin and eosin. With the naked eye the area is seen which is more intensively painted with grey. Microscopically there is pointed to the area which is represented by hemopoiesis cells of different stages of differentiation. In the nidus of extramedullar hematosis the remains of disturbed canals, single glomerules with pronounced necrobiotic changes are seen. There are great dystrophic changes of epithelium of sinuous canals. **Designate:** 1 – kidney glomerules, 2 – canals, 3 – leukemic infiltrates.

10 Leukemic infiltration of myocardium. Preparation is painted with hematoxylin and eosin. In pericardium an area of hemopoiesis cells accumulation of different stages is seen. Kernels of these cells are hyperchromic. Under the pericardium the fatty bag is seen which growth between the cardiomycytes and looses the myocardium. Cardiomycytes are atrophic with pronounced dystrophic changes – transversal banding is absent, sarcoplasma is homogenous, mostly of intensively coloured pink with eosin (manifestation of coagulate necrosis). Sometimes cardiomycytes are fragmented which is transversal fibers ruptures. Sometimes the lengthwise garnetting of cardiomycytes is seen, sarcoplasma emptiness – cytolysis (the manifestation of coagulate necrosis), sarcoplasma has a light pink painting, less eosin colouring.

Designate: 1 – cardiomycytes, 2 – leukemic infiltrates.

11 Spleen lymphogranulomatosis. Preparation is painted with hematoxylin and eosin. The picture of spleen is erased. The area of hyperplasia of lymph tissue is seen, the sells have different sizes, intensity of painting, sometimes among them there single giant Berezovsky-Sternberg cells are met – the accumulation of hyperchromic kernels. The lighter areas of

necrosis and sclerosis are also seen painted in pink. Light centers in lymph follicles are necrotizing. The vessels are plethoric. Thus in the spleen the all stages of lymphogranulomatosis are seen: granulematosis, necrosis and sclerosis. **Designate:** 1- spleen parenchyma, 2 – necrosis areas, 3 – sclerosis areas.

12 Renal amyloidosis. Preparation is painted with congo-rot, amyloidosis is pictured with red. The amyloidal accumulations in the vessels walls, in organ stroma are seen. Such changes are common in the cose of the amyloidosis disease. Plasmocytes produce the gamma globulins which go out via kidneys and constipate them; and first of all kidney filter - glomerules. Besides products of bones destruction of albuminous character also constipate the kidneys.

Designate: 1- glomerules, 2 – canals, 3 – amyloidosis.

13 Lymph node under lymphogranulomatosis. Preparation is painted with hematoxylin and eosin. The picture is erased. The areas of lymph tissue hyperplasia are seen, cells of different sizes, intensity of painting, among them there single giant Berezovsky-Sternberg cells are met – the accumulation of hyperchromic kernels are seen. The lighter areas of necrosis and sclerosis are also seen coloured in pink. Light centres in lymph follicles are necrotizing. The vessels are plethoric. Thus in the lymph node all stages of lymphogranulomatosis are seen: granulematosis, necrosis and sclerosis.

Designate: 1- lymphocytes, 2 – sclerosis,
3 - Berezovsky-Sternberg cells.

Situation Tasks:

1 A dead man who had suffered from a stomach ulcer for a long time has died of massive stomach hemorrhage (in the stomach and intestine hole there is more than 2,5 l (0,66 gallon) of blood). What type of anaemia is represented? Which paint of skin and tissue the deceased will have? What

microscopic changes will be there in his internals? What changes are there in the hemopoietic organs?

2 An ill woman of 22 has icteric sclera and skin, the spleen is increased. In blood test the erythrocytes quantity is lowered, they are of falcate form. Which type of anaemia is represented? What is the name of the disease? What is the pathogenesis of disease development? Which macroscopic changes are there in the spleen?

3 An ill woman has metrorhagy of more than two months has not asked for a medical help. The weakness, paleness, tachycardia, hard breath increased. What type of anaemia is represented? What changes are there in the peripheral blood? What changes are there in hematosis organs? What changes are there in the internals and tissues?

4 A child had the weakness, languor, nasal bleeding, and fever. At the time of the checkup the increasing of lymph nodes of mediastinum, spleno- and hepathomegalias, increasing of lymphocytes quantity in blood were discovered. There is a great number of lymphoblasts in the lymphocytes. What form of leucosis you can expect?

5 The ill man suffered from the hematosis disease for 25 years, old. The cause of death is bronchopneumonia. Post-mortem examination showed the systematic increasing of lymph nodes, they are succulent, intergrowed in the bag shape with 12 cm (4,72 inches) diameter. The spleen is 800 g (28,22 ounces) weight, the marrow is red. In peripheral blood there are 85x10 ml lymphocytes. What disease can you expect? What histological changes can be there in spleen, liver, and lungs?

6 There is an ill man with an isolated increasing of lymph nodes in the throat from the right side. Peripheral blood test shows the norm. The histological examination of biopsy of the increased lymph node showed the erased picture of node, the absence of follicles, focal hyperplasia of lymph tissue of the granuloma type, in which the giant polykernel cells, areas of

necrosis and sclerosis are met. What disease can you expect? Which cells are important for the diagnostics?

Answers for the Situation Tasks:

1 It is acute posthemorrhagic anaemia. The skin and tissues of a dead man will be pale painted, anaemic. Microscopically in the internals there will be the spanaemia, dystrophic changes. In the hematosis organs there will be the manifestations of hyperplastic changes.
2 It is the hemolytic anaemia. Falcate cells anaemia. The disease develops because of the erythrocytes destruction which are defective in their morphologic and functional features. In the spleen the hyperplastic processes, hemosiderosis develop.
3 The ill woman has a posthemorrhagic anaemia. In the peripheral blood there will be the lowering of erythrocytes, hemoglobin, kernel erythrocytes are possible. In the hematosis organs the hyperplastic changes will develop. In internals and tissues there will be the manifestations of the spanaemia, dystrophic changes.
4 It is lymphoblastic leucosis.
5 It is lympholeucosis. In internals there will be the leukemic infiltration.
6 It is possible to expect the lymphogranulomatosis. Berezovsky-Sternberg cells have the diagnostic significance.

Test Tasks:

1 An ill man suffered from often gastrointestinal hemorrhages, has died of insult. Post-mortem examination showed the succulent red marrow of shaft of femur. What process developed in the marrow?
A. Hormonal hyperplasia.
B. Work hypertrophy.
C. Compensatory hyperplasia.

D. Vicarious (substitutional) hyperplasia.
E. Hypertrophic overgrowth.

2 Medical examination of an ill woman's oral groove showed he tongue tunic atrophy with red spots (Hunter's (Moeller's) glossitis), yellow sclera. Blood test showed the painting index more than 1. What anaemia does a woman have?
A. Iron deficient.
B. Hemolytic.
C. Acute posthemorrhagic.
D. B-12-folicdeficient.
E. Chronic posthemorrhagic.

6 years old girl has the general weakness, trophic (venous tasis) ulcers on the skin, painful articulations, pale skin. Blood est Hb=70 g/l (2,47 ounces per 0,26 gallon), falcate rythrocytes. What pathology a child has?
A. Hemoglobinopathy.
B. Malignant pernicious anaemia.
C. Acute leucosis.
D. Toxic anaemia.
E. Rheumatism.

4 An ill woman has worked for a long time with benzol, the anaemia is progressing. Hemorrhagic syndrome appeared. Sternum biopsy material shows the fatty tissue, the lack of hematosis niduses with the single myelopoesis cells. What pathology does an ill woman have?
A. Chronic myeloleucosis.
B. Pernicious anaemia.
C. Hemolytic anaemia.
D. Hypoplastic anaemia.
E. Posthemorrhagic anaemia.

5 12 years old boy has increased cervical nodes. Biopsy material shows the prolypheration niduses of lymphocytes, eosinophils, giant polykernel Berezovsky-Sternberg cells, areas of necrosis and fibrosis. What disease is this?
A. Lymphosarcoma.
B. Histiocytosis.
C. Lymphogranulomatosis.
D. Chronic lympholeucosis.
E. Myelomic disease.

6 10 years old child has increased lymph nodes of all groups, spleen, and liver. Histological examination of cervical node showed the absence of lymphoid follicles, the whole node tissue is changed by the round kernels and narrow basophile cytoplasm, node picture is erased. What disease is this?
A. Lymphosarcoma.
B. Lymphoid leucosis.
C. Lymphogranulomatosis.
D. Myelomic leucosis.
E. Myelomic disease.

7 Post-mortem examination of 40 years old woman showed increased lymph nodes of all groups, flat and fungous bones marrow hyperplasia (marrow pyopoiesis), the increasing of spleen to 6 kg (13,23 pounds), and liver to 4 kg (8,82 pounds). What disease is it?
A. Chronic lympholeucosis.
B. Chronic myeloleucosis.
C. Myelomic disease.
D. Lymphogranulomatosis.
E. True polycythemia.

8 Cervical node examination showed the erased picture, diffusive spread of lymph cells, the presence of eosinophils,

giant bikernal cells, niduses of necrosis and sclerosis. Which type of lymphogranulomatosis is represented?

A. With lymph tissue domination.
B. With lymph tissue oppression.
C. Mixed cellular.
D. Mixed.
E. Nodular sclerosis.

Answers to the Test Tasks:

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

Illustrations to theme

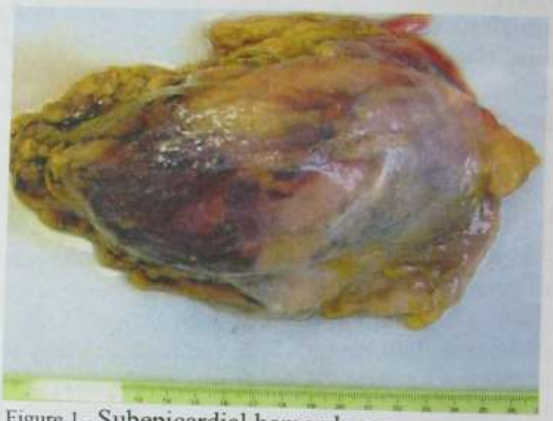


Figure 1– Subepicardial hemorrhages.

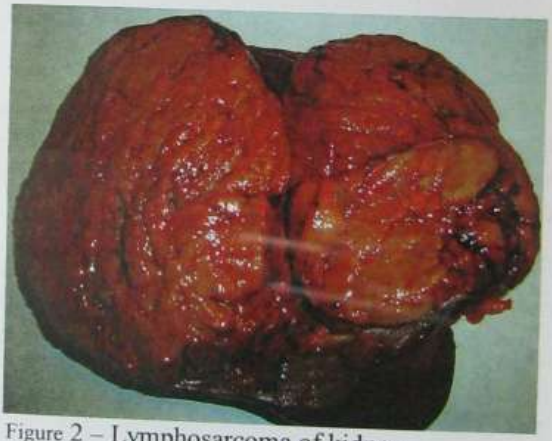
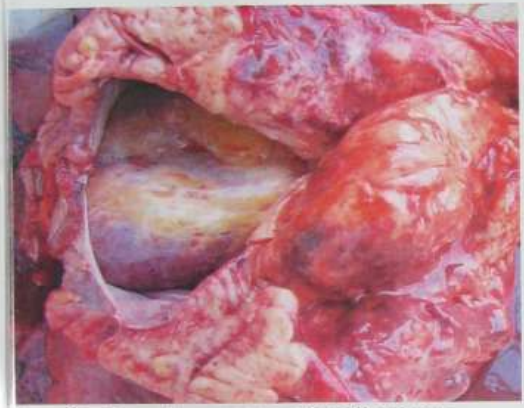


Figure 2 – Lymphosarcoma of kidney.



igure 3 – Lymphosarcoma of mediastinum.

igure 4 – Metastasis of lymphosarcoma in kidney

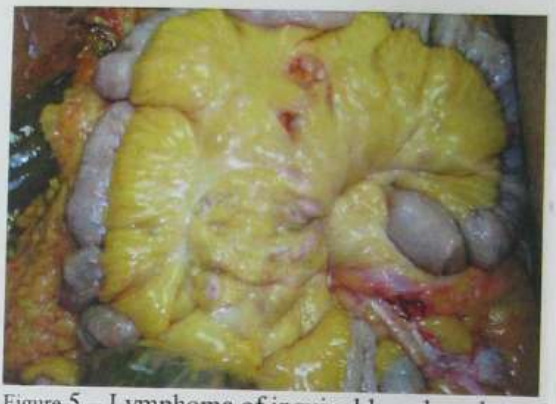


Figure 5 – Lymphoma of inguinal lymph nodes.

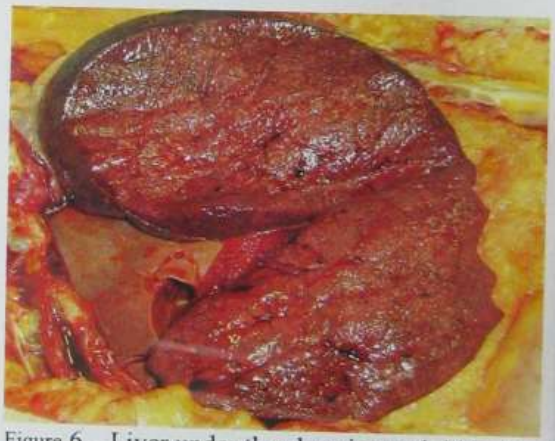


Figure 6 – Liver under the chronic myeloid leukemia.

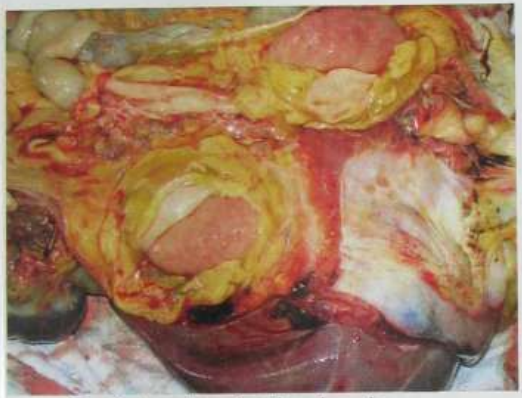


Figure 7 – Iinternal under the chronic posthemorrhagic anemia.

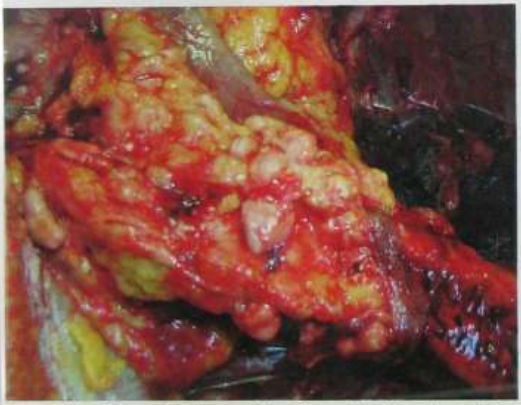


Figure 8 – Lympholeucosis of aortic lymph nodes.

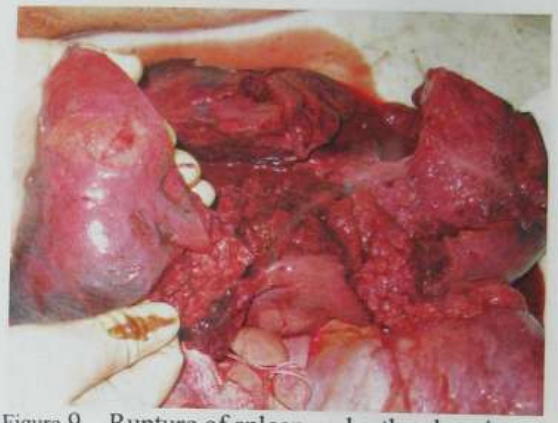


Figure 9 – Rupture of spleen under the chronic myeloid leukemia.

