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DEPARTMENT OF PATHOLOGICAL ANATOMY
MEDICAL FACULTY

Textbook of Techniques

To Study of General Pathological Anatomy

Part 1

General edition by Professor O.D. Mishnev

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Steps of sample description

Some samples must be prepared (or crayoned).

1 Sample identification
2 Stain
3 Microscopic or Gross picture
4 The name of process or disease in the sample
5 Define the process (or disease) shown in the given sample
6 Name the classifications
7 Name the stages of the process (or the disease)
8 Etiology (causes)
9 Specify general stages of the pathogenesis (or morphogenesis)
10 Outcome (or results)
11 Consequences (or complications)
12 Specify the diseases which can contain this pathologic process or specify the pathological processes manifested in this disease.

Abbreviations:
des-design; **H & E-** hematoxilin and eosin

Unit 1: HEMODYNAMIC DISORDERS (Hyperemia, stasis, hemorrhage, edema)

Hyperemia is blood volume increase within the organ

There are arterial & venous Hyperemia, General & local, Acute & chronic

Classification of local arterial hyperemia: a) inflammatory; b) postischemic; c) vocational (syn. Decompression); d) angionevrotic; e) collateral; g) with arteriovenous fistula. Chronic venous hyperemia as venous congestion is one of the most important part in the clinical picture. It occurs systematically in nutmeg liver, the kidney & the spleen or the lungs. It occurs locally in nutmeg liver. *Pathogenesis:* the right- sided heart failure (or congestive right heart failure) leads to chronic passive congestion with nutmeg liver, cyanotic induration of the kidneys, cyanotic induration of the spleen (syn. congestive splenomegaly). Congestion of capillary beds is closely related to the development of edema, so congestion & edema are common to occur together.

Hemorrhage is blood outcome from the vessel or the heart.

There are three mechanisms of bleeding: 1 **per rhexin**- with rupture of the vessel; 2 **per diapedesin**- with hyperpermobility of the small vessels (capillaries, arterioles, venules); 3 **per diabrosin-** with erosion (corrosive) of the vascular wall (pus, enzymes of the tumor, gastric juice).

Classification of hemorrhage: 1) According to the vessel & heart: 1 venous, 2 arterial, 3capillaries, 4 parenchymal, 5 flow from cardiac chambers.

2) According to the site: 1 external, 2 internal: a) into the organ; b) into the body cavity.

1definition: external hemorrhage is the blood outflow to environment.

EXTERNAL hemorrhage: 1 nasal hemorrhage – **epistaxis**; 2 blood vomiting - **hematemesis;** 3 irregular bleeding between the periods – **metrorrhagia**;
4 the presence of blood in the urine – **hematuria;**

5 tarry stool as a sign of bleeding in the gastrointestinal tract- **melena**; 6 the presence of blood in the phlegm- **hemapthoe.**
INTERNAL hemorrhages within the organs are 1 hemorrhagic infiltration;
2 hematoma; 3 petechii; 4 ecchymosi (see abridged dictionary of medical terms).
The types of the internal hemorrhage into the body cavities are: 1 hemothorax;
2 hemopericardium; 3 hemoperitoneum; 4 hemarthrosis.
Hemorrhagic diathesis is an increased tendency to hemorrhage within lots of organs.

Microsamples:
1 Nutmeg liver (chronic venous hyperemia in the liver) H & E ***design***
2 Brown induration of the lung H & E; Pearls stain
3 Hemorrhagic infiltration within the brain H & E ***des***
4 Intravascular microcirculatory blood Stasis within the brain H & E ***des***
5 Collateral hyperemia of esophageal veins H & E

Macrosamples:
1 Nutmeg liver
2 Brown induration of the lung
3 Collateral hyperemia of esophageal veins
4 Inflammatory hyperemia of the appendix
5 Cyanotic induration of the kidney
6 Hematoma within the brain
7 Chronic ulcer of the stomach

1 №8 NUTMEG LIVER H & E **des**
Microscopically: the central vein and the vascular sinusoids of the centrilobular regions of the liver are distended with blood. The central hepatocytes become atrophic secondary to chronic hypoxia. The peripheral hepatocytes suffer due to less severe hypoxia, fatty changes develop.
Grossly: The central regions of the hepatic lobule become red-blue, surrounded by a zone of uncongested liver substance descriptively referred to as nutmeg liver.
The liver is some what enlarged, firm with smooth surface.
The nutmeg liver is a chronic venous hyperemia (passive congestion) in the liver.
Definition: a chronic venous hyperemia (passive congestion) is the increase of venous blood volume within the organ resulting from impaired venous return from a tissue.
Etiology: for nutmeg liver, it is right-sided heart failure, less common in the obstruction of the inferior vena cava; for nutmeg liver there is also obstruction of the hepatic vein with Chiari-Budd syndrome.
Morphogenesis: passive venous congestion – atrophy of hepatocytes- sclerosis- portal (nutmeg) cirrhosis of the liver.
Result of chronic venous hyperemia (chronic passive congestion) of the liver is in portal (nutmeg) cirrhosis of the liver.
Diseases: 1 chronic lung diseases (pneumosclerosis, chronic bronchitis, emphysema);
2 congenital heart diseases; 3 heart valvular diseases (mitral stenosis and insufficiency);
3 cardiomyopathy; 4 postinfarction cardiosclerosis.