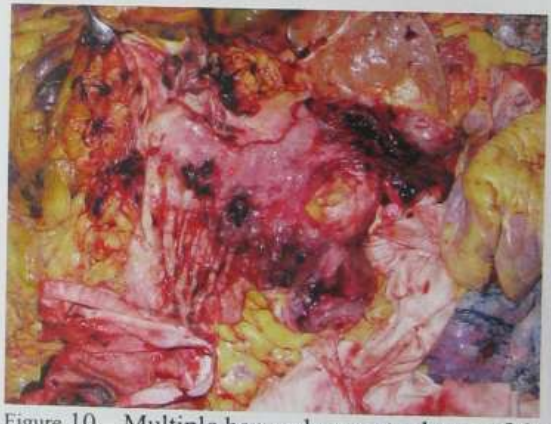
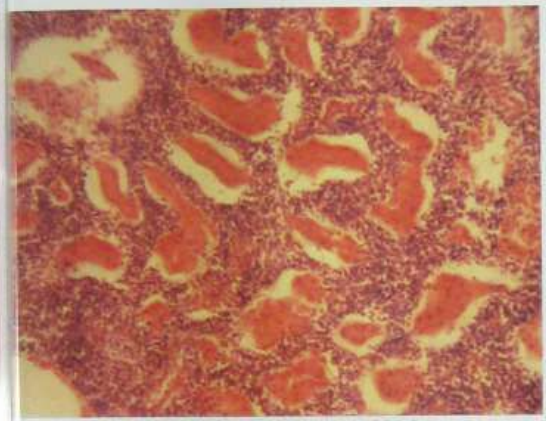
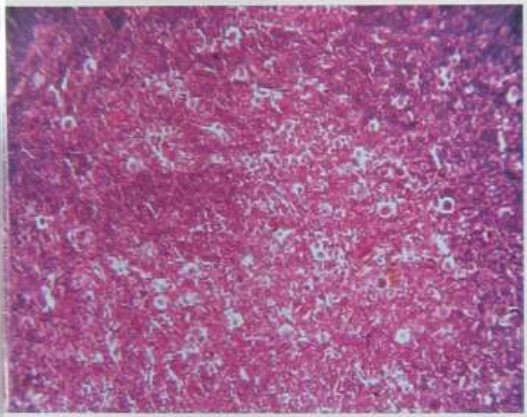


Figure 10 – Multiple hemorrhages at ulcers of the stomach



igure 11 – Leukemic infiltration of kidney.



igure 12 – Lymph node under lymphogranulomatosis, ixed-cellular variant.

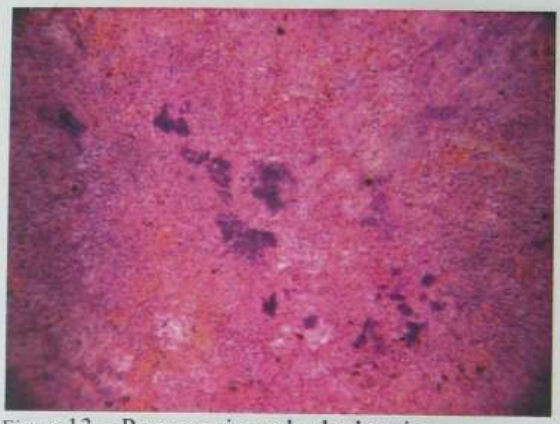


Figure 13 – Pneumonia under leukemia.

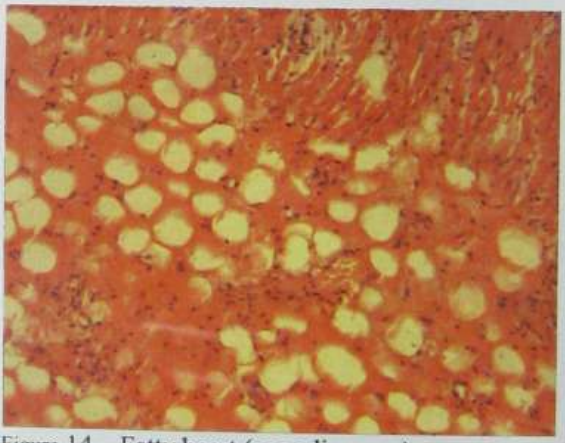


Figure 14 – Fatty heart (cor adiposum).

Diseases of the cardio-vascular system

Specific aims:

- *To explain structurally the functional description of the cardio-vascular system.*
- *To interpret the modern pictures of etiology and pathogenesis of atherosclerosis.*
- *To analyze the morphological description, the stages of atherosclerosis and organ defeats at the time of it.*
- *To analyze etiology, pathogenesis and factors of risk of ischemic illness of heart.*
- *To analyze the clinic-morphologic description of stenocardia.*
- *To interpret reasons, classification, dynamics of biochemical and morphological -functional changes in myocardium at the time of the heart attack of myocardium.*
- *To interpret morphology of sharp, relapsable and repeated heart attack of myocardium, and also consequences, complications, causes of death.*
- *To interpret clinic-morphologic description, complication, causes of death from chronic ischemic illness of heart.*
- *To interpret the clinic-morphologic description, complications, causes of death at essential hypertension (hypertensive illness) and at second (symptomatic) hypertensions.*
- *To interpret the clinical-morphological description of hypertrophy of myocardium, the insufficiency of left and right ventricles*
- *To analyze the violation of immune homeostasis and system making progress disorganization of the connecting tissue at the time of the rheumatic illnesses.*
- *To determine etiology, patho - and morphogenesis, and also morphological changes, complications and consequences at the time of rheumatic illnesses.*

- *To determine etiology, pathogenesis, morphological displays of vasculitis.*
- *To analyze morphological changes, complications and consequences at the time of endo- and miocarditis of different genesis.*
- *To interpret the mechanism of education, the varieties of the purchased and innate defects of heart, their complication and causes of death.*

Actuality of theme: illnesses of the cardio-vascular system occupy the main place in the general structure of morbidity, invalidisation and death rate of men. That is why the knowledge of the morphological bases of this pathology is necessary not only for the study of their clinical displays but also for clinic-anatomic analysis, the determination of tactic of treatment and prophylaxis.

Aim: to study etiology, pathogenesis, morphological displays of atherosclerosis, hypertensive illness, ischemic illness of heart, miocarditis, cardiomiopathia, defects of heart, diseases of vessels, and also to be able to distinguish their clinic-morphological forms and most frequent complications.

Task:

1 To know etiology, pathogenesis, morphological displays of atherosclerosis, hypertensive illness, ischemic illness of heart, vasculitis, defects of heart, cardiomiopathies, miocarditis.

2 To learn to diagnose the morphological displays of the above mentioned cardio-vascular illnesses on macroscopic and microscopic levels.

3 To be able to distinguish clinic-morphological forms and most frequent complications, and also causes of death at the time of atherosclerosis, hypertensive illness, ischemic illness of heart, defects of heart, miocarditis, vasculitis.

Theme 23 Atherosclerosis and arteriosclerosis. Ischemic illness of heart

Main questions for the individual training:

Cardio-vascular system. Structurally functional description. Cells of vascular wall and their participating in reactions of the damage.

Atherosclerosis and arteriosclerosis. Common data (epidemiology, risk factors). Modern pictures of etiology and pathogenesis of atherosclerosis. Morphologic description and stages of atherosclerosis, the structure of atherosclerotic plague. Organ defeats at the time of atherosclerosis. Arteriosclerosis, the morphological description.

Aneurysm and stratifications of arteries. Aneurysm: classification, value, morphology. Stratification of aorta: concept, the mechanisms of development, morphological description, clinical syndromes, complications.

Ischemic illness of heart (coronal illness). Concept, epidemiology, connection, with atherosclerosis and hypertension. Etiology and pathogenesis, risk factors. Stenocardia: classification, clinic-morphological description. Heart attack of myocardium: causes, classification, dynamics of biochemical and morpho -functional changes, in myocardium. Morphology of sharp, relapsable and repeated heart attack of myocardium. Consequences, complications, causes of death. Sudden coronal (ischemic) death. Chronic ischemic illness of heart: clinic-morphological description, complication, causes of death.

Theme 24 Hypertension and arteriolosclerosis

Main questions for the individual training:

Adjusting to normal blood pressure. Hypertension, common data (epidemiology, diagnostic criteria). Essential hypertension (hypertensive illness) and second (symptomatic) hypertension. Hypertension of high quality and malignant motion of

hypertension. Hypertensive illness: factors of risk, causes of development, pathogenesis, morphological changes, in vessels, heart, other organs.
Hypertrophy of myocardium: the classification, clinic-morphological description; left and right ventricles insufficiency.

Theme 26 The system of vasculitis: unspecific aortoarteritis, knot periarteriitisis, granulematosis of Vegener, obliterate thrombangitis

Main questions for the individual training:

Classification, etiology, pathogenesis. Basic uninfectious vasculitis: knot periarteriitisis, arteriitis of Takayasu, granulematosis of Vegener, obliterative thrombangitis (illness Vinivarter -Burgher), illness Kavasaki. Epidemiology, etiology, pathogenesis, morphological description. Vasculitis of other groups (purpura of Shenlein - Genokh, reumatoid vasculitis). Illness of Reyno. Pathogenesis, clinic-morphological description.

Theme 27 The endocarditis of Lefler, idiopathic myocarditis, is innate and the defects of heart are purchased

Main questions for the individual training:

Cardiomiopathia: classification. Dilatation, hypertrophy, restrictive cardiomiopathia.
Defeat of endocard (endomiocardial fibrosis, endomiocarditis of Lefler, endocardial fibroelastosis): value of genetic factors, patho - and, clinic-morphological description, causes of death. Infectious endocarditis.
Myocarditis. Determination, etiology. Viral, microb and vermin myocarditis, giganticcellular myocarditis of Fidler. Patho – and clinic-morphological description, consequences, causes of death. Diseases of myocardium, conditioned the

oxic (alcohol, medications), metabolic and other influencing. Patho - and, clinic-morphological description, prognosis. The defects of heart are purchased: the mechanism of education, varieties. The defects of heart are innate by s violation of the division of heart cavities (defects of interatrial and interventricles partitions, atrio-ventricular communication). The defects of heart are innated by the violation of the division of arterial barrel (general arterial barrel; complete transposition of pulmonary artery and aorta; stenosis and atresia of pulmonary artery; stenosis, koarktatsiya that atresia of aorta). Difficult innate defects of heart (triad, tetrad and pentad of Fallo).

Equipment of the lessons:

Macropreparations: atherosclerosis of aorta with a transition in iterocalcinosis, atherosclerosis of aorta with aneurysm of its abdominal department, exfoliating aneurism, gangrene of foot at atherosclerosis of vessels of lower limbs, hypertrophy of left ventricle of heart, atherosclerosis of kidney arteries and atherosclerotic, arteriosclerotic (initially wrinkled kidney), transmural heart attack of myocardium, sharp aneurysm of heart with a break, postattack (largfocus) cardiosclerosis, concentric hypertrophy of heart, eccentric hypertrophy of heart, stenos atherosclerosis of coronal artery of heart with thrombosis and heart attack of myocardium, smallfocus cardiosclerosis, chronic aneurysm of heart, atherosclerosis of iliac artery with an obturated blood clot (Syndrome of Lerish), gangrene of thin bowel.

Micropreparations: lypoidosis of aorta (sudan III), atherosclerosis of aorta(hematoxylin and eozin), stenose atherosclerosis of coronal artery of heart (paints. hematoxylin and eozin), arteriosclerotic (paints. hematoxylin and eozin), organized heart attack of myocardium, largefocus cardiosclerosis(paints. pikrofuksinom), obliterative trombangit,

nekrotic stage of myocardial infarction" (paints hematoxylin and eozin), hypertrophy of myocardium (paints hematoxylin and eozin).

Sliding seats and tables which are in the archive of department, for example: the prelipid stage of atherosclerosis is a hypertrophy of myocardium, spasm of arterioli, fibrinoid change of endocardium at rheumatism, exfoliating aneurysm, gangrene of foot, hypertrophy of the left ventricle of heart, arteriolonephrosklerosis, heart attack of myocardium, sharp aneurysm of heart with a break, postmyocardial infarction cardiosclerosis, fibroplastic endocarditis, fibrinous pericarditis, brown induration of lungs, muscat liver.

I Preauditorium individual training for the practical training

Theoretic Material Summary

Atherosclerosis is a chronic disease which arises up as a result of the violation of fatty and albuminous exchange. On determination of IHPO, atherosclerosis is "various combinations of changes of internal membrane of arteries, which shows up as a focus laying of lipids, difficult connections of carbohydrates, elements of blood and circulatory in it matters, the formation of the connecting tissue and laying of calcium". Atherosclerosis damages vessels of elastic and elastic-muscular types. After the prevalence illness occupies the first place in cardio-vascular pathology. Lately it collected character of epidemic, especially among the citizens of highly developed countries. It occurs mainly in people of mature age - after 30-35.

Etiology. It is a polyetiologic disease. There are plenty of risk factors which are instrumental in the increase of level of aterogenic lipoproteins in blood and to penetration of them in the wall of vessel: arterial hypertension, saccharine diabetes, obesity, hypokinesia, smoking, hyperlipidemia and

islipoproteinemia, inherited inclination, age, sex (more requent occurs in men), psychoemotional overstrain, etc.

There are some theories of the development of atherosclerosis : he infiltrative theory of Anichkov, the nervous metabolic heory of Myasnikov, the immunological theory of Klimov and Nagornev, the viral theory, the gerontology theory of Davidovskiy, the thrombogenic theory of Rokitansky.

Pathogenesis. The pathogenetic essence of atherosclerosis consists of the focus laying in intimae of arteries of so-called atherogenic lipoproteids in reply to the damage of endothelium.

Lipoproteids show by themselves spherical particles which consist of kernel and external membrane. In the complement of kernel enter triglyceride and ethers of cholesterol, in the complement of external membrane are protein (apoproteids), phospholipids and nonetherifide cholesterol. Four classes of lipoproteids circulate in blood, which differ in sizes and maintenance of cholesterol and albumens - chylomikrones, lipoproteids of very low and high closeness. Atherogenic are considered to be lipoproteids of very low and low closeness, which contain the large supply of cholesterol (to 45%) and little albumen. Lipoproteids of high closeness, opposite, a protein (55%) and comparatively little cholesterol have much (16%). They execute an antiatherogenic function, that prevents the development of atherosclerosis.

Pathological anatomy. In the development of atherosclerosis four stages are selected –the stage prelipid, the stage of lipid spots, the stage of fibrosis plagues and the stage of the complicated defeats (ulceration, calcinosis, thrombosis).

The prelipid stage is characterized by such processes, as a loss of glycocalix - protective polysaccharide layer of endotheliocytes, the expansion of intraendothelial cracks, the activating of endocytosis in endothelial cells. Intima swells up. In subendothel space lipoproteids begin to penetrate from plasma of blood in growings amounts.

The main transport form of cholesterol is lipoproteids of low closeness. They carry cholesterol from liver to the cells of organism. Mechanism by which cholesterol is transported in a cell, receptor-mediated is called endocytosis. Cells parenchymatos and specific receptors, capable of linking lipoproteids of low closeness, have connective tissue types (fibroblasts, fibres of smooth muscles of arteries) on the surface (apo-v, Å-receptors). This co-operation takes place in the area of the special diaphragm structures, adopted by the bordered pits. After co-operating with the particles of lipoproteid the bordered pits incurve inward cells and are torn away, forming bordered endocytic vacuole. They contact with lizosoma and fission. An exempt cholesterol is utilized on the necessities of cell, for example on the synthesis of membranes, hormones. Receptor-mediated of endocytosis is regulated after the mechanism of feed-back. At the increase of cholesterol the amount of Apo-v diminishes in a cell, Å-receptors on its membrane, and fastening of lipoproteids is limited. That is why it does not bring a transport over of cholesterol of receptormediated way to his piling up in a cytoplasm.

It is lately proved that in the genesis of atherosclerosis a leading role is played not by native lipoproteids of low closeness, but by their modified variants. Name such change of structure of lipoproteid particle modification, when it stops to be recognized Apo-v, by the Å-receptors of fibroblastiv and other cells and is not taken in by them. The modification of lipoproteids takes place in blood and vascular wall. To the major modified forms belong:

à) glycated lipoproteids, such which added glucose;

b) peroxide-modified lipoproteids, which appeared under act of free radicals and products of peroxide oxidization of lipids;

c) autoimmunic complexes of lipoproteids antibodies;

d) lipoproteids, that tested partial degradation at the time of the act of proteolytic enzymes.

Modified lipoproteids, which entered subendothelial space from blood or appeared in a vascular wall, carry with macrophagocytes. On the surface of these cells, next to typical Apo-B, by E-receptors, receptors are located other to the type, adopted scavenger -receptors (scavenger is garbage). scavenger - absorption of modified lipoproteids greatly differs from endocytosis native lipoproteids, mediated through Apo-B, E-receptors. This mechanism is not regulated by the principle of feed-back that is why inward macrophagocytes the enormous amount of lipoproteids of low closeness penetrates uncontrollably, rich in cholesterol. The activity of lyzosomal enzymes can appear insufficient for the breaking up of his ethers, and gradually the cytoplasm of macrophagocytes is overfilled with lipid vacuoles with the accumulated ethers of cholesterol. Under a microscope it reminds suds, that is why such cells were adopted foamy. The transformation of macrophagocytes in foamy cells is the irreversible stage of atherosclerotic process.

Lipoproteids of high closeness counteract converting of macrophagocytes into foamy cells. They easily penetrate at intimae, saturated cholesterol and similarly easily go back into blood. Macrophagocytes have on the surface the specific receptors for lipoproteids of high closeness. The particles of lipoproteids after binding to the receptors are taken in, but do not fission the enzymes of lizosom. Enriched in cholesterol, they go out from macrophagocytes after the mechanism of exocytosis and migrate in a vascular river-bed. Sucking of cholesterol by this mechanism is important for those cells which take in modified lipoproteids through apo-B,E-receptors, that are noncontrolled. Purging them from surplus of cholesterol, lipoproteids of high closeness slow development of atherosclerosis by such method.

Another characteristic of morphological feature of atherogenesis is the proliferation of cells of smooth muscles in

intimae of vessels. Miocytes migrate here from the middle membrane of arteries (media) under act of factors of chemotaxis, and the reproduction of them depends on the factors of growth - thrombocytic, fibroblastic, endothelial. Miocytes which migrated at intimae and began to propagate themselves the transform from retractive cells into metabolic active. Without regard to the absence of scavenger -receptors, they acquire property to take in modified lipoproteids and accumulate ethers of cholesterol. Foamy cells also appear from them.

Lipid spots (strips) appear in different departments of the arterial system, but before all in aorta. From cellular elements foamy cells, T-lymphocytes and fibres of smooth muscles, prevail in over them. On this stage ethers of cholesterol are mainly in cells. Around there is insignificant excrescence of the connective tissue. Lipid spots do not hinder blood stream.

Foamy cells, overloaded with cholesterol, collapse in the course of time, and cholesterol is outpoured in out of cellular space. It irritates the surrounding tissues as extraneous body and causes brief cellular proliferation at first, and afterwards - maks progress as fibrosis. The accumulations of foamy cells and out of cellular lipids, bedding between elastic fibres, make light intima. Glycosaminglycanes are put aside in it, γ-globulin, fibrin.

The fibres of smooth muscles which migrated at intimae from middle membrane grow into secretory cells. They begin to increase the production of connective tissue albumens - elastin, collagen. Fibrosis tissue which surrounds a lipid hearth as a capsule is formed from them. This structure was called the fibrous plague. It is dense macroscopically, oval, white or white yellow color, rises above the surface of intimae. That part which knobs in lightening of vessel, yet more dense and that is why it creates the hindering of blood stream.

Fibrous plagues consist of amorphous mass, which tailings of elastic and collagenic fibres, cholesterol, enter in the complement foamy cells are not blasted. If in plagues the processes of disintegration prevails over the formation of necrotic masses, such plagues are called atheromatosis. Foamy cells, lymphocytes, plasmocytes, newformed vessels, accumulated on periphery of plague. From lumen of vessel is marked off hyalinised by the connective tissue (overlay of plague). Complications begin on this stage.

In the area of fibrous plagues parietal blood clots often appear. Their appearance is explained by the breaks of fibrous capsule of plagues, and also by the demage of endothelium under them.

Ulceration of plagues - is also a frequent phenomenon. An ulcer has unequal edges, the bottom of it is formed by a muscular layer or advevtitia. The defects of plagues are often covered by blood clots. If atheromatous masses get into bloody river-bed, they become the cause of brain embolism of and embolism other organs.

Another complication of fibrous plagues –is liming (atherocalcinosis). This process is complete with atherosclerosis. Salts of lime are put aside in atheromatous masses, the fibrous tissue and intermediate matter between elastic fibres. Plagues collect stony consistency. The focus of calcinosis are localized mainly in abdominal aorta, coronal arteries, arteries of pelvis and thighs.

Depending on overwhelming localization of atherosclerosis in that or other vascular pool we point out the following clinic-morphological forms: atherosclerosis of aorta, atherosclerosis of coronal vessels of heart, atherosclerosis of arteries of cerebrum, atherosclerosis of arteries of kidneys, atherosclerosis of arteries of intestine, atherosclerosis of arteries of lower limbs. The description of these forms is resulted in a table.

Hypertensive illness (HI) or essential hypertension is a chronic disease with the protracted and proof increase of arterial pressure. Symptomatic hypertension, which arises up at the time of diseases of the nervous system, kidneys, vessels. Types of symptomatic hypertension are also distinguished: kidney (nephrogenic, renovascular), endocrine (illness/syndrome of Icenko-kushing, second aldosteranism, to pheochromocytoma), neurogenic (trauma, tumor, abscess, hemorrhage in a cerebrum, defeat of hypothalamus and barrel of brain), vascular (coarctation of aorta, other anomalies of vessels, polycytemia).

Etiology and pathogenesis of hypertensive illness is not fully found out. That factor which needs to be considered the starting one is not set, as a result of action of which arterial pressure begins to exceed critical border - 140 and 90 mm Hg. It is possible, that there are a lot of causes, and only at unfavorable for an organism co-operation they are able to put out of action the mechanisms of correction of arterial pressure and to increase it over the norm border. The important place in the origin of illness is taken disorders of adjusting of vascular tone (Lung, Myasnikov) is illness of unreacting emotions, and also surplus use of kitchen salt in a meal, which is combined with genetic propensity to hypertension. It is possible to select among the mechanisms of development of HI: nervous, reflex, hormonal, kidney, inherited.

All influencing which are able to promote the cardiac troop landings or peripheral resistance or the first and the second simultaneously can be considered the etiologic factors of hypertensive illness. To the majority of them belong: the increase of the volume of plasma, the increase of the cardiac troop landings, the hyperactivity of the sympathic nervous system, the violation of kidney functions.

Sympathic hyperactivity -is one of the strongest factors of the development of the essential hypertension. This state

affects functions of some organs which can be considered the targets of the sympathic influencing. Except for heart, arterioles, veins and kidneys belong here.

The pathological anatomy of HI depends on its motion which can be of high quality and malignant. In the first case we select three clinic-morphological stages – the preclinical or transient, the stage of widespread changes of arteries, or organic, and the stage of the second changes, or organ.

The transient (functional) stage clinically shows up the periodic brief increase of arterial pressure, and morphologically – by the hypertrophy of muscular layer and hyperplasia of elastic structures of arteriole, the spasm of arteriole and moderate compensate hypertrophy of the left ventricle of heart.

The stage of widespread changes of arteries is characterized by constantly promoted arterial pressure. Walls of shallow arteries and arterioles are in a state of proof reduction and hypoxya. Their penetrating rises. Plasma impregnates the structures of vascular walls (plasmorrhagia), and the latter are destroyed. The elements of destruction, and also protein and lipids of plasma are eliminated through a wall by resorbtion, but it, as a rule, is incompleted, that results in the development of hyalinosis and arteriolosclerosis. The vascular wall is thickened, and the lumen of arteriole becomes narrower.

In large arteries, unlike the changes of arteriole mentioned above, elastofibrosis develops and atherosclerosis. Elastofibrosis is a compensate answer for proof hypertension as hyperplasia and the breaking up of the internal elastic membrane of vascular wall. The development of atherosclerosis is related to the destruction of the vascular wall, the accumulation of cholesterol and promoted arterial pressure.

The typical clinic-morphological display of this stage is a hypertrophy of the left ventricle of heart, and also dystrophy and necrobiosis of cardiomyocytes.

The stage of the second organ changes is characterized by the destructive, atrophy and sclerotic changes of internal organs. There is diffuse smallfocus cardiosclerosis in the hypertrophied heart, in kidneys arteriosclerotic nephrosclerosis develops or initially wrinkled kidneys which are symmetric diminished here, dense consistency, with shallow tuberositas on a surface, the thickening of cork layer on a cut. At a microscopy the bulge of afferent arteriole appears with expressed them by hyalinosis, glomerules of sclerous and hyalinous, tubules are obsolete, stroma is scleroused.

For the malignant clinical course of hypertensive illness such characteristic as frequent hypertensive crisis is present (it is a sharp increase of arterial pressure, which arises up as a result of the spasm of arteriole). The morphological signs of crisis is goffering and the destruction of basal membrane, location of endothelium as paling, plasmarrhagia, fibrinoid necrosis of walls of arteriole, thrombosis. Heart attacks and hemorrhages develope in internal organs.

Depending on the predominance of structural alteration of vessels in a certain pool and related to it clinic-morphological changes, select kidney, cerebral and cardiac clinic-morphological forms of hypertensive illness.

The kidney form of hypertensive illness is characterized by sharp and chronic displays. Before sharp displays, which remove mainly the malignant character of the illness, take heart attacks, arterionecrosis and capillarnecrosis glomerules of kidneys. The latter can entail sharp kidney insufficiency. Sometimes arteriole- and capillarnecrosis completed with fleeting (malignant is Headlight).

Chronic displays are expressed by the development of the initially wrinkled kidney. Thus the majority of nephrons through insufficient blood supply become atrophied and scleroused, those are the shallow areas of microcavities macroscopically. Other nephrons are compensately

hypertrophied and come forward above the surface of kidneys as grey-red granules. Kidneys become dense, their surface is fine-grained, a cork layer is thin, a capsule is taken off with difficulty.

The cerebral form of hypertensive illness makes basis of cerebro-vascular diseases, and cardiac - together with the cardiac form of atherosclerosis - ischemic illness of heart.

The causes of death of HI sick can be hemorrhages in a cerebrum, heart attacks, malignant nephrosclerosis, dug up of aorta.

Ischemic illness of heart name the violation of its functions, conditioned absolute or relative insufficiency of coronal blood supply. In connection with large social meaningfulness of this pathology it is selected IHO in independent nosology unit. Ischemic illness shows up in arrhythmias, ischemic dystrophy of myocardium, heart attack of myocardium, cardiosclerosis. It develops mostly in men after 50 and occupies the first place in invalidisation and death rate of patients with cardio-vascular pathology. Ischemic illness pathogeneticaly is related to atherosclerosis and hypertensive illness and on the essence is their cardiac form with the general factors of risk. To ischemic illness can lead other defeats of coronal arteries, in particular at rheumatism, knot periarteriitisis.

Etiology and pathogenesis, risk factors. Direct causes of ischemia of heart more frequently all is a spasm, thrombosis or embolism of coronal arteries, and also functional overload of myocardium in the conditions of sclerotic oclusion of these vessels. But there are only local factors of ischemia and necrosis of cardiac muscle. In the origin of ischemic illness as a cardiac form of atherosclerosis and hypertensive illness an important role is played by the row of favorable terms - hyperlipidemia, arterial hypertension, surplus mass of body, immobile way of life, smoking, saccharine diabetes and gout,

chronic emotional overstrain, inherited inclination. At combination for the same person during 10 of such factors, as hyperlipidemia, arterial hypertension, smoking and surplus mass, there will be ischemic illness of heart in the half of cases.

Ischemic illness of heart has undulating motion. In the background there is chronic (relative) insufficiency of coronal blood circulation, there are flashes of sharp (absolute) insufficiency. That is why we distinguish the acute and chronic forms of ischemic illness of heart. The sharp form shows up ischemic dystrophy of myocardium of -stenocardia and heart attack (by necrosis) of myocardium, chronic - cardiosclerosis. The latter is diffuse small- and largfocus and postattack largfocus. Sometimes cardiosclerosis is complicated with chronic aneurysm of heart.

It is known that providing of myocardium blood for a healthy man is carried out the system functionally eventual arteries. The diameter of anastomoses between right, middle and left coronal arteries does not exceed 40 mkm, collaterals are not developed. At the time of physical training blood supply of myocardium is provided due to hyperemia of intraorganic branches of coronal vessels. Hyperemia is caused by metabolits that appear during activating of tissue exchange. In addition, metabolic expansion of coronal arteries is combined with the oppression of sensitiveness of a-adrenoreceptors to the vasoconstrictors influencing. Due to these mechanisms the increase of volume speed of coronal blood flowing always answers the growings requirements of myocardium in oxygen.

Patients with the stenous sclerosis of coronal arteries have the continuous piling up of vasoactive metabolits in the focus of ischemia that exists permanent dilatation vessels of microcirculatory river-bed, which diminishes their functional reserve. These vessels are not able to provide the increase of volume speed of coronal blood flowing the physical training.

For patients with atherosclerosis even in the conditions of rest there is a deficit of blood supply of myocardium. Morphologically it reminds a mosaic, built of normal cardiomyocytes and cardiomyocytes with changed structure and function (dystrophy and necrosis - in one, hyperplasia - in other places). Clinically it shows up such characteristic as pains and electrocardiography changes, however enzymemia (increase of activity of transaminase, lactatdehydrogenase and other enzymes in blood), which testifies to the presence of heart attack is absent. This state is called stenocardia. We distinguish its unstable and stable forms.

Morphologically stenocardia is characterized by ischemic dystrophy of myocardium. It is flabby, in the focus of ischemia, pale and filling out. Histologically we find out paresis of vessels, sometimes fresh blood clots, interstitial is swollen, red corpuscles stasis, the disappearance of transversal banding cardiomyocytes, diapedesis hemorrhages. Electronic - microscopic and histochemical changes are taken to diminish the amount of granules of glycogen, the swelling and destruction of chondriosome and tubules of sarcoplasmatic net. These changes are conditioned by the violation of the tissue breathing, the strengthening of anaerobic glycolysis, breaking up of breathing and oxidizing phosphorilation. In development of destructive changes of cellular organelles an important role is played by disengaged catecholamines and to the changed water-electrolyte exchange (loss of magnesium, potassium and phosphorus but piling up of sodium, calcium and water).