Clinical signs: Chronic passive congestion is the passive hyperemia in affected parts of vein as venous blood flow is impaired. An increase of deoxygenated hemoglobin in blood increases with cyanosis as the blue tint with hypoxia of surrounding tissues is noted. Physician palpates the soft, firm liver.

2 №21 BROWN INDURATION OF THE LUNG H & E; Pearls' stain. **des**

Microscopically: The pulmonary alveolar capillaries are congested (chronic venous hyperemia). With persistent elevation of pulmonary venous pressure, the capillaries may become tortuous and rupture to produce in small hemorrhage into alveolar spaces. Alveolar macrophages phagocytosis of red blood cells is noted and eventually becomes filled with hemosiderin. Persistence of septal edema induces fibrosis within the alveolar walls.

Hemosiderin contains iron revealed by Pearls' stain.

Grossly: The lungs become dark brown firm and short air is noted.

Classifications: see above

Etiology: Left-sided heart failure.

Diseases: 1 heart valvular diseases (mitral stenosis, insufficiency); 2 cardiomyopathy; 3 postinfarction cardiosclerosis; 4 arterial hypertension.

Pathogenesis of chronic venous hyperemia or chronic passive congestion within the lungs: It occurs as hyperemia of the lung which capillary bed between alveoli with diapedesis of erythrocytes within alveolar spaces. Erythrocytes are destructed with formation of hemosiderin (hemoglobinogenic pigment), accumulated into siderophages. Chronic hypoxia, mechanical and resorption lymph insufficiency and sclerogenic affect of SH-ferritin composed hemosiderin lead to diffuse sclerosis of the lung.

Results are in progressive hemosiderosis and pneumosclerosis

Clinical signs: 1rusty sputum; 2 shortness of breath.

3 №16A HEMORRHAGIC INFILTRATION WITHIN THE BRAIN H&E **des**

Microscopically: Blood saturates within the cerebral tissue without its destruction. This type of the intraorganic hemorrhage is named hemorrhagic infiltration.

Grossly: Another type of the intraorganic hemorrhage is referred to as hematoma. Hematoma is the cavity filled with Blood with drawn from the cerebral tissue.

Definition: hemorrhagic infiltration is the blood saturation of the tissue.

The mechanisms of their formation is rupture of the vessels (Latin term is ***per rhexin***)

Diseases: Essential and symptomatic Arterial hypertension; Atherosclerosis; Aneurisms; Tumor; Leukemia; Trauma; Sepsis; Rheumatism; DIC-syndrome; Typhus fever

Result of hemorrhage into the brain may be a cyst.

Clinical signs: neuralgic symptoms or death of the patient many occur.

4 № 9 INTRAVASCULAR MICROCIRCULATORY BLOOD STASIS WITHIN THE BRAIN H & E ***des***

Microscopically: erythrocytes slug & adhesion into vascular lumen is noted.

Definition: stasis is the cessation of the natural blood stream in a living organism

Pathogenesis: blood stasis is characterized by location slowing the circulation with

increasing permeability of the microvasculature walls and the concentration of red cells in small vessels with increased viscosity of the blood and dilated small vessels.
Stages: prestasis; stasis; poststasis.
Results: 1 the restoration of the blood stream into small vessels; 2 thromboses: 3 diapedesis.
Clinical signs: a pain of the organ.

5 № 10 COLLATERAL HYPEREMIA OF ESOPHAGUS VIENS H & E

Microscopically: The veins of the submucous membrane of the esophagus are enlarged thinned with blood esophageal varices.
Grossly: There are esophageal varices showing dilated submucosal veins.
Definition: This is collateral local venous hyperemia as an adaptive compensatory process, when the general vessel is obstructive.
Pathogenesis: Increased resistance to portal blood flow is named portal hypertension. With the rise in portal system pressure, bypasses develop wherever the systemic and portal circulations share capillary beds.
There are three collateral anastomoses (or portosystemic shunts): 1 esophageal; 2 abdominal; 3 rectal.
Abdominal wall collaterals appear as dilated subcutaneous veins extending from the umbilicus toward the rib margins are the so- called Medusa's head (caput medusae).
Diseases are hepatic cirrhosis or portal vein thrombosis.
Result for esophageal varices may be in external massive hemorrhage after variceal rupture.
Clinical signs: hematemesis, melena.

Inflammatory hyperemia of the appendix

Grossly: the inflamed appendix is red, swollen. This is a manifestation of the local arterial hyperemia.

Cyanotic induration of the kidney

Grossly: the kidney is somewhat enlarged, solid and cyanotic. This is a manifestation of the general chronic venous hyperemia.

Hemorrhage into the brain as hematoma

Grossly: there is a cavity filled with clotted blood enclosed within a cerebral tissue.

Chronic ulcer of the stomach

Grossly: The peptic ulcer of the stomach has a vessel in its base.
Vascular lumen is closed by thrombus. This is the sign of former external hemorrhage named melena with erosion fallow of the vascular wall by gastric juice.
Mechanisms are the so- called *per diabrosin*.

Unit 2 HEMODYNAMIC DISORDERS (Thrombosis; embolism)

Thrombosis is blood clotting within the vascular system or the cardiac chambers of a living organism. Thrombus is the product of thrombosis.

Classifications

1.1 red or stasis thrombus (venous thrombosis or phlebothrombosis);
1.2 gray-white thrombus (arterial thrombosis);
1.3 mixed thrombus (aortic or cardiac chamber thrombosis);
1.4 hyaline thrombus (microcirculatory thrombosis).
2.1 mural thrombus (aorta, vessels, cardiac chamber); 2.2 occlusive thrombus (vessels).