Long durated coronal spasm, thrombosis or occlusion of coronal vessels are causes of the transition of ischemic dystrophy of myocardium at the time of heart attack. Heart attack of myocardium is circulatory ischemic necrosis of cardiac muscle that is why, except for the changes of electrocardiogram, enzymemiya is typical for it. Morphologically it is ischemic heart attack with hemorrhagic

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crownom. It is classified by the time of origin, by localization, distribution and motion.

Complete necrosis of cardiomyocytes is formed within a day. At first myocardium in the pool of the damaged artery is flabby, unevenly vascularity. Histologically the accumulations of leucocytes appear in capillaries, emigration of them, diapedesis hemorrhages, relaxation of cardiomyocytes, the disappearance in the latter of glycogen and oxide restoration enzymes. During the following hours the outlines of fillings out cardiomyocytes become wrong, transversal banding disappears.

Macroscopically the area of a heart attack expressly appears only through 18-24 hours after the origin of illness. A necrotic area acquires grey-red color, it is limited by the ribbon of hemorrhage and something comes forward above the surface of cut as a result of edema. The phenomenon of edema disappears in subsequent days, necrotic tissue falls back, becomes dense, yellow grey. On periphery a demarcation billow which consists of leucocytes is formed, fibroblasts and macrophagocytes. The latter take part in resorbtion of dead masses, lipids and tissue detritus accumulate in their cytoplasm. Fibroblasts take part in fibrinogenesis. The process of organization of heart attack lasts for 7-8 weeks. The connecting tissue germinates from the area of demarcation from the round of the stored tissue in the area of necrosis. Newformed connecting tissue at first is magnificent, as granulation, afterwards passes in rough fibrose. In it and round it islands of hypertrophied cardiomyocytes appear. Investigation of this process is the formation of a dense scar – the morphological basis of postattack largefocus cardiosclerosis.

The acute heart attack of myocardium has the most frequent complication as cardiogenic shock, fibrillation of ventricles, asystole, sharp cardiac insufficiency, miomalation,

sharp aneurysm and break of heart, parietal thrombosis and pericarditis.

There is melting of myocardium in the cases of predominance of autolisis of dead tissue - miomalation. Myocardium in these cases is helpless to counteract interventricle pressure of blood. Wall of heart is thickeningand knobs outside, that results in formation of additional cavity - aneurysm of heart. Compensately parietaly blood clot appears in it. It covers the tears of endocardium and strengthens durability of wall. At insufficient thromboformation blood penetrates under endocardium and necrotic tissue what conduces hearts to the break. Blood is outpoured in the cavity of cardiac shirt (hemopericardium). Parietal blood clots arise up mainly at transmural and subendocardial heart attacks. They can be the source of embolism, for example, of kidney vessels.

At subepicardial and transmural heart attacks there is the reactive exudative inflammation - fibrinous pericarditis often enough

Cardiosclerosis makes the structural basis of chronic ischemic illness of heart. It can be atherosclerotic diffuse smallfocus or can be developed at hypertensive illness, and also postattack largfocus. The first form is related to hypoxia of myocardium. The connective tissue replaces the places of dystrophy, atrophy and dead cardiomyocytes, and also overgrows in perivascular spaces. Macroscopically such cardiosclerosis is presented as white perivascular layers and narrow ribbons in all layers of heart muscle.

The organization of heart attacks is completed by largefocus cardiosclerosis. Sometimes it is the vast fields of connecting tissue, which take all layer of wall of heart. In such cases it is thinned and knobs under pressure of blood - an aneurismatic sack appears.

At the time of chronic ischemic illness of heart constantly there are terms for development of the repeated

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At the time of chronic ischemic illness of heart constantly there are terms for development of the repeated

heart attack of myocardium with all characteristic complications.

Cardiogenic shock, fibrillation of ventricles, asystole, sharp cardiac insufficiency, come forward in the early period of heart attack direct causes of death. In the course of time the first place will be taken up by the break of heart and thromboembolia of vessels of cerebrum. At the time of chronic ischemic illness of heart death is caused by cardiac insufficiency, thromboembolic complications and break of wall of aneurysm.

Cardiomiopathia is an illness with the insufficient retractive function of cardiomyocytes as a result of dystrophic changes of myocardium, which are unconnected with coronal blood circulation or rheumatic defeats.

Classification. Cardiomiopathia is divided into primary (idiopathic): dillatation (congestive), hypertrophy (constrictive, obstructive), restrictive; but the second: intoxication (alcohol, salts of heavy metals, uremia)infectious, exchange inherited (amyloidosis, glycogenosis) and purchased (thireotoxicosis, gout, hyperparathireosis, avitaminosis), alimentary (malabsorption, cirrhosis of liver).

Dillatation cardiomiopathia is characterized by the considerable expansion of cavities of heart, hypertrophy and dystrophy of myocardium and decline of his retractive function. Often arises up after the carried viral infection (Koxaki), drinking of alcohol.

Hypertrophy cardiomiopathia is characterized by the expressed hypertrophy of myocardium as a result of the promoted sensitiveness to catecholamines with the disorganization of miofibrils and the diminishing of volume of cavities of heart.

Restrictive cardiomiopathia is characterized by the rigidity of walls of the ventricles of heart, which develops as a result of endomiocardial fibrosis, fibroelastosis, fibroplastic

eozinofil endocarditis. The cavities of ventricles can even be diminished, and the cavities of atriums broaden.

The second cardiomiopathia is characterized by the development of dystrophic changes in cardiomyocytes as a result of action of that or other etiologic factors that is why their displays can differ.

Complications of cardiomiopathies can be: sudden death, thromboembolic syndrome, chronic cardiac insufficiency.

Vasculitis is an inflammatory disease of vessels which is often accompanied by destructive changes in a wall.

Classification. We distinguish local and system vasculitis. Depending on localization we select aortitises, arteriitisises, arteriolitises, capillaritises, phlebitises. In addition, vasculitis can be endo-, mezo-, peri-, panvasculitis. Originally the infectious and immunodefensive vasculitis are distinguished.

System vasculitis is shown up in different types of inflammatory reaction: alterative-exudative, productive, necrotic, destructively productive, granulematous. In the pathogenesis of the development of the morphological changes the basic place is taken by the immune reactions of hypersensitiveness.

Distinguish: primary vasculitis:

- the defeat of aorta and its large branches with granulematous gigantcellular reaction (unspecific aortoarteriitisis or illness of Takayasu, temporal arteriitisis or illness of Khorton);
- the defeat of arteries of the middle and shallow arteries with destructively productive reaction (knot periarteriitisis, allergic granulematosis, system necrotic vasculitis, granulematosis of Vegener);
- the defeat of arteries of shallow caliber, capillaries, veins (obliterative thrombangitis or illness of Burgher);

second vasculitis:

- infectious (syphilis, tuberculosis, rickettious, sepsis);
- the system diseases of connective tissue;
- the vasculitis of hypersensitiveness (whey illness, malignant new formations).

Unspecific aortoarteriitisis (arteriitisis of Takayasu) or arteriitis of young women shows up the productive granulematous inflammation in the wall of aorta, the cause of which can be different factors. The bulge of wall, the formation of aneurysm, parietal blood clots, the deformation of aorta is developed.

Knot periarteriitisis (illness of Kussmaulya-Mayera) is characterized by the development of necrotic imunnocomplex vasculitis in the arteries of middle and shallow sizes of every localization, but more frequent in kidneys, heart, the digestive system, the nervous system, skeletal muscles. The necrosis of middle membrane and internal elastic membrane with infiltration of wall by lymphocytes, plasmatic cells, eozinofils are typical. Aneurysm of vessels, hemorrhages, knots and blood clots develop. In kidneys immunocomplex arteriolitis and glomerulonephritis develop. A defeat of kidneys and arterial hypertension are often the causes of death at knot periarteriitis. The defeat of coronal arteries predetermines the evelopment of ischemic damage of myocardium. In the organs of the digestive system there are ischemic damages of guts at knot periarteriitis, gangrene can develop sometimes. There are myalgias in the skeletal muscles, artralgias, arthritises. Aneurysm which can be torn and can cause the mortal bleeding or heart attacks of cerebrum develop in the vessels of cerebrum.

Granulematosis of Vegener shows up the defeat of vessels of mainly overhead respiratory tracts, rarer kidneys and other organs with the development of alterative, exudative and productive (granulematosis) inflammatory changes. Investigation is hyalinosis, sclerosis, the formation of

aneurysm in the wall of vessels and sclerosis and the deformation of organ. Mesangiocapillar glomerulonephritis often develops.

Obliterative thrombangitis (illness of Vinivarter - Burgher) is a productive inflammatory defeat of mainly shallow arteries and veins of lower limbs with the development of blood clots, the obliteration of vessels and gangrene of extremity. Microabscesses can develop with necrotic changes in tissues. More frequent arises up in men who smoke.

Defects of heart are proof rejections in its structure and predetermine the violation of function. We distinguish the purchased and born defects.

The purchased defects develop as a complication of rheumatism, atherosclerosis, syphilis, bacterial endocarditis. The eventual link of pathogenesis of the purchased defects of heart is the sclerotic deformation of valves in connection with the chronic inflammation and the disorganization of connecting tissue. Hereupon there is the insufficiency of valve (it is not closed up fully) or its stenosis, more frequent there is the combined defect – the combination of stenosis and the insufficiency of that valve. After localization we distinguish the defects of mitral, aortic, three-leaved valves and valves of pulmonary artery. The purchased defects can be compensated and decompensated. The signs of general venous plethora develop at decompesated defects, that is morphological picture of chronic cardiac insufficiency which is often the cause of death of such patients.

Born defects of heart depending on the degree of hypoxia can be cyanotic and white. At dark blue defects circulation of blood is carried out by anomalous ways from right to left (general arterial barrel, complete transposition of pulmonary artery and aorta, stenosis and atresia of pulmonary artery or aorta, combined defects of Fallo). Blood flows around the small circle of blood supply or passes through it only

partly. At the time of white defects hypoxia is absent. Blood circulation of is carried out from left to right. Depending on the violation of morphogenesis of heart all of defects are divided into three groups:

- Defects with the violation of the division of cavities of heart: partial or complete defect of interventricles partition, isolated defect of interatrial partition (wide oval opening). These are white defects; the three-chambered heart is often formed;
- Defects with the violation of the division of general arterial barrel: complete absence of division, transposition of pulmonary artery and aorta: aorta flows away from the right ventricle, and pulmonary artery from the left ventricle behind aorta;
- combined defects: triad (defect of interventricle membrane, stenosis of pulmonary artery and hypertrophy of right ventricle), (defect of interventricle membrane, stenosis of pulmonary artery, dextraposition of aorta and hypertrophy of right ventricle), (defect of interventricle membrane, stenosis of pulmonary artery, dextrapoition of aorta and hypertrophy of right ventricle, defect of interatrial membrane) of Fallo.

Miocarditises is a group of diseases which is characterized by the inflammation of cardiac muscle. According to etiology we select primary and secondary miocarditises. More frequent are secondary miocarditises: - infectious (viral, bacterial, mycotic and), infectiously allergic (at rheumatic illnesses, gigantcellular arteriitis, granulematosis of Vegener, generalized sarkoidosis), toxic (uremia, diphtherial toxin, substances of phosphorus), medical.

Gigantcellular idiopathic myocarditis of Abramov-Fidler is shown up by the focus of necrosis of cardiomyocytes, by diffuse inflammatory infiltration of myocardium with lymphocytes, eozinofils, plasmatic cells, giant cells and ends with cardiosclerosis.

Algorithm of the practical part of the lesson

udy and be ready for the verbal description of the acropreparations

Atherosclerosis of aorta with transition in aterocalcinosis. ll the stages of atherosclerosis are expressly determined on eparations: yellow spot and ribbon, fibrous plagues, hermanous, ulceration, sclerosis and calcinosis. At the initial splays of atherosclerosis (yellow spots and ribbons) aorta is ot deformed. Intimae is yellow. Pay attention to the fact , that llow spot and ribbon are located mainly near places of origin arteries. At presence of atheromatous the internal surface of ssel has an unequal kind as a result of the presence of plural llow explosions. It should be noted that at the developed of herosclerotic defeat of vessel all displays of process are pressly determined. Thus sharp distortion of internal surface vessel is especially evidently. Thrusting out of yellow rrespond to atheromas, white - as a result of the development the connecting tissue - atherosclerosis. Most atheromas have haracter of ulcers. Such ulcers of internal surface of aorta are ie place of the formation of blood clots and can be the source f embolisms. Atherocalcinosis is determined near sectional ible by conducting a knife for the surfaces of plague. It is thus ossible to hear a clang.

Exfoliating of aneurism of aorta. It mainly is the nvestigation of the destruction of internal and middle iembranes of vessel. Macropreparation is the transverse ection of aorta. Between internal and external membranes iere is an accumulation of blood (intramural haematoma). The umen of aorta of cracklike, sharply narrowed, that conduces odies and deaths to draining of blood of lower part. Another nvestigation of exfoliate aneurysm is possible - blood follows rom exfoliate aneurysm in lumen of aorta through the ulcer elow located in the wall of aorta. There is an unreal river-bed

of aorta, which is afterwards covered with endothelium. Blood supply of organs and tissues of the lower part of a body is worsened insignificantly.

3 *Gangrene of foot at the time of atherosclerosis of vessels of lower limbs.* On the skin of foot the area of black is expressly determined with maceration. Such changes in tissues of foot arose up as a result of stopping of blood supply which is the complication of atherosclerosis of arteries of a leg.

4 *Concentric hypertrophy of the left ventricle of heart.* Wall of the left ventricle of heart is 2 sm thick. Papillar muscles are thickened. Lumen of the left ventricle is concentric narrowed. Myocardium of fibred structure is with the thin layers of grey color. On this stage of hypertrophy of myocardium or tonogenic hypertrophy is compensated.

5 *Arteriolonephrosclerosis (a kidney is initially wrinkled).* A kidney is diminished, dense. The surface is unequal, grainy as a result of even duty of deepenings and appearances as corns. Deepenings are predefined scars in place of separate scleroused glomerules. So long as in a afferent vessel – in arteriole hyalinosis and sclerosis are developed, proper glomerule is scleroused- arteriosclerotic glomerulosclerosis. Nearby glomerules, afferent arteries which are not yet damaged, compensate inlarged, because execute greater load. On a cut notedly thinning of bark, a picture is effaced, evidently is darker bars which go from deepenings on a surface through cork and medullar matter. Blood vessels of gate of kidney are as gaping of the thick-walled white tubes.

6 *Transmural heart attack of myocardium.*On a cut the walls of the left ventricle the area of heart attack of myocardium is visible, which spreads on all thickness of wall of heart and presented the area of tissue of pinky color, which is marked off the ribbon of brown color. The pinky color of area of heart attack testifies that death came after days or anymore from the

eginning of attack of illness. Brown color on periphery - it emorrhagic crown - collaterals and hemorrhages are extended.

Acute aneurysm of heart with a break. Nearer to the surface f heart the area of necrosis, saturated with blood, is etermined. Necrosis of a heart takes all of its layers with inning of wall to 0,5 cm and break of myocardium. In the tored areas there is the thickness of wall of left ventricle and nterventricles membrane 1,5 cm.

Postattack largefocus cardiosclerosis. The lumen of coronal essel of is stenoused by an atherosclerotic plague. The wall of he left ventricle is thickened. The muscle of heart is omogeneous. In the area of apex there is a hearth of onnective tissue with unclear contours, which occupies the onsiderable area of transverse section of wall of heart is ostattack largefocus cardiosclerosis.

Atherosclerotic nephrosclerosis. A kidney is dense, the rface of largeneven with plural involvements and the resence of the thin-walled cysts. In the gate of kidney are vidently vessels which are damaged by atherosclerotic rocess, lumen of arteries is narrowed to 60%. Specify the ossibilities of complication and the cause of death.

0 *Gangrene of thin bowel.* Wall of bowel is black. In ransparent vessels which blood supply bowel, are evidently ed obturative blood clots. Why does a bowel have such color? Specify the clinic-anatomical form of atherosclerosis.

11 *Atherosclerosis of iliac artery with an obturative thrombosis (syndrome of Lerish).* Intima of aorta is disfigured by atheromatous plagues. Lumen of iliac artery is filled with red blood clot which fully recovers the entrance in general iliac rteria. The investigation of such changes in vessels is the development of sharp ischemia of tissues of lower limbs.

12 *Stenos atherosclerosis of coronal artery of heart with hrombosis and heart attack of myocardium.* On the cut of the eart wall of the left ventricle the area of light color, which

occupies a considerable area is visible. A coronal vessel is thickened, scleroused, on the transversal cut of artery evidently there is the narrowing of its diameter, and in lumen there is obturative blood clot.

13 *Chronic aneurysm of heart*. On the preparation of heart it is evident, that the wall of the left ventricle is sharply refined, and substituted for cardiac muscle with connecting tissue. In this area of the left ventricle there is thrusting out of the wall outside spherical form.

14 *Eccentric hypertrophy of heart*. In macropreparation the wall of the left ventricle is thickened, and lumen of chambers-is wide. It is the beginning of decompensation. As a result of hyalinosis of arterioles blood supply of myocardium is worsened, in that time when loading grows. Hypoxia of myocardium conduces to dystrophy and atrophy of cardiomyocytes, from what retractive ability of them diminishes, that conduces to stretching of myocardium by high bloody pressure; myocardium is thickening, chambers are stretching. It is a decompensate hypertrophy of heart - an organ is megascopic mainly due to the stretching of lumen of chambers, the transversal sizes of heart grow.

Study the micropreparations of the theme and be ready to show on the picture the main points of the pathologic process with the following descriptions:

1 *Atherosclerosis of aorta*. Colouring of hematoxylin and eozin. The elastic fibres of focus are blasted, with the presence of lipophagocytes, there are the focus laying of lime and destruction of intimae. To ***designate***: 1-blasted elastic fibres, 2- laying of lime, 3- lipophagocytes.

2 *Stenous atherosclerosis of coronal artery*. Colouring of hematoxylin and eozin. A transversal cut of coronal artery of heart and adjoining fatty tissue is evident. Lumen of coronal

rtery is considerably narrowed due to atherosclerotic plague-tenous atherosclerosis. It is located eccentrically, in the wall of a vessel, reverse to myocardium. It is explained by the fact hat part of artery which adjoins to myocardium is on more lense bedding, comparatively with the opposite. At the sistolic wave of blood, this department is not exactly injured. Microscopically it is evident, that the fibred structure walls of rtery is damaged, transferable homogeneous rose mass cholesterol and protein of plasma of blood). Navy blue drops ppear in a plague, it is a deposit of salts of lime. In nyocardium there are dystrophic changes of cardiomyocytes, henomenon of diffuse cardiosclerosis, called excrescence of he connective tissue is between cardiomyocytes. To ***designate:*** -atherosclerotic plague, 2- laying of lime, 3- excrescence of onnecting tissue.

Arteriolonephrosclerosis. Colouring is after the method of an Gizon. Connecting tissue is coloured in rose and red. Glomerules are of different sizes and color. Shallow glomerules are coloured in rose color, there are little kernels in hem, prevail fibred structures of connecting tissue. In windings tubules an epithelium is with the signs of destructions, disintegration mainly of apical part of cells. In lumen of tubules products of the destruction of epithelium are rose. Arteries out of glomerules are changed their walls are thickened, homogenized, little kernels, lumen is narrowed - hyalinosis. There are large glomerules which have a lot of kernels - hypertrophy is in it. In a cerebral layer is lightening of direct lumen, there is blood- hematuria.

To ***designate***: 1- hyalinosis of arteries, 2- hyalinosis of glomerules, 3- hypertrophied glomerule.

4 *Necrotic stage of attack of myocardium*. Colouring of hematoxylin and eozin. An area of myocardium coloured in the saturated rose color is evident. Cardiomyocytes in this area are deprived of kernels, sarcoplasma is homogeneous, absent

transversal banding. Eozinofilia is peculiar for the necrotised tissues. Absence of kernels testifies to the fact that that death came later days from the beginning of the attack of the illness. Round the area of necrosis vessels and hemorrhages are evidently extended, hemorrhagic crown and also the accumulation of cells: leucocytes, lymphocytes, histiocytes - that a demarcation area which is the beginning of organization. It specifies on that a few days passed from the beginning of necrosis, - near a week. To ***designate***: 1-necrosis of cardiomyocytes, 2- cellular infiltration, 3- excrescence of connecting tissue.

5 *Postattack largefocus cardiosclerosis*.The preparation is tinted after the method of van Gizon. Parenchyma (cardiomyocytes) coloured in light-green color, stroma in rose or pale red. Evidently focus excrescence of the connective tissue, perimisium, that round muscular bunches, in a less measure - endomisium - round every muscular fibre. Consequently, diffuse cardiosclerosis, predefined permanent hypoxia as a result of the narrowing of lumen of coronal vessels in the combination with focus takes a place. Thus, in this micropreparation largefocus rough postattack cardiosclerosis which developed on a background of diffuse cardiosclerosis take place, that is peculiar for chronic ischemic illness of heart. To ***designate***: 1- largefocus cardiosclerosis, 2- stenous vessel, 3- diffuse excrescence of connecting tissue.

6 *Organized heart attack of myocardium*. The preparation is tinted with hematoxylin and eozin. In the tissue of cardiac muscle is evident area which is coloured in rose, around there is cellular infiltration with histiocytes and hematogenic cells, forming of the connective tissue. Increased vascularisation is marked in the demarcation area. Nearby cardiomyocytes are stored, megascopic in a diameter and coloured more intensively. To ***designate***: to 1-areas of necrosis, 2- perifocal demarcation area, 3- excrescence of connecting tissue.

7 *Hypertrophy of myocardium*. The preparation is tinted with hematoxylin and eozin. Cardiomyocytes are evidently hypertrophied in the tissue of cardiac muscle, the intensive painting of cytoplasm and kernel by the proper dyes, the sizes of kernel are megascopic, the quantitative correlation of stroma decreased comparing with parenchyma. ***To designate***: 1- hypertrophied cardiomyocytes, 2- hypertrophied kernels, 3- excrescence of connecting tissue.

8 *Lipoidosis of aorta*. The preparation is coloured by sudan [222]. On the internal surface of aorta is evident laying of the fatty inclusions which are coloured in yellow. Elastic fibres of aorta wall are made light, fillings out with the focus of liposclerosis is laying of the fatty inclusions and excrescence of rough fibrose the connective tissue. To ***designate:*** 1- laying fat, 2- light elastic fibres, 3- excrescences of connecting tissue.

9 *Obliterative trombangit*. The preparation is tinted by hematoxylin and eozin. In the preparation is evident the inflammatory infiltration of the arterial vessel wall. To the intima of artery thrombotic masses densely adhering of mixedcellular composition. A blood clot fills a vessel with the simultaneous excrescence of the connective tissue and the complete obliteration of lumen. To ***designate***: 1-inflammation of vessel walls, 2- blood clot in lumen of vessel, 3- excrescence of connecting tissue.

Situation tasks

1 A patient came to the clinic with complaints on periodic pain in a sural muscle at the time of walking, pain and dark skin of the first finger of foot. What is it a clinic-morphological form of atherosclerosis? Give the explanation to the symptom of lameness.

2 A patient suddenly had pain atherosclerosis in small of the back. In a month the indexes of remaining nitrogen were increased, pneumonia developed and lungs were swollen, the

skin became grey. What changes of kidneys were found out on a section?

3 A patient suddenly died because of atherosclerosis. During life roentgenologic observed usura of breastbone. What changes of aorta were found out on a section?

4 At biochemical research of a patient with hypertensive illness blood got such indexes: albumen - 68,2%; urea - 33,3; creatinine - 0,9; potassium - 5,8; sodium - 129; calcium - 2,16; chlorine - 101,6. Explain the laboratory information and morphological changes which resulted in the violation of indexes.

5 During research of ECG of patient with hypertensive illness the displacement of ax to the left, signs of ischemia of myocardium were found. Give the morphological ground of these indexes.

6 A patient with hypertensive illness had edema on feet, cyanosis, trophic ulcers. Give the morphological ground of the indicated displays.

7 A patient suddenly had smarts behind a breastbone with an irradiation in a shoulder-blade: lower jaw, electrocardiologicaly the ischemia of myocardium and phenomenon of hypertrophy of the left ventricle of heart is marked. In two hours from the beginning of illness attack he died. What stage of illness do we speak about? By what reagents is possible macro- and microscopic diagnostics? What electronicmicroscopical changes are typical for this stage? Specify the possible causes of death.

8 A man who smoked 2 packs of cigarettes a day, suddenly felt squeezing pain behind a breastbone, which was not taken off by nitroglycerine. On the third day a patient died. Specify the cause of stenocardia. What possible microscopic changes are there from the side of a heart? Specify the risk factors?

9 On the second year after the heart attack of myocardium in a patient the considerable expansion of scopes of heart is

marked, pulsation in the area of apex, difficulty in breathing, cough with ferruginous phlegm, enlarged of liver, anasarca are diagnosed. What disease did a patient have? Give the explanation of the indicated symptoms.

10 In a patient with superfluous mass of body chronic postattack aneurysm of the left ventricle of heart, megascopic liver are diagnosed. Death came suddenly. Specify the morphological changes of heart and possible cause of death. What disease is in a background?

Answers for situation tasks.

1 Atherosclerosis of lower limbs. At the physical training nonoxyfied products which draw pain of sural muscle are accumulated in the conditions of ischemia.

2 Atherosclerotic nephrosclerosis. A kidney is sclerotic changed with rough scars and microcysts.

3 Aneurysm of ascending department of aorta, dug up or stratification.

4 Uremia developed as a result of arteriolonephrosclerosis.

5 These ECG marks the hypertrophy of left ventricle of heart. As a result of spasm of hyalinised arterioles the signs of ischemia often come.

6 The noted signs are the display of chronic cardiac insufficiency which is accompanied by general venous plethora.

7 The stage of ischemic dystrophy (prenecrotic). Nitroblue of tetrasolium, Shif's, cardiogenic shock, swollen lungs, unrhythmical shock.

8 Atherosclerosis of coronal vessels of heart, spasm. Heart attack of myocardium, atherosclerotic cardiosclerosis. Smoking of tobacco.

9 Chronic aneurysm of heart. Chronic decompensation of heart, which was accompanied by venous stagnation in organs and tissues.

10 Postattack cardiosclerosis, hypertrophy on periphery of scar of cardiomyocytes with fatty dystrophy. Chronic cardiac insufficiency, thromboembolia. Obesity.

Test task

1 During the necropsy of man, 48 years in intimae of aorta of the abdominal department the flat yellow bars, which do not rise above its surface were found. The presence of leiomyocytes is histologically marked, macrophagocytes with foamy cytoplasm. At colouring of sudan ^{222} in these cells are marked yellow granules. Specify the credible stage of atherosclerosis.

A. Prelipid.
B. Lipoidosis.
C. Liposclerosis.
D.Atheromatosis.
E.Atherocalcinosis.

2 During histological and histochemical research of coronal vessels of heart of man, who died suddenly, amorphous masses, which consisted of crystals of cholesterol, fragments of elastic and collagenic fibres are determined. The masses are marked off from lumen of arteries by hyalinised the connective tissue. Specify the credible stage of atherosclerosis.

A. Prelipid.
B. Lipoidosis.
C. Liposclerosis.
D. Atheromatosis.
E.Atherocalcinosis.

3 During necropsy of old man, who died of sharp heart attack of myocardium, an aorta in an abdominal department bursts saccate. Its wall is refined, with yellow and white bars, areas of

stony closeness. Specify the name of the pathologically changed aorta.
A. Displasia.
B. Atrophy from pressure.
C. Atrophy disfunctional.
D. Hypertrophy working.
E. Aneurysm.

4 An old man entered clinic with the complaints about sharp pains in an abdominal region. Death came in a few minutes. On a section in the abdominal department of aorta the saccate thrusting was found out. A wall is refined with the presence of defect with unequal edges; the surrounding tissues are saturated with blood. Complication of what form of arteriosclerosis took place in this case?
A. Ischemic illnesses of heart.
B. Abdominal ischemic illness.
C. Atherosclerosis of aortas.
D. Syphilitic mesaortitis.
E. System vasculitis.

5 A man, who died from the cardio-vascular insufficiency, at necropsy in the coronal arteries of heart numerous atherosclerotic plagues were found out which close 2/3 of lumen of vessel. At histological research of myocardium diffuse surplus development of the connective tissue and proliferation of fibroblasts are marked in interstitium, dystrophy and hypertrophy of cardiomyocytes. Specify a credible disease.
A. Sharp ischemic illness of heart (heart attack of myocardium).
B. Sharp ischemic illness of heart (stage of ischemic dystrophy).
C. Chronic ischemic illness of heart (diffuse cardiosclerosis).

D. Chronic ischemic illness of heart (postattack cardiosclerosis).
E. Chronic ischemic illness of heart (chronic aneurysm of heart).

6 A patient died of uremia. On a section fibrinous inflammation of serous and mucus membranes, swollen cerebrum and lungs were found out. In kidney arteries are numeral atherosclerotic plagues which close 2/3 of lumen. In kidneys there are plural band scars, polycystosis. Specify the form of nephrosclerosis .
À. Primary wrinkled kidney.
B. Secondary wrinkled kidney.
C. Amyloidal wrinkled kidney.
D. Atherosclerotic wrinkled kidney.
E. Born polycystosis of kidneys.

7 A patient died from the chronic cardiac insufficiency. The syndrome of lameness was marked during life. On a section atrophy and dryness of skin and atrophy of muscles of shin, gangrene of the first finger of foot were found out. What were the credible changes of vessels?
A. Thromboflebitis.
B. Vasculitis.
D. Capillaritis.
E. Atherosclerosis.

8 A man, 40 years, died suddenly after a considerable psyhoemotional overstrain. Histologically and histochemically in myocardium of the left ventricle of heart paretic expansion of capillaries, focus eozinofilia of cardiomyocytes with the loss of them banding, diminishing of number of granules of glycogen were found. Intimae of coronal arteries is waval,

endothelicytes take a place as a tile. Specify the credible pathology.

A. Sharp heart attack of myocardium, stage of ischemic dystrophy.
B. Sharp heart attack of myocardium, stage of necrosis.
C. Sharp heart attack of myocardium, stage of scarring.
D. Repeated heart attack of myocardium.
E. Relapsable heart attack of myocardium

Answers for the tests:
1.B; 2.D; 3.E; 4.B; 5.C; 6.D; 7.E; 8.A.