1 The thrombus may be obstructive into the artery and the cause of infarction in the organs, into the vein –it may be the cause of edema and ulcer.

2The thrombus into deep veins of low extremity may be embolising in pulmonary artery causing death.

The thrombus into the aorta or the heart may be embolising in artery system of lots of organs.

Etiology: Virchov's triad as local causes: 1) destruction of integrity of the vascular wall (endothelial injury); 2) impairment; 3) disturbance of blood flow.

The systemic (generalized) factors: 1 imbalance between coagulation and anticoagulation systems; 2 increase of viscosity and amount of regular blood elements.

Pathogenesis: stages of thrombus formation:

1Agglutination of the thrombocytes (platelets); 2 coagulation of fibrinogen; 3 agglutination of the erythrocytes; 4 precipitations of the plasma proteins.

Results of thrombus are in:

1 organization; 2 canalization; 3 calcification (phleboliths); 4 septic dissolution; 5 embolisms; 6 aseptic dissolution.

Diseases: 1 Atherosclerosis; 2 Vasculitis; 3 Malignant tumors; 4 Vegetation of the valves; 5 Nonbacterial endocarditis; 6 DIC-syndrome; 7 Traumas.

Embolism is the circulation with blood or lymph stream of abnormal masses (emboli) to occur in any site within the cardiovascular system.

Classification

1 the volume of emboli: 1 single; 2 multiple; 3 repeated.

2 according to the type of embolus: 1 thromboembolism; 2 fatty; 3 bubble of air; 4 nitrogen; 5tissue embolism; 6 foreign bodies; 7 microbial (bacterial).

3 according to movement of emboli with blood flow: 1 direct embolism; 2 retrograde, (backward); 3 paradoxical embolism.

Microsamples:

1 Mixed thrombus with the start of organization ***des***
2 Fatty embolisms of the lung **des**
3 Metastatic abscesses in the kidney **des**
4 Tissue embolisms (cancerous cells) in the lung

Macrosamples

1 Atherosclerosis of the aorta. Mural thrombus in the aorta.
2 Ball -valve thrombus in the left atrium.
3 Verrucae endocarditis in the mitral valve.
4 Postmortem fibril rolls
5 Thromboembolism in the pulmanal artery
6 Abscesses in the liver
7 Carcinoma metastasis in the liver

1 № 26 MIXED THROMBUS WITH THE START OF OPRGANISATION H & E **des.**

Microscopically: the thrombus contains fibrin, red cells, platelets, leukocytes and precipitation proteins. It is attached to a vascular wall where the connective tissue grows into thrombus.

Grossly the thrombus consists of head, body, and tail.

It is characterized by firm adherent, gray-white and red stripes, also friable.

The diseases: see above.

Clinical correlations: Thrombosis may be as complication of a lot of diseases.

1The thrombus may be obstructive into artery and be the cause of infarction and gangrene of the organs; in case of the vein it may cause hemorrhage, edema, and trophic ulcer.

2 The thrombus into deep veins of the leg may be embolising in the pulmonary artery causing death.

3 The thrombus into the aorta or the heart may be embolising in arterial system of many organs.

4 The favorable outcome: organization of the thrombus when thrombus consolidation on the wall and decreases thromboembolism development.

5 The favorable outcome: canalization gives the partial resumption of blood stream.

2 № 30 FATTY EMBOLISMS OF THE LUNGS stain Sudan 111 **des**

Microscopically: there are a lot of drops of lipids into the capillary lumen between alveoli.

Definition: Fatty embolism is the circulation with blood or lymph stream of fatty masses (emboli) which may occur anywhere within the cardiovascular system.

Etiology: 1 trauma (fracture of the tubular [cylindrical] bone; 2 crushing of the subcutaneous fat; 3 mistaken oil injection to bleeding.

Pathogenesis: the hemodynamic disturbances with pneumonia to occur; death may be rare.

when 2/3 capillaries of the lung are obturated by fatty drops with acute heart right-sided failure or death may occur when fatty drops obturate small vessels of the brain.

Results are in block of blood stream or emulation of the fat.

Clinical signs: 1shortness of breath; 2 cyanosis.

3 № 91 METASTATIC ABSCESSES IN THE KIDNEY H *&* E ***des***.
Microscopically
There are a lot of microbial emboli into the lumen of multiple small vessels of the kidney. Leukocyte infiltration surrounds microbial emboli with dissolution of the tissue is named abscess.
Grossly
There are multiple small green- yellow purulent foci on the cut and the surface of the kidney
Definition
Embolism is the circulation with blood or lymph stream of abnormal mass (emboli) to occur anywhere with blood within the cardiovascular system.
Metastasis shows the development of secondary purulent foci discontinued with the primary purulent focus.
Etiology: Bacterial colony, fungus.
Pathogenesis: the primary focus may be anywhere, from purulent thrombophlebitis microbial emboli in the small vessels of the lung and then other organs: the kidney; the heart; the brain; the spleen; the liver.
Result is in multiple purulent metastases as abscesses.
Diseases: 1 sepsis; 2 appostematous nephritis; 3 bacterial endocarditis; 4 acute pyelonephritis (as hematogenic pathway).
Clinical correlations: 1 acute renal failure; 2 pyuria; 3 high temperature
4 low back pains; 5 disuria.

4 № 89 TISSUE EMBOLISMS (CANCEROUS CELLS) WITHIN THE LUNG H & E
Microscopically: There is a complex of malignant tumor cells into the vessels lumen of the pulmonally parenchyma.
Grossly: There are multiple solid round white nodules within the lung.
Definition: this is tissue embolism with its outcome in metastases of the malignant cells. Metastasis shows the development of secondary implants (metastases) discontinued in the primary tumor, possibly in distant tissues.
Classification and *Etiology:* tissue embolism includes a) embolism with malignant cells; b) embolism with amniotic fluid; c) embolism with segments of the traumatic tissues.
Pathogenesis: ***theory of metastatic cascade*** (see tumor): 1 malignant tumor cells penetrate deep into surrounding tissue; 2 they penetrate into the blood and lymph vascular lumen; 3 single cell or individual cells are separated within blood or lymph stream; 4 they keep tissue viability; 5 they migrate into venules and lymph vessels; 6 they register with vascular endothelium of the organs; 7 they realize the invasion of microvessels and can Grow within new sites and new company.
Result is in multiple metastases of malignant tumor.
Diseases: malignant tumors.
Clinical correlations: Generalization of the malignant tumor process.

Ball -valve thrombus in the left atrium.
Ball –like thrombus is formed from thrombus pieces of the mitral valve leaflet lost in contact with a leaflet thrombus and is polished by blood stream.

Verrucae endocarditis in the mitral valve.
Small verrucous vegetations are visible along the line of closure of the mitral valve leaflets, with previous small thrombus.
Postmortem fibril rolls
They are soft, smooth, elastic and they must be differentiated with thrombus.
Thromboembolism in the pulmonary artery
Small and large emboli show medium-size and small pulmonary arteries.
Abscesses in the liver
Pyogenic (bacterial) hepatic abscesses may occur as solitary or multiple lesions, ranging from millimeters to massive lesion of many centimeters in diameter. Occasionally, fungi or parasites can be identified.
Carcinoma metastases in the liver
There are a lot of small and large firm and soft locations as nodes of gray-white and white yellow color.

Unit 3 NECROSIS. INFARCTION.

Definition: ***Necrosis is one of the morphological patterns of death: the death of cells or tissue parts or organ parts in a living organism.*** There are two patterns of death in the living organism: a) necrosis; b) apoptosis.
Classification is according to etiology: 1 Hypoxia; 2 Physical agents; 3 chemical agents and drugs; 4 Infectious agents; 5 genetic injury; 6 malnutrition.
Classification is according to pathogenesis: 1 direct action; 2 indirect action.
Clinic pathologic forms: 1 coagulation necrosis; 2 liquefactive necrosis; 3 gangrenous necrosis; 4 infarct; 5 sequester; 6 fatty necrosis.
Classification: there are two types of necrosis according to denaturation of proteins and enzyme digestion: 1 coagulation is necrosis with a predominance of proteins. Its variety is named caseous necrosis; 2 liquefactive one is necrosis with a predominance of enzymes and water.
Classification of gangrenous necrosis: 1 dry 2 wet gangrene. Wet gangrene is associated with microorganisms.
Classification of wet gangrene: 1 bedsore (syn. Decubitus) is the type of wet gangrenous necrosis of the skin and soft tissues exposed to long term pressure; 2 noma is the type of wet gangrenous necrosis of cheeks or the perineum developed in debilitated children.
Results of necrosis: 1 restitution; 2 scar; 3 cyst formation; 4 myolysis; 5 rupture; 6 petrifaction; 7 ossification; 8 encapsulation; 9 fistula formation.
Microsamples:
1 Necrosis of the splenic lymphatic follicles (changes of the nuclei) ***des.***
2 Necrosis of the skeletal muscles with petrifaction ***des.***
3 Ischemic infarction of the kidney ***des***
4 Hemorrhagic infarction of the lung
Macrosamples:
1 Caseous necrosis (tuberculosis of the kidney, dorsal vertebras).
2 Infarctions of the kidney or the spleen.
3 Postinfarction Scars of the myocardium.

4 Brown induration of the lung with red infarction
5 Gangrene of the foot, the intestine & other organs (appendix, lung)
6 Osteomyelitis (chronic suppurative process).

1 № 1 NECROSIS OF THE SPLENIC LYMPHATIC FOLLICLES (CHANGES OF THE NUCLEI) H & E ***des.***
Microscopically: the nuclei of the lymphocytes into the lymphatic follicles reveal changes: a) karyopycknosis, b) karyorrhexis, c) karyolysis. The cytoplasm of the cells exhibits changes: a) plasmorrhexis, b) plasmolysis, c) precipitation of proteins. The changes are ***necrosis or irreversible injures of the cell.***
Grossly: the spleen is enlarged with smooth capsule, rotten cherry-like one on the cut.
Karyopycknosis is a kind of necrosis characterized by nucleus shrinkage and densification.
Karyorrhexis is a kind of necrosis characterized by nucleus fragmentation.
Karyolysis is a kind of necrosis characterized by nucleus fading away and dissolving.
Pathogenesis: 1 ischemia with oxygen absence and formation of free radicals caused by lipids peroxydation; 2 Calcium imbalance; 3 ATP exhaustion; 4 loss of selective permeability of membranes.
The signs of necrosis or irreversible injures of the cell are changes of the mitochondria, loss of ATP, destruction of membrane.
Diseases: Typhus fever;
Outcome: atrophy of the lymphatic follicles and sclerosis or regeneration.
Clinical sign: decrease of splenic functions.