Illustrations to theme

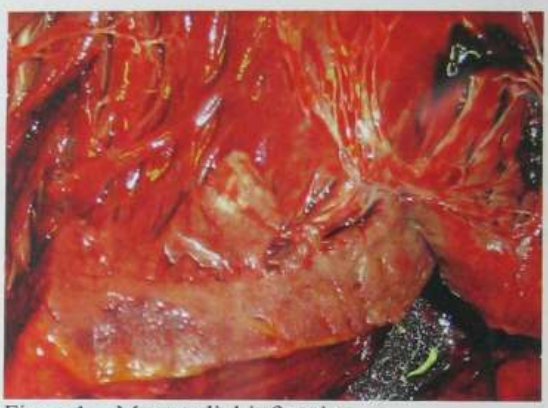

Figure1 – Myocardial infarction.

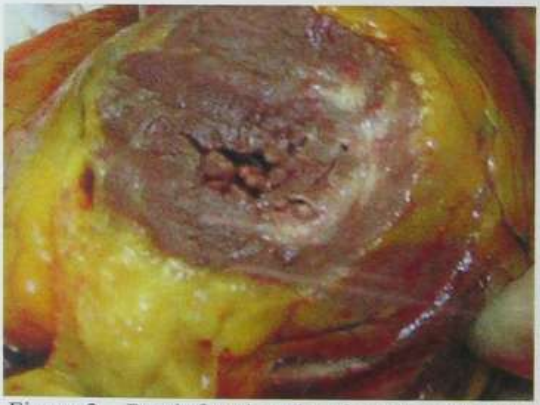

Figure 2 – Postinfarction (largfocus) cardiosclerosis.

Figure 3 - Concentric hypertrophy of left ventricle of heart.

Figure 4 –Chronic aneurysm of heart.

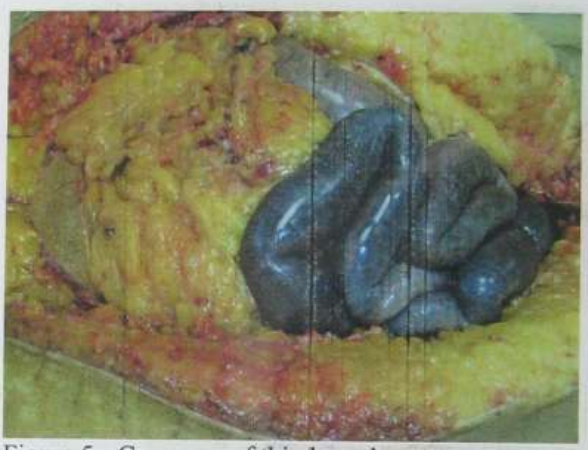

Figure 5 - Gangrene of thin bowel.

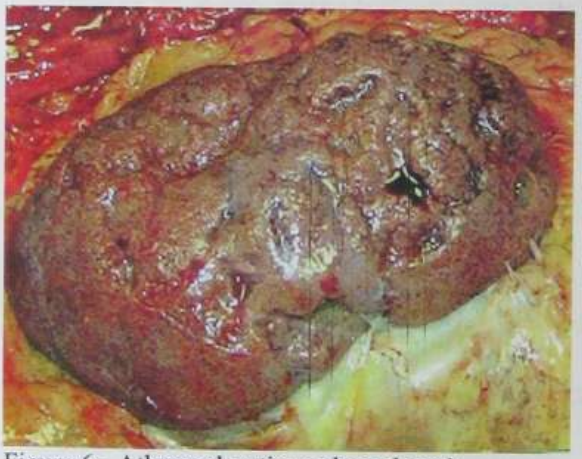

Figure 6 - Atherosclerotic nephrosclerosis.

Figure 7 – Atherosclerosis of aorta and iliac artery with an obturative thrombosis.

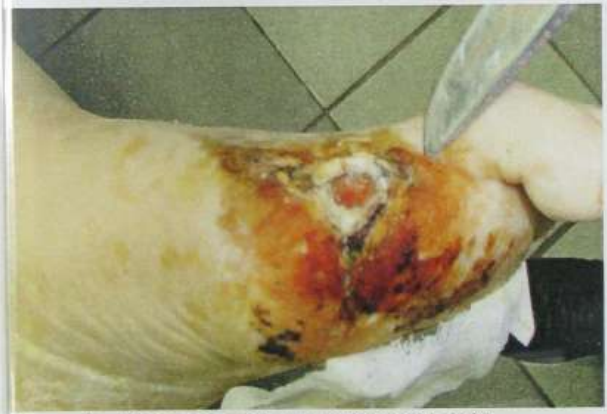

Figure 8 – Gangrene of foot at atherosclerosis of vessels of lower limbs.

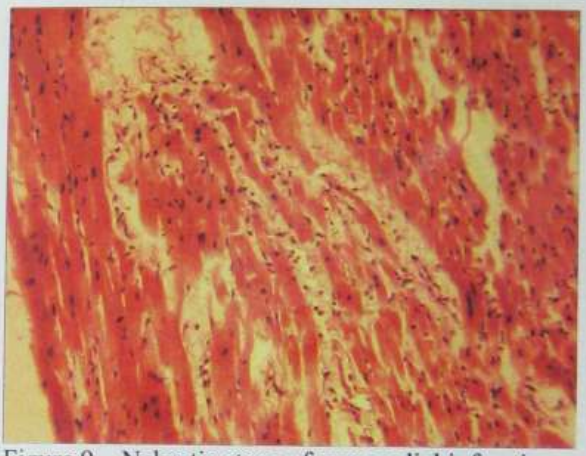

Figure 9 – Nekrotic stage of myocardial infarction.

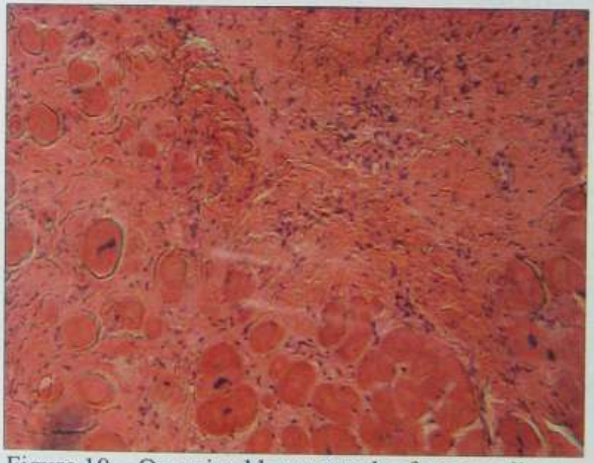

Figure 10 – Organized heart attack of myocardium.

Theme 25 ***Systemic Diseases of Connective Tissue with Autoimmunization. Rheumatism. Rheumatoid Arthritis. Systemic Lupus Erythematosus. Scleroderma. Dermatomyositis. Bechterew's (Strumpell's) disease***

Subject Actuality: systemic diseases of connective tissue and rheumatic diseases are defined by primary lesion of connective tissue and immune disorders with general morphologic changes of microcirculation vessels. They develop on the basis of systemic progressive disorganization of connective tissue that places such diseases as rheumatism, rheumatoid arthritis, systemic lupus erythematosus, systemic scleroderma (systemic sclerosis) and periarteritis nodosa into one group. The knowledge of the subject is necessary for studying these diseases at clinical university departments.

Aim: learning the etiology, pathogenesis and pathologic anatomy of the systemic diseases of connective tissue (rheumatic diseases).

Task:

1 To know the definition of systemic diseases of connective tissue (rheumatic diseases).
2 To know the main etiological factors, pathogenesis, morphologic changes and complications of rheumatic diseases.
3 To learn to distinguish between the main clinicoanatomic forms of rheumatism.
4 To be able to diagnose rheumatic illnesses on the basis of their morphologic presentations.

Main questions for the individual training:

Immune homeostasis disturbances and systemic progressive disorganization of connective tissue in rheumatic diseases.

Rheumatism: etiology, classification, patho- and morphogenesis, morphologic description and diagnostic

methods, clinical symptoms and syndromes, prognosis. Endocarditis, myocarditis, pericarditis and pancarditis: classification, clinicopathologic description, complications. Infectious endocarditis: morphologic description. Visceral lesion in rheumatism. Rheumatism peculiarities in children.

Rheumatoid arthritis: aetiology, immunopathogenesis, morphogenesis, morphology of articular manifestations (phases of rheumatoid polyarthritis progression), clinical presentations, complications and consequences. Juvenile rheumatoid arthritis: clinicopathologic description. Stages of synovitis. Visceral manifestations of rheumatoid arthritis, complications, causes of death.

Bechterew's disease: etiology, pathogenesis, pathologic anatomy.

Systemic lupus erythematosus: etiology, pathogenesis, pathologic anatomy. Immunomorphologic changes of skin, vessels, heart, kidneys. Groups of tissue and cell transformations. Complications, causes of death.

Systemic scleroderma (systemic progressive sclerosis): etiology, pathogenesis, pathologic anatomy. Visceral manifestations of systemic scleroderma. Complications, causes of death.

Dermatomyositis: etiology, pathogenesis, pathologic anatomy, clinicoanatomic forms. Complications, causes of death.

Lesson equipment:

Macropreparation: acute verrucous endocarditis, recurrent verrucous endocarditis, valvular disease (mitral stenosis), fibrinous pericarditis, concentric cardiac hypertrophy, nutmeg liver, brown induration of lungs, spinal osteoarthritis, rheumatic fibroblastic endocarditis, primarily contracted kidney in lupous glomerulonephritis.

Micropreparation: mucoid edema of endocarditis in rheumatism, acute rheumatic verrucous endocarditis (tinted

with hematoxylin and eosin), productive (granulomatous) rheumatic myocarditis nodosa, lupous glomerulonephritis, nutmeg liver, brown induration of lung (tinted with hematoxylin and eosin, Pearls' test), rheumatic recurrent verrucous endocarditis, cardiac valve sclerosis due to valvular disease, lupous nephritis (tinted with hematoxylin and eosin), spleen sclerosis in lupus erythematosus (tinted with hematoxylin and eosin), autoimmune parotitis in Shegren's disease (tinted with hematoxylin and eosin).

Slides and tables corresponding with the macro- and micro-specimens, available in the department's archives.

I Preauditorium individual training for the practical training

Theoretic Material Summary

Rheumatic Diseases

Rheumatic diseases are a group of chronic diseases characterized by systemic lesion of connective tissue and blood vessels. In their etiology a significant role is played by a clinically apparent or latent streptococcic infection and the pathogenetic mechanisms mainly consist of allergic reactions of delayed and immediate type. There develops progressive disorganization of connective tissue – a mucous edema, a fibrinoid edema and necrosis, cellular reaction (granulomatosis) and sclerosis.

Although the pathogenesis of rheumatic diseases is single-type, every nosologic form has its characteristic peculiarities. In rheumatism, for instance, the sensitizing factor is the antibodies against the β-hemolytic streptococcus of A-type that have affinity to antigens of cardiac connective tissue. That is why rheumatism usually affects patient's heart.

Rheumatoid arthritis mainly affects the connective tissue of articular capsules. The immune complexes where the

antibodies are immunoglobulins of various types (Ig M, Ig G, Ig A) are important for the pathogenesis of the disease.

In systemic lupus erythematosus the DNA metabolism is disturbed and antibodies are produced against the components of the nucleus and the cytoplasm – DNA, RNA, histones, nucleoproteins. This causes polymorphic changes in many organs and tissues but mainly in skin, vessels, kidneys and heart.

Visceral Manifestations of Rheumatic Diseases

Rheumatism	Arteritis, arteriolitis, capillaritis, endocarditis, myocarditis, pericarditis, serofibrinous polyarthritis, glomerulonephritis, erythema nodosum of skin, polyserositis, juvenile chorea, pneumonia, hypodermic nodes
Rheumatoid arthritis	Arteritis, arteriolitis, progressive destructive polyarthritis, fibrous and bony anchylosis, osteoporosis, polyserositis, glomerulonephritis, pyelonephritis, renal amyloidosis, cardiosclerosis
Systemic lupus erythematosus	Arteriolitis, capillaritis, vasculitis, intermediate inflammation of internal organs followed by sclerosis, periarterial bulbous spleen sclerosis, hyperproduction of immunoglobulins, DNA loss, appearance of lupous cells, erythema of skin (butterfly circuit), Libman-Sacks endocarditis, glomerulonephritis, polyarthritis without articular deformations
Scleroderma	Arteriolitis, capillaritis, sclerosis, hyalinosis, skin atrophy (parchment-skin), sclerodermic heart (macrofocal cardiosclerosis), sclerodermic kidney (cortical necrosis), basal pneumofibrosis
Periarteritis nodosa	Vasculitis (destructive, destructive-and-productive, productive), infarcts and postinfarction sclerosis of internal organs, haemorrhage, glomerulonephritis

Systemic scleroderma is characterized by sclerotic and atrophic changes of skin. Deranged synthesis of collagen is

considered to be the decisive factor for scleroderma development.

Periarteritis nodosa is defined by a complex immune mechanism of arterial lesion of small and medium calibre which leads to secondary transformations of internal organs. It is considered that the fibrinoid necrosis of middle coat of blood vessels causes the development of proliferative reaction of cells in the outer coat, which is followed by sclerosis and formation of nodes.

The group of rheumatic diseases is constantly growing owing to new nosologic forms included into it, whose pathogenesis is connected with systemic disorganization of connective tissue and blood vessels. Bechterew's disease and dermatomyositis fall into this category. Bechterew's disease is a chronic rheumatic disease consisting of lesion of articular-and-ligamentous apparatus of spine that leads to bony anchylosis. Dermatomyositis is a rheumatic disease that manifests itself mainly in systemic lesion of transversely striated muscles and less in that of non-striated muscles.

Rheumatism is a chronic disease with prevailing lesion of heart and blood vessels. Its progression is undulating, periods of exacerbation alternate with remissions. Its development is associated with β-hemolytic streptococcus of A-type. However, rheumatism cannot be regarded as a simple streptococcic infection. Penetrating to the body through tonsils, streptococci release toxins and cause in the places of invasion cell destruction and inflammation that usually manifests itself in tonsillitis. The toxins and cell destruction products are the antigens against which antibodies are produced. Recurrent exacerbation of tonsillitis serves as a starting point of the development of the disease.

It is proved that some streptococcic ferments break up glucosamine-and-protein complexes in connective tissue. As a result of immune response to streptococcic components and

tissue destruction products, a wide range of antibodies and immune complexes appears in the blood which creates preconditions for autoimmune processes.

Four stages of connective tissue disorganization are observed in the development of rheumatism – mucous edema, fibrinoid changes, granulomatosis and sclerosis. Mucous edema is surface and reverse disorganization of connective tissue characterized by intensified metachromatic reaction to glucosaminoglycanes and hydration of basal substance. For a clinician it is important to know that this phase is reversible. Early diagnosis and beginning of treatment may bring complete recovery.

Fibrinoid changes (swelling and necrosis) are irreversible. They are characterized by homogenization of collagen fibres that get impregnated with plasma proteins, including fibrin.

The stage of granulomatosis manifests itself morphologically in inflammatory reaction of cells. It was first described in the form of nodular masses in heart stroma by Aschoff (1904) and in 1930 V.Talalayev singled out three phases in the development of rheumatic granuloma – alterative-exudative, proliferative and sclerotic. Correlating them to clinical data he showed that the whole cycle of granuloma development lasts 4-6 months.