2 №7 NECROSIS OF THE SKELETAL MUSCLES WITH PETRIFICATION H & E ***des.***
Microscopically: This is coagulation necrosis of the skeletal muscles without nuclei, without banding striatura of bright pink color and deposition of calcium salt.
Grossly: The skeletal muscle is solid of yellow color, waxy like, the so-called Zenker's necrosis.
The definition: coagulation necrosis is necrosis of the tissue in which denatured proteins are richer than enzymes and water.
Cause: right toxin actions.
Diseases: Typhus fever; typhoid fever; toxic dysentery; toxic diphtheria.
Pathogenesis: proteins and enzymes are denatured by the cellular injury and intracellular acidosis.
Results: organization with scarring, formation petrification.
Clinical signs: pains; loss of muscular contractility.

3 №5 INFARCT AS ISCHEMIC NECROSIS OF THE KIDNEY H&E ***des.***
Microscopically: Infarct of the kidney exhibits coagulation necrosis with loss of nuclei and clump of the cytoplasm but with preservation of basic outlines of glomerular and tubular architecture. Then Demarcate inflammation; Hyperemia of the vessels with hemorrhage and Normal tissue architecture can be seen.

Grossly: White -yellow color with red border; solid and cone-shaped. Its basis is on the surface under a capsule and apex is directed to hilus.
The definition: An infarct is an area of ischemic necrosis within a tissue or an organ, produced by the occlusion of its arterial supply or its venous drainage.
Classification: 1hemorrhagic (or red) infarct; 2 ischemic (or white); 3 ischemic infarct with hemorrhagic border.
Causes: 1 stenotic atherosclerosis of the artery; 2 thrombus; 3 embolus; 4 prolonged spasm of the artery.
Stages of pathogenesis: 1 ischemia; 2 necrosis; 3 organization as formation of a scar.
Results: 1 scar; 2 abscess.
Factors to influence development of an Infarct: 1 nature of vascular supply; 2 rate of development of occlusion; 3 vulnerability to hypoxia; 4 oxygen contents of blood.
Diseases: 1 myocardial infarction as ischemic heart disease; 2 complications of atherosclerosis; 3 cerebral infarction.
Clinical signs: 1 pain in the lower back; 2 proteinuria; 3 hematuria.

4 № 33 HEMORRHAGIC INFARCTION OF THE LUNG H&E.

Microscopically: it is ischemic coagulative necrosis of the lung parenchyma in the area of hemorrhage,
Grossly: Infarct appears as elevated, solid and red blue area. It has a triangular form with the apex pointing toward the hilus of the lung. In many cases an occluded vessel can be identified near the apex of the infarct. Base is on the pleural surface.
The adjacent pleural surface is often covered with a fibrinous exudate.
Definition: Hemorrhagic (or red) infarct is accompanied 1 by venous occlusions, 2 loose tissues, 3 double circulation tissues and 4 previously congested tissues.
Classification: red infarct can occur in the lung, intestine, liver, brain.
Causes: The 95% amount of all red infarct of the lung is caused by thromboembolism of the pulmonary arteries. Marantic thrombosis of the pulmonary artery.
Pathogenesis: a) an increase in pulmonary artery pressure due to blockade of flow and vasospasm caused by neurogenic mechanisms and release of mediators; b) ischemia of the downward stream of pulmonary parenchyma.
Results are in: 1 scar formation; 2 peripheral pneumonia; 3 abscesses in the center.
Diseases: 1 Thrombosis within the large deep veins of the legs; 2 cancer; 3 surgery performed on the low extremities; 3 severe trauma; 4 congestive heart failure diseases.
Clinical signs: 1 chest pain; 2 dyspnea; 3 hemaptysis; 4 pleural friction rubbing.

Caseous necrosis (tuberculosis of the kidney, dorsal vertebras).
Grossly: the caseous necrosis is of yellow- white color and cheese-like.
Definition: Caseous necrosis is a distinctive form of coagulative necrosis.
“caseous” is derived from cheese- like appearance in gross study.
Diseases: tuberculosis, syphilis, Hodgkin’s disease.
*Result*s are in organization; encapsulation; petrification; ossification.

Gangrene of the foot, the intestine and other organs (appendix, lung)

Grossly: The foot is dry, thinner, of black color, or the foot is swollen, enlarged, of yellow- green.

Definition: Gangrene is a necrosis of tissues contacting with the environment factors. This is dry gangrene.

Causes: 1 stenotic atherosclerosis; 2 thromboses; 3 embolisms; 4 arteritis.

Diseases: 1 Atherosclerosis; 2 Diabetes mellitus; 3 Typhus fever.

Causes of death: Intoxication.

Osteomyelitis (chronic suppurative process).

Osteomyelitis is the inflammation of bones and bone marrow.

It develops as a complication of acute infection with residual necrotic bone referred to as the sequester.

Definition: sequester is a dead piece of tissue localized between living tissues without autolysis or organization.

Result is in sarcomas and secondary amyloidosis.

Clinic signs: fever, malaise, hyperleukocytemia, local pain, swelling, redness.

Unit № 4 CELLULAR INJURIES (PARENCHYMAL DYSTROPHY).

Definition: Parenchymal disproteinosis is the reversible injury of the cells connected with abnormality of protein metabolism.

Definition: Dystrophy is the pathologic process connected with disturbances of tissue metabolism, leading to structural disorders.

Classification ***1 parenchymal disproteinosis***: a) hydropic dystrophy; b) hyaline droplet dystrophy; c) hyperkeratosis (or horny dystrophy).

2 ***according to the sites of structural changes***: a) parenchymal dystrophy; b) stromal vascular dystrophy; c) mixed dystrophy.

3 ***according to the metabolic changes:*** a) disproteinosis; b) lipidosis; c) carbohydrates abnormality; d) mineral and pigmental abnormality.

4 according to the nature: a) acquired; b) hereditary.

5 ***according to a spread:*** a) general; b) local.

Lysosomal storage diseases caused by mutations in enzyme proteins

In Glycogenoses, enzymatic defects in the synthesis or breakdown (degradation) of glycogen result in massive stockpiling, with secondary injury and cell death.

1 Glycogen storage diseases or Glycogenoses; 2 Sphingolipoidoses is Tay-Sachs disease with accumulation of GM2 gangliosides; 3 Gaucher disease with accumulation of glucocerebrosides; 4 Sulfatidoses is Niemann- Pick disease with accumulation of sphingomyelin.

Microsamples:

1 Hydropic dystrophy of the kidney **des.**

2 Fatty dystrophy of the heart **des.**

3 Glycogen accumulation in renal tubular epithelium **des.**

4 Ichthyosis.

Macrosamples:
1“Tiger heart”: fatty change in myocardium.
2 Fatty liver (steatosis; “Goose liver”).

1 № 34 HYDROPIC DYSTROPHY OF THE KIDNEY H&E **des.**
Microscopically: small clear vacuoles may be seen within the cytoplasm;
Electron microscopically: These represent distended and pinched-off segments of the endoplasmic reticulum.
Grossly: When all cells in an organ are affected, there is pallor, with increased turgor and: weight.
Definition: Hydropic dystrophy or degeneration is a type of parenchymal disproteinosis with the cellular swelling and with fluid babbles in the cytoplasm to appear.
Etiology: a) hypoxia, b) high temperature; c) starvation; d) infectious diseases; e) exo-toxins.
Pathogenesis of the Hydropic dystrophy: cells are incapable of maintaining ionic and fluid homeostasis. K-Na pomp component of the cellular membranes is destroyed and Na ions are accumulated within cellular plasma. Accumulation of the protein within cell plasma may also occur*: 1 nephrotic syndrome appears in membrane and enzyme systems destruction with disturbance of reabsorption of the water and the protein. The mechanisms are called infiltration.*
The diseases: glomerulonephritis, nephrotic syndrome.
*Organs: **the kidney, the liver, the skin, the adrenals, nervous system, muscles.***
Outcome: 1 if the etiologic agent is not manifested, the cells return to normal state; 2 if the etiologic agent acts, there may be liquefactive necrosis as irreversible injury.
Clinical correlations: 1proteinuria; 2 polyuria; 3 hypoproteinemia;

2 № 166 FATTY DYSTROPHY OF THE HEART (stain Sudan III) **des.**
Microscopically: Lipids are found in the myocardiocytes as small droplets (focal intracellular fat deposits).
Grossly: the heart and its chambers are enlarged, myocardium is of soft consistency, its subendocardial surface shows apparent bands of yellow myocardium alternating with bands of darker, red-brown, uninvolved heart (“tiger effect”) with mild hypoxia. The process is local, involving groups of cardiomyocyties around small veins.
Diffuse yellow color of the myocardium can be seen with sever hypoxia.
Definition: Fatty change (fatty dystrophy) is a pathologic process as parenchymal lipidosis characterized by occurrence of lipid vacuoles in the cytoplasm.
It is a less universal reaction, principally encountered in cells participating in fat metabolism.
Classification: see above
Organs: the heart (tiger-skin like heart); the liver (goose liver); the kidney; the skeletal muscles.
Etiology: hypoxia (anaemia or chronic heart failure); toxins; protein malnutrition; hormonal abnormalities.
*Pathogenesis: **for the heart, first mechanisms are named decomposition:***

1. Tissue hypoxia as a result of ischemia, or inadequate oxygenation of the blood (for example in cardio respiratory failure), or loss of the oxygen-carrying capacity of the blood (for example in anaemia or carbon monoxide poisoning). The increasing of lipids within cardiomyocyties with inhibition of fatty acid oxidation and alteration of mitochondrial structure and function.
2 Microbiologic agents (infections), such as viruses, rickettsiae, bacteria, fungi, and higher forms of parasites.
3. Intoxication. Agents commonly known as poisons may cause severe damage at the cellular level by altering membrane permeability and osmotic homeostasis. Other agents are air pollutants, insecticides, carbon monoxide, asbestos, therapeutic drugs, and social "stimulus" such as ethanol.

The diseases:

Ischemic heart diseases, myocarditis, chronic obstructive lung diseases, anaemia, alcohol addiction, diphtheria.

During faucial diphtheria, the toxin acts to develop carnitin metabolism.

Outcome:

1. May be reversible with complete recovery of structure.
2. Irreversible injury (necrosis) may develop.

Clinical correlations:

The "Tiger heart" is a morphologic equivalent for decompensation of the myocardium.

3 № 54 GLYCOGEN ACCUMULATION IN RENAL TUBULAR EPITHELIUM (Best's stained by Carmine) **des.**

Microscopically: excessive intracellular deposits of glycogen are seen in the cytoplasm of tubular epithelium highlighted as red-violet globules within the cell. The glycogen accumulation is the store for glucose.

Definition

Carbohydrate dystrophy is a pathologic process as parenchymal dystrophy accompanied with chronic disorder of carbohydrates metabolism.