The alterative-exudative phase is characterized by accumulation of macrophages around the fibrinoid necrosis focus, which transform into big cells with a hyperchromic nucleus. Such granuloma is called "floriferous". It indicates an acute process going on.

At the time of the proliferative phase the cells become elongated, there appear fibroblasts and the quantity of fibrinoid masses decreases. The "fading granuloma" develops. It indicates the attenuation of the process.

In the phase of sclerosis the fibroblasts substitute the fibrinoid necrosis zone, and argyrophil and collagen fibres are synthesized. The granuloma assumes the properties of a scar. This indicates the remission of the disease.

In typical progression of rheumatism it is the heart that is affected first and foremost. There develops endocarditis, myocarditis, less often – pericarditis. Sometimes one can observe acute polyarthritis characterized by swelling of big joints, quick passage from one joint to another, and restoration of their functions during remission. Chorea, erythema annulare, formation of hypodermic nodes that used to be typical of rheumatism, is relatively rare nowadays.

According to localization, endocarditis can be valvular (valvulitis), chordal and parietal. In most cases the rheumatic process affects the mitral and the aortic valve. Depending upon the prevailing alterative or regenerative process, one distinguishes between four types of rheumatic valvular endocarditis:

a) diffuse endocarditis characterized by diffuse mucous edema of connective tissue without endothelium lesion;

b) acute verrucous endocarditis defined by fibrinoid transformation of connective tissue and endothelium desquamation with accumulation in the places of lesion of thrombotic masses in the form of warts;

c) fibroplastic endocarditis that develops as a result of the above mentioned forms and is characterized by excrescence of the newly formed connective tissue, emboly of blood vessels and regeneration of epithelium; the valve is thickened and transformed by scars which causes its deficiency (acquired valvular disease);

d) recurrent verrucous endocarditis characterized by recurrent disorganization of the newly formed connective tissue, endothelium lesion and fibrin deposition due to sclerosis and

hyalinosis of the valve; this process indicates a recurrent rheumatism attack.

Myocarditis is a constant manifestation of rheumatism. Three forms of it are singled out:

a) granulomatous, characterized by the presence of "floriferous", "fading" and sclerotic rheumatic granulomas in perivascular connective tissue;

b) diffuse exudative interstitial myocarditis characterized by edema, hyperaemia and considerable infiltration of intersticium with lymphocytes, histiocytes, neutrophils and eosinophils, and solitary Aschoff-Talalayev granulomas;

c) focal exudative interstitial myocarditis that manifests itself in slight focal infiltration of intersticium with lymphocytes, histiocytes and neutrophils. Under favourable conditions myocardite develops into cardiosclerosis.

Pericarditis is a sort of serous, serofibrinous or fibrinous exudative inflammation. It often ends with the formation of adhesions. Obliteration of pericardial cavity and calcification of the formed connective tissue may also occur (stone heart).

The combination of endo- and myocarditis is referred to as rheumatic carditis, and that of endo-, myo- and pericarditis – as rheumatic pancarditis.

Vasculitis at the time of rheumatism has systemic nature and is observed in all organs and tissues. Capillary permeability increases drastically, it manifests itself clinically in nodular erythema. It often occurs that skin capillaries are wrapped in pericyte muffs and endothelium is in the state of proliferation. In the end there develops sclerosis around capillaries with the formation of rheumatic nodes.

Polyarthritis is usually serofibrinous in rheumatism. Articular cartilage is not damaged so there can be no articular deformation.

Juvenile chorea is a cerebral form of rheumatism. It occurs more often in children. Because of vasculitis there develop dystrophic changes of nerve cells in the brain as well as destruction focuses and haemorrhages that are the morphologic basis of clinical presentations.

Rheumatism complications are connected in most cases with heart lesion: valvular defects and embolisms in verrucous endocarditis, internal infarcts, encephalomalacia, limb gangrene, commissures and obliteration of pericardial cavity.

The most frequent cause of death of rheumatism is decompensated valvular defect and thromboembolic complications.

Rheumatoid arthritis is a chronic disease based on progressive disorganization of connective tissue of synovial membranes and articular cartilages. Its characteristic feature is the development of nonsuppurative proliferative synovitis followed by articular deformations. It often causes damage of skin, blood vessels, heart, lungs, muscles and other organs and tissues. It affects mainly women. The cause of the disease is unknown but one points out genetic susceptibility to autoimmune reactions to collagen of Type 2. For that matter T-lymphocytes release inflammatory mediators and lytic cytokines that destroy joints. Microbial infection, especially viruses, is often the starting point for the disease. The body produces antibodies to its own Ig G, which is the rheumatoid factor.

Morphologic changes mainly manifest themselves in the lesion of musculoskeletal system. There develops synovitis that has three stages. *The first stage* is characterized by edema of synovial membrane and villi with the development of disorganization of connective tissue: mucoid and fibrinoid intumescence, fibrinoid necrosis. The villi necrotize and there develops "rice body". There are signs of inflammatory reaction of cells in tissues. *The second stage* manifests itself in the

growth of villi and proliferation of synoviocytes, in inflammatory cellular infiltration, in the formation of granulation tissue on the joint surface, erosions in articular cartilage, exposure of bone and epiphyses, in osteoporosis. The granulation tissue narrows the joint space, decreases articular mobility and causes luxations and subluxations. *The third stage* manifests itself in fibrous and bony anchylosis and develops after long progression of the disease. It is defined by complete articular immobility, the formation of rheumatoid nodes around joints with signs of destructive changes in connective tissue.

The main visceral manifestations of rheumatoid arthritis are polyserositis, vasculitis in lungs and heart with disorganization of connective tissue and inflammatory cellular infiltration with lymphocytes, plasmocytes and histiocytes. The heart may be affected by endocarditis with the development of valvular disease, the lungs – by pneumosclerosis.

One of the complications is renal amyloidosis with the development of uraemia which is often the cause of patient's death.

Bechterew's (Strumpell's) disease (poker back) or anchylosing spondylitis, rheumatoid spondylitis is a chronic rheumatic disease characterized by the lesion of articular-and-ligamentous apparatus of spine that ends with its immobility. In its *etiology* and *pathogenesis* the main role is played by infectious and allergic factors, spinal trauma and heredity. More often it affects men. The pathologic anatomy is characterized by the development of destructive-inflammatory changes in the tissues of small spinal joints with the destruction of articular cartilage and the development of bony anchylosis. Similar transformations develop in intervertebral disks. The spine becomes completely immobile. It also damages internal organs: aorta, heart, lungs. There develops renal amyloidosis which is often the cause of death.

Systemic lupus erythematosus (SLE) (Libman-Sacks disease) is a systemic disease marked by autoimmunization that has acute or chronic progression and is characterized by the lesion of skin, vessels and kidneys. More often it affects young women. *The cause* of the disease is unknown. A nonspecific provoking factor is ultraviolet radiation and pregnancy. The disease may develop after a viral infection. Hereditary factors play important role too. In its *pathogenesis* a significant role is played by the imbalance of the function of T-suppressors and T-helpers with the formation of multiple organ antibodies (lupous factor – antinuclear antibodies). The *pathologic anatomy* is characterized by the development of fibrinoid changes in the walls of microcirculation vessels with the formation of vasculitis that ends with secondary ischemic changes in organs in the form of dystrophy and necrosis. *Skin* is affected by cheek erythema – "red butterfly" – due to proliferative-destructive vasculitis in the derma; edema and focal perivascular lymphohistiocytic infiltration. *Kidneys* are affected by lupous glomerulonephritis or mesangioproliferative glomerulonephritis. A characteristic peculiarity is the deposition of immune complexes and capillary thickening in the form of "wire loops", fibrinoid necrosis focuses, hematoxylin bodies, hyaline thrombi. Glomerulonephritis results in contraction of kidneys and the development of renal insufficiency which is often the cause of patient's death. The patient's *heart* is affected by nonbacterial verrucous Libman-Sacks endocarditis where hematoxylin bodies can be found in the necrosis focuses. In contrast to rheumatism no mucoid or fibrinoid intumescence can be observed. In spleen one can find periarterial "bulbous sclerosis". Among complications and causes of death of SLE one should highlight lupous nephritis and the development of renal insufficiency.

Systemic scleroderma (systemic sclerosis) is defined by the development of diffuse sclerosis and hyalinosis of

connective tissue in various organs and tissues. The *etiology* and *pathogenesis* is unknown. Important for the disease development are viral infections and hereditary factors with autoimmunization. *Pathologic anatomy.* Major changes develop in the heart, kidneys, gastrointestinal tract, blood vessels and skin. In the *heart* one can observe sclerosis and contraction of mitral valve cusps, subendocardial cardiosclerosis with the development of cardiovascular collapse – "sclerodermic heart". In coronary vessels one can often find concentric sclerosis and hyalinosis. Around vessels there is inflammatory infiltration with lymphocytes, macrophages and plasmatic cells. *Skin* is affected by diffuse or focal epidermal atrophy, sclerotic transformations and hyalinosis of connective tissue. In dermal vessels one can observe vasculitis and later reduction of bloodstream. Due to insufficient vascularization there appears necrosis and exulceration focuses in the skin. The latter becomes dense, with focuses of hyperpigmentation and hemangiectasia. The face becomes masklike. In *kidneys* there develops progressive vasculitis, concentric thickening of interlobular arteries, their trombosis, cortical necroses and infarcts, parenchyma sclerosis with the development of renal insufficiency. In *lungs* one can observe carnification due to diffuse fibrosis, thickening of alveolar septa, arteriolar sclerosis. In *gastrointestinal tract* one can observe sclerotic transformations of submucous and muscular layer, swallowing and absorption derangement, slowing-down of motility, development of cachexy.

Dermatomyositis is characterized by the lesion of transversely striated muscles and less by that of non-striated muscles. More often it affects skeletal, pharyngeal, laryngeal, ocular and diaphragmatic muscles. Muscles undergo atrophic and dystrophic changes, lose their striation, their fermentative activity and glycogen supplies decrease, sometimes coagulation necrosis occurs. Muscles are gradually substituted

by connective tissue and fat masses. In the heart one can observe dystrophy of cardiomyocytes, intermediate myocarditis with productive vasculitis, edema of intercellular substance, infiltration with lymphocytes, macrophages and plasmatic cells. The process ends with diffuse cardiosclerosis and atrophy of cardiomyocytes. In lungs alveolar septa are thickened. In gastrointestinal tract one can observe atrophic and dystrophic transformations of muscular cells, perivascular lymphomacrophage infiltrations, sclerosis of mucous and submucous layer. Other organs undergo inflammatory and sclerotic changes.

II Algorithm of the practical part of the lesson

Study and be ready for the verbal description of the macropreparations:

1 *Acute verrucous endocarditis*. The size of valves, cords and papillary muscles is normal. Mitral cusps are dingy and thickened. One can see soft grey "warts" on cords.

2 *Fibroblastic endocarditis*. Mitral valve is considerably thickened and has slight deformation. Cords are thickened. Parietal endocardium is half transparent. So, rheumatic endocarditis is usually diffuse, i.e. it affects simultaneously valves, cords and parietal endocardium.

3 *Recurrent verrucous endocarditis*. The size of the left ventricle of heart is bigger and its weight is increased. Papillary muscles and the cardiac wall is hypertrophied, the valve is sclerosed, with necrotic and thrombotic deposits. The valve cusps are inosculated and thickened as a result of connective tissue excrescence. Cords are also greatly thickened, shortened and inosculated. Parietal endocardium is white and thickened.

Identify the clinical valvular disease.

4 *Valvular disease (mitral stenosis)*. The size of heart is bigger and its weight increased due to hypertrophy of both ventricles. Cardiac cavities are delated, mitral valve cusps are

considerably thickened, white, dense, with calcification here and there. Cords are considerably shortened and thickened. The left atrioventricular opening is considerably narrowed (it resembles a buttonhole). The cardiac muscle in section is dingy.

5 *Fibrinous pericarditis*. The heart is bigger in size. Pericardium is thickened due to yellow-grey fibrin deposits. Epicardium is rough and covered with fibrin threads. Such changes in pericardium and epicardium give the impression of hair – "hairy heart". In the other specimen - "adhesive pericarditis" – one can see that both leaves of pericardium are thickened due to fibrin organization. Between the leaves of pericardium there are thick adhesions of connective tissue. A separate macro-specimen represents "stone heart". Both leaves of pericardium are thickened and the pericardium lumen is obliterated. Deposition of calcareous salts occurs in the connective tissue, the heart is immured into "stone" – "stone heart".

6 *Concentric cardiac hypertrophy*. In horizontal section of heart one can see drastic thickening of the left ventricle wall and interventricular septum. The cavity of the left ventricle is smaller. *Which heart diseases are characterized by this type of hypertrophy?*

7 *Nutmeg liver*. The liver is larger in size, dense. The parenchyma in section is motley, yellow-grey with dark red specks and looks like a nutmeg: dark blue areas against a light yellow background. The motley is caused by the fact that central veins and sinusoids are thickened, plethoric, and at the periphery of particles there are hepatocytes with atheroma which gives the light yellow background.

8 *Brown induration of lungs*. The macro-specimen represents a lung in section. The lung is enlarged in size, dense and brown. The organ's tissue is of rusty colour which is caused by considerable accumulation of hemosiderin in alveoli and

stroma. At the time of rheumatism it is usually the left heart that is affected: valves, endocardium and myocardium. The left ventricle cannot pump the blood over from the lesser to the greater circulation. So the right heart forces blood into lungs and the left one is not able to pump it over. Lung capillaries are overfilled with blood, thickened and the permeability of their walls increases. Erythrocytes penetrate by way of diapedesis from vessel lumens into lung tissue and into alveoli. Beyond vessel lumens erythrocytes are regarded by tissues as foreign bodies and they are absorbed by macrophages in which haemoglobin is converted into hemosiderin and the latter is of light brown (rusty) colour. The colour's intensity depends upon the duration of congestion. Macrophages with hemosiderin are called siderophages. Siderophages in patient's expectoration are called "heart disease cells". Lungs' consistency is dense due to the development of pneumosclerosis. The latter's genesis is connected with the proliferation of fibroblasts and their activation due to hypoxia.

Study the micropreparations of the theme and be ready to show on the picture the main points of pathologic process with the following descriptions:

1 *Mucoid edema of endocarditis in rheumatism*. The specimen is tinted with blue toluidine solution. It can be seen that myocardium becomes blue. But certain areas of tissue turn pink. It is the so called phenomenon of metachromasia that occurs in the places of mucoid edema of tissue. Such changes in endocarduim occur at the initial stages of endocardium lesion in rheumatism. Indicate what the stages of the disease progression will be. **Designate**: 1 – affected endocardium, 2 – unchanged endocardium, 3 – cardiac hystiocyte.

2 *Acute rheumatic verrucous endocarditis*. The specimen is tinted with hematoxylin and eosin. In outer areas of the valve cusp one can observe occasional basophilia, fibrinoid necrosis

and endothelium destruction. In the places of endothelium lesion one can see thrombotic deposits – "warts". At the basis of such transformations in the valve cusp there occurs lymphohistiocytic infiltration. **Designate**: 1 – fibrinoid necrosis, 2 – thrombus (wart), 3 – lymphocytes.

3 *Productive (granulomatous) rheumatic myocarditis nodosa.* The specimen is tinted with hematoxylin and eosin. In the perivascular connective tissue of the myocardium one can observe rheumatic granulomas consisting of macrophages and fibroblasts. There are almost no fibrinoid masses in the node centre. **Designate**: 1 – granuloma, 2 – fibroblasts, 3 – cardiac hystiocytes.