Glycogen accumulation is a pathologic process associated with abnormalities in the metabolism of either glucose or glycogen within the cells.

Classification

Carbohydrate parenchymal dystrophies are divided into disorders of 1) glycogen and 2) glycoproteids. Disorders of glycogen metabolism are: 1) diabetes mellitus and 2) hereditary glycogen storage diseases (Glycogenoses) or thesaurismosis.

Etiology and pathogenesis

Type 1 Diabetes mellitus results from severe, absolute lack of insulin caused by a reduction in the beta-cell mass. Mechanisms of the islet cell destruction are: genetic susceptibility, autoimmunity, and environmental insult (attack).

Type 2 Diabetes mellitus occurs due to a collection of multiple genetic defects, each contributing to its own predisposition risk and each being modified by environmental factors. Most of hypothesized defects remain unidentified. The two metabolic defects that characterize type 2 diabetes are derangement in beta-cell secretion of insulin and inability of peripheral tissues to respond to insulin (insulin resistance).

Outcome:
1. May be reversible with complete recovery of structure.
2. Intercapillarial glomerulosclerosis.
3. Tubulonecrosis (necrotizing papillitis).

Clinical correlations:
1) Glucosuria, 2) cylinderuria, 3) acute renal failure.

4 № 61 ICHTHYOS FETALIS H&E **des.**
Microscopically: The stratum of the keratin is enlarged in the skin in hyperkeratosis.
Definition: Ichthyosis is a type of Hyperkeratosis characterized by extensive lesion of the skin or lesion of all the skin. Hyperkeratosis is the pathological process with parenchymal protein dystrophy associated with a quantitive abnormality of the keratin.
Etiology: Gene disorders;
Pathogenesis: Abnormality of keratin metabolism.
Outcome: Ichthyosis is the hereditary disease of the infancy skin due to hyperkeratosis of the epidermis leading to death.

Macrosample
Fatty liver (steatosis; "Goose liver").
Grossly: the liver is enlarged, soft, yellow and greasy.
Etiology: toxins, protein malnutrition, diabetes mellitus, obesity, alcohol abuse.
*Pathogenesis**: for the liver, first mechanisms are named, associated infiltration with:***
Free fatty acids from adipose tissue or ingested food are transported into hepatocytes. Within the liver, they are converted into cholesterol or phospholipids or oxidized to ketone bodies. Lipoproteins traverse the circulation. Hepatotoxins (like alcohol) alter mitochondrial structure and function to decrease the synthesis of apoproteins. Hypoxia inhibits fatty acid oxidation and starvation increases fatty acid mobilization from peripheral stores.
Outcome: 1 Hepatitis; 2 Cirrhosis; 3 Reverse to normal structure.

Unit № 5. STROMAL DYSTROPHY. HYALINOSIS. AMYLOIDOSIS.
Definition: There is a group of stromal vascular disproteinosis with destruction of the connective tissue and deposits of abnormal proteins in the stroma.
Classification of stromal vascular dystrophy: 1 amyloidosis; 2 hyalinosis;
3 mucoid swelling; 4 fibrinoid swelling/
Definition: Amyloidosis is the pathologic process characterized by developing of amyloid - pertinacious substance deposited between cells in various tissues and organs of the body. Amyloidosis is the group of diseases, with a common sign of amyloid depositions.
Amyloidosis is a pathologic process of the stromal vascular disproteinosis.
Classifications of amyloidosis:
1. Based on chemical composition:
1.1. AL-amyloid: composed of immunoglobulin light chains (amyloid light chain) associated with multiple myeloma and other monoclonal B-cell proliferations.

1.2. AA-amyloid: made up of immunoglobulin protein absence (amyloid associated) composed by the liver.
2. Based on the associated clinical setting:
2.1. Immunocyte dyscrasias with amyloidosis;
2.2. Reactive systemic amyloidosis;
2.3. Heredofamilial amyloidosis;
2.4. Localized amyloidosis;
2.5. Senile Amyloid.
3 Based on anatomic distribution:
Major organ involvements are the following: amyloidosis of the kidney, spleen, liver, heart, endocrine organs.

Microsamples:
1 Amyloidosis of the spleen ("sago spleen"). Congo red stain **des**
2 Amyloidosis of the kidney. Congo red stain **des**
3 Hyalinosis of spleen vessels. **des**
4 Obesity (lipomatosis) of the heart. **des**
5 Mucoid swelling of the cardiac valve.

Macrosamples:
1 "Icing spleen": Hyalinosis of spleen capsule.
2 "Sago or tapioca spleen".
3 "Lardaceous spleen".
4 Amyloidosis of the kidney.
5 Brown atrophy of the heart.
6 Subcutaneous fats in obesity.

1 № 42 AMYLOIDOSIS OF THE SPLEEN ("SAGO SPLEEN"). Congo red stain **des**
Microscopically: amyloid deposits associated with capillaries end reticuloendothelial cells in the marginal zone of the lymphoid follicles are seen as amorphous pink casts. Congo-red stained amyloid shows pink or red colour of the deposits. Under polarized light the Congo red-stained amyloid shows green birefringence. This reaction is shared by all forms of amyloid and is due to the crossed beta-pleated configuration of amyloid fibres.
Grossly: amyloidosis of the spleen often causes moderate or even marked enlargement. Amyloid deposits virtually limited to the splenic follicles produce tapioca-like granules on gross examination ("sago spleen"). The spleen appears firm in consistency and reveals pale, grey, waxy deposits on the cut surface.
One more gross type of spleen amyloidosis is named "lardaceous spleen" when amyloid deposits maybe seen within the splenic sinuses and all splenic pulps.
Etiology: several aspects of amyloid origins are still not clear.
Pathogenesis: Systemic amyloidosis (generalized) may be primarily connected with Immunocyte dyscrasias or secondary as the complication of chronic inflammations or destructive process of the tissue. Heredofamilial amyloidosis forms a separate heterogenic group of the diseases.