4 *Lupous glomerulonephritis*. The specimen is tinted with hematoxylin and eosin. In slight enlargement one can see hyaline thrombi and fibrinoid necrosis focuses in certain glomerule loops. In great enlargement one can observe thickening of basal membranes of capillaries which look like "wire loops", pathologic nuclear transformations – karyorrhexis (hematoxylin corpuscles), cellular infiltration and proliferation of mesangium. **Designate**: 1 – fibrinoid necrosis of glomerule, 2 – thickened capillary membranes, 3 – cellular infiltration of mesangium.

Situation Tasks:

1 A 53-year-old patient, disabled person of Group 2, had had a rheumatic heart disease for years. At exacerbation of rheumatism with increasing cardiovascular collapse there developed left-side hemiplegia and the patient died. What clinicopathologic form of rheumatism is implied? What changes of brain caused the development of left-side hemiplegia? What changes in mitral valve cusps of heart can indicate exacerbation of rheumatism?

2 A patient died of chronic cardiovascular collapse. The incision showed thickening of mitral valve cusps which are

opaque and milk-white, the opening itself is narrowed. What sequential transformations of valve endocardium can give such a macroscopic picture? Name the dystrophy type in the valve cusps. At what stage of morphologic changes was the process reversible?

3 A 30-year-old woman had suffered from a rheumatic heart disease since childhood. She was taken to the hospital with edemas on limbs, ascites, the edge of the liver protruded out of the right hypochondrium. The diagnosis was mitral stenosis. In section the liver was motley, kidneys were dense, with cyanosis. Lungs were dense and brownish. What changes can one observe in the valve at histologic examination? Name the changes in the liver and kidneys. Identify the nature of changes in lungs.

4 After long insolation a child fell ill suddenly: the blood pressure increased, there appeared signs of nephrotic syndrome. The therapy produced little effect, renal insufficiency gradually progressed and a year later the patient died. In section kidneys are bigger in size, motley, with dotty haemorrhages, dark red pyramids, on the surface. What disease causes such changes in kidneys? Define these changes. What hypersensibility reactions do they reflect?

Answers to the Situation Tasks:

1 Cardiovascular form. Cerebral thromboembolism resulted in brain infarct. Exacerbation of rheumatic process is indicated by fibrinoid necrosis in the endocardium of mitral valve as well as by fresh thrombotic deposition.

2 Transformations in endocardium had the following progression: mucoid intumescence, fibrinoid intumescence and necrosis, inflammatory cellular reaction, hyalinosis, sclerosis. In the cusps there developed mesenchimal degeneration. Morphologic changes are reversible at the stage of mucoid intumescence.

3 At histologic examination one can find hyalinosis in the valve. In the liver one can observe nutmeg liver, in kidneys – cyanotic induration, in lungs - brown induration of lungs.
4 The child suffered from systemic lupus erythematosus. The changes in kidneys relate to lupous glomerulonephritis. In the organs there developed autoimmune hypersensibility reactions of immediate type.

Test Tasks:

1 At the autopsy of a middle-aged man one finds numerous haemorrhages in skin, in serous and mucous tunics and in conjunctiva, as well as thickening of ungual phalanxes, jaundice, focuses of necrosis of hypodermic fatty tissue, endocarditis polypoulcerosa of aortic valve with perforation of one of the cusps, sclerosis and deformation of others. Histologically one observes infiltration of internal organs' stroma with lymphocytes, histiocytes and macrophages, endo- and perivasculitis. There are no neutrophils in the infiltration. Identify the presumable disease.
A. Idiopathic myocarditis.
B. Rheumatism.
C. Atherosclerotic defect of aortic valve.
D. Septic endocarditis.
E. Fibroblastic parietal endocarditis.

2 The female patient has suffered from rheumatism complicated by mitral defect since childhood. In the recent years there signs of cardiovascular collapse and cough with rusty expectoration have frequently occurred. Name the complication that has developed in lungs.
A. Brown induration of lungs.
B. Emphysema.
C. Atelectasis.
D. Pneumosclerosis.

E. Bronchiectasis.

3 The female patient had suffered from a rheumatic heart disease for a long period of time. She was hospitalized with complaints of short breath, edemas on legs, ascite and enlarged liver. She died of chronic cardiac insufficiency. In section one could observe mitral stenosis. Which of the morphogenetic factors is the most probable?
A. Sclerosis and thickening of cusps.
B. Shortening of tendinous fibres.
C. Sclerosis and shortening of cusps.
D. Inosculation of cusps.
E. Small thrombi on the surface of valves.

4 At the incision of a patient who had suffered from rheumatoid arthritis one found enlargement of kidney that was of yellow-white colour with waxy hue and quite dense. Tinted with Congo-rot, it showed deposition of pink masses in capillary loops of glomerules, on the walls of arterioles, arteries, in basal membrane of tubules, in the stroma. What complication of rheumatoid arthritis developed in the patient's body?
A. Acute necrotic nephrosis.
B. Secondary renal amyloidosis.
C. Fibroblastic glomerulonephritis.
D. Rapidly progressing glomerulonephritis.
E. Post-infectious glomerulonephritis.

5 At histologic examination of the patient's heart auricle for mitral stenosis one has found Aschoff-Talalayev granulomas. What genesis of heart disease suggests itself?
A. Rheumatic.
B. Septic.
C. Congenital.

D. Syphilitic.
E. Atherosclerotic.

Answers to the Test Tasks:

1.D; 2.A; 3.D; 4.B; 5.A.

Illustrations to theme

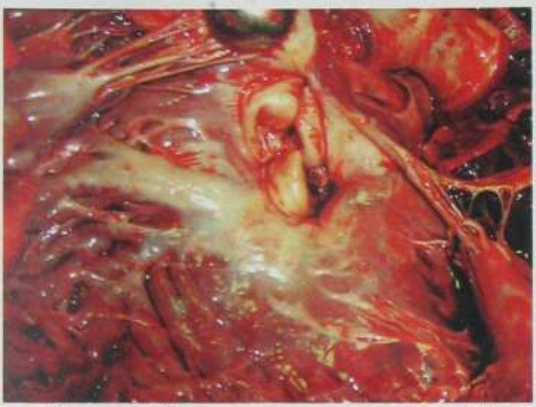

Figure 1 – Recurrent verrucous endocarditis.

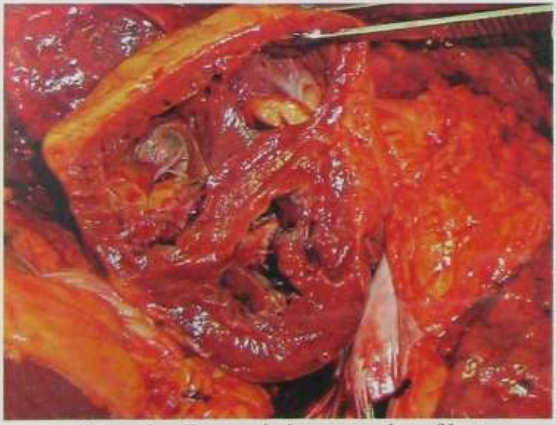

Figure 2 – Eccentric hypertrophy of heart.

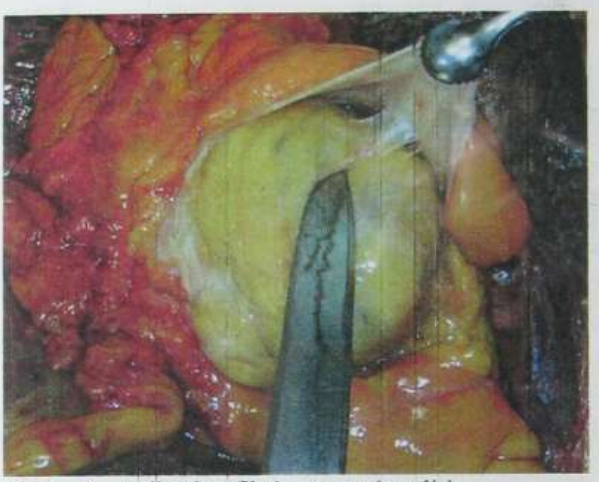

Figure 3 – Adhesive fibrinous pericarditis.

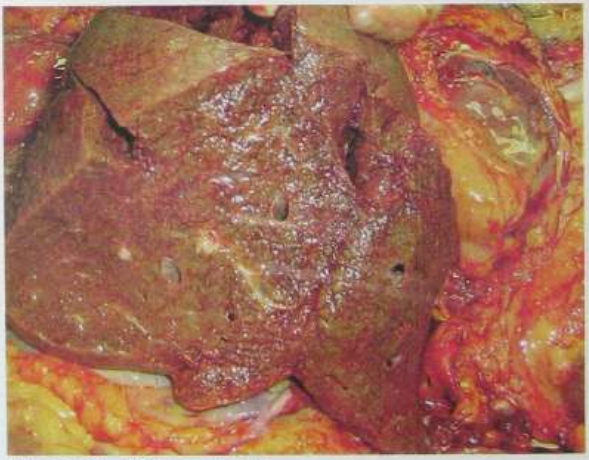

Figure 4 – Nutmeg liver.

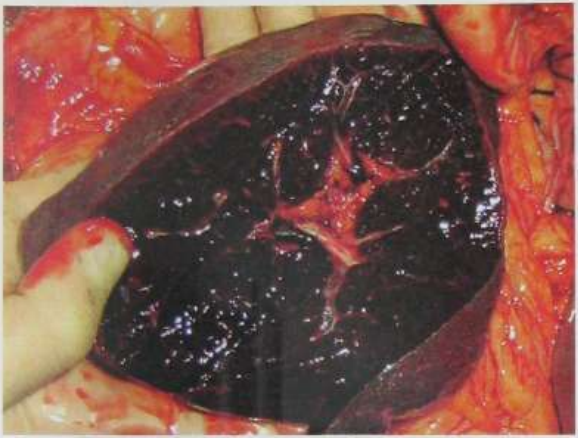

Figure 5 – Cyanotic induration of spleen.

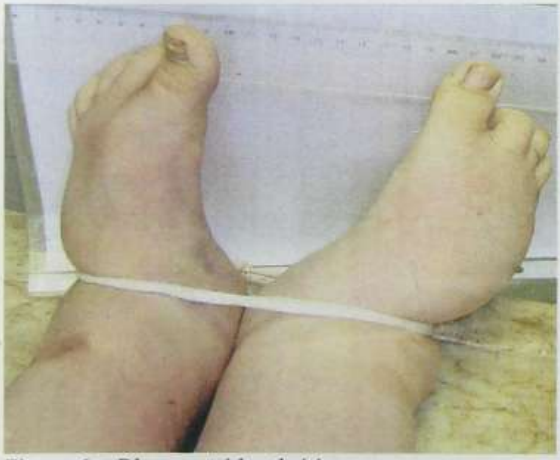

Figure 6 – Rheumatoid arthritis.

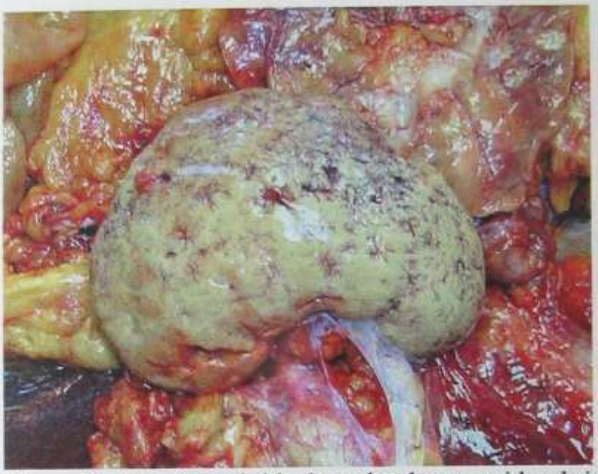

Figure 7 – Renal amyloidosis at the rheumatoid arthritis.

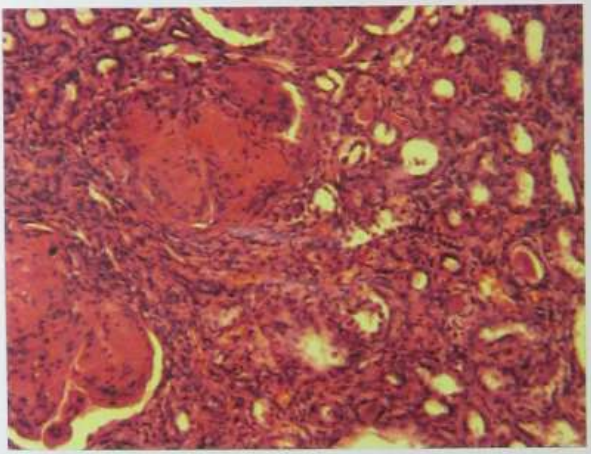

Figure 8 – Renal amyloidosis.

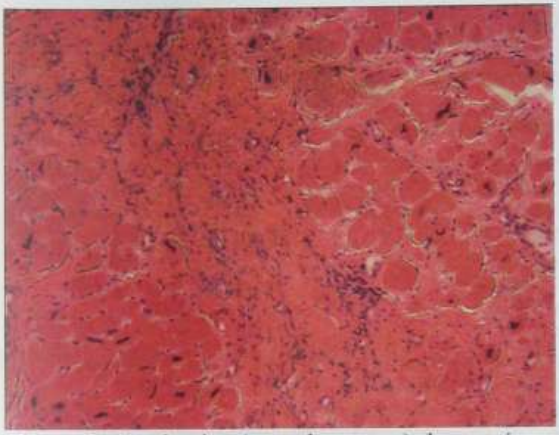

Figure 9 – Productive (granulomatous) rheumatic myocarditis.

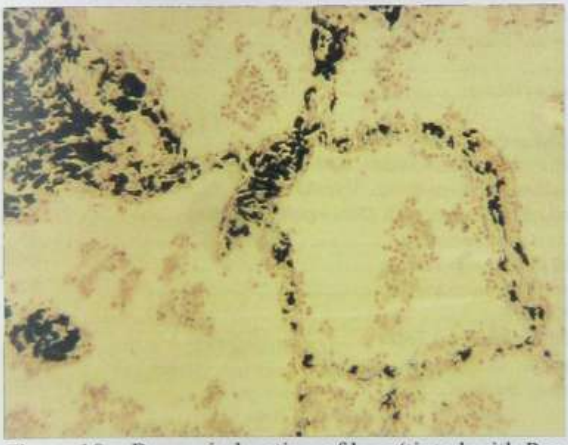

Figure 10 – Brown induration of lung(tinted with Pearls' test).

CONTENTS

Content module 5

Навчальне видання

Романюк Анатолій Миколайович,
Карпенко Людмила Іванівна

Короткий курс системної патоморфології

Навчальний посібник для іноземних студентів III курсу
Медичного інституту
У чотирьох частинах
ЧАСТИНА 3

едактор Н.О.Кравченко
омп'ютерне верстання А.А.Качанової

ід. до друку 02.07.2007.
ормат 60x84/16.Папір офс. Гарнітура Times New Roman Cyr. Друк. офс.
м. друк. арк.6,51. Обл. - вид. арк.5,28.
ираж 75 пр.
ам. №750.

идавництво СумДУ при Сумському державному університеті
0007, м. Суми, вул. Р.- Корсакова, 2
відоцтво про внесення суб'єкта видавничої справи до Державного реєстру
К № 2365 від 08.12.2005.
адруковано у друкарні СумДУ
0007, м. Суми, вул. Р.- Корсакова, 2.