Diseases: Amyloidosis.
Clinical signs: Splenomegaly may be rare. Biopsy followed by Congo red staining is the most important tool in the diagnosis of amyloidosis.

2 № 44 AMYLOIDOSIS OF THE KIDNEY. Congo red stain. **des**.
Microscopically: The amyloid deposits are found principally in the **glomeruli**, but they are also present in the **interstitial peritubular tissue** as well as in the walls of the blood vessels. The glomeruli are the first to develop focal deposits within the mesangial matrix and with diffuse or nodular thickenings of the basement membranes of the capillary loops to occur on progression, the deposition encroaches on the capillary lumina and eventually leads to total obliteration of the vascular tuft. The interstitial peritubular deposits are frequently associated with the appearance of amorphous pink casts within the tubular lumina. Amyloid deposition may be found on **tubular membranes.** Amyloid deposits may develop **in the walls of blood vessels** of all sizes, often causing marked vascular narrowing.
Grossly: the kidney appears unchanged, or it be abnormally large, pale, grey, and firm. In severe cases the kidney may be reduced in size. The kidneys are named **big, white waxy kidneys**.
Definition and classification see above.
Diseases: **secondary amyloidosis as complication of bronchiectatic disease; tuberculosis of lung and bones; pyogenic Osteomyelitis; rheumatic diseases.**
Outcome: Nephrosclerosis (secondary shrinkage or contracted kidney).
Clinical appearance: chronic renal failure (uraemia).
Cause of death uraemia

3 № 38 HYALINOSIS OF SPLEEN VESSELS H & E **des**
Microscopically: pink colour substance within vascular wall with narrowing of its lumen.
Grossly: The vascular wall is thick, white and solid with narrowing of the lumen.
The splenic capsule may be thick, white and solid and the spleen with hyalinosis of its capsule is the so-called “icing” or “glassy” spleen.
Definition: Hyalinosis is the stromal vascular disproteinosis with the extracellular deposits of a homogenous, glassy, pink appearance like hyaline cartilage.
Etiology: Collagenous fibres may appear hyalinized but etiology is not clear;
High permeability of the vascular wall with extravasations of plasma protein (plasmorrhagia).
Pathogenesis: Arterial hypertension and diabetes mellitus are characterized by Hyalinosis of walls of the small arteries and arterioles with plasmorrhagia and deposits of proteins in the wall.
Diseases: 1 diabetic micro- and macro- angiopathy; 2 arterial hypertension;
3 rheumatic diseases; 4 heart valve diseases; 4 senile involution of the organs.
Outcome: sclerosis, mucus production, lysis by macrophages, lipidosis.
Clinical appearance: chronic decrease of blood stream with atrophy of the organs.

4 № 45 OBESITY (LIPOMATOSIS) OF THE HEART H & E **des**
Microscopically: Fatty cells (lipocytes) can be seen within the cordial stroma with myocardiocytes atrophy.
Grossly: The heart is enlarged with fat infiltration and atrophy of the myocardium.
Definition: Fatty stromal dystrophy (or degeneration) is characterized by increase or decrease of the fatty components stores.
Classification: 1obesity; 2 fatty atrophy.
Etiology for obesity: 1 genetic agents; 2 environmental; 3 psychologic factors.
Pathogenesis: Leptin occurs in the blood. Hypothalamus contains leptin receptor. Hypothalamus produces neuropeptides. Neuropeptides act on receptors. Together with thyroid adrenal and with adrenergic nerves they regulate energy glow and food intake with regulation of fatty stores.
Diseases: 1 endocrinal diseases; 2 cerebral diseases; 3 diets.
Outcome: cardiac decompensation; (heart failure, cardiac insufficiency)
Clinical appearance: decrease of cardiac output.

5 № 36 MUCOID SWELLING OF THE CARDIAC VALVE. Toluidin blue stain.
Microscopically: The focus of the mucoid swelling is coloured by Toluidin blue with violet-pink colour is revealed. The phenomenon is named metachromasia.
Grossly: we can not see mucoid swelling with naked eye.
Definition: Mucoid swelling is the type of stromal-vascular disproteinosis, characterized by surface and reversible disorganization of the connective tissue and increase of permeability of vessels and tissues.
Classification: can see above stromal-vascular disproteinosis.
Etiology: the immune mediated injury (hypersensitivity reaction)
Pathogenesis: The host response to streptococcus infectious agent is antibody specific, that antibodies can cross-react with self antigens (as anticardiac antibodies) with damage to the connective tissue.
Diseases: Rheumatic heart disease.
Outcome: 1 returns to normal structure; 2 fibrinoid swelling and fibrinoid necrosis occur.
Clinical appearance: valve prolapsus.

Unit 6. DISORDERS OF PIGMENTS (CHROMOPROTEIDS) AND MINERALS. PATHOLOGIC CALCIFICATION**.** FORMATION OF STONES.

Definition: PIGMENTS are coloured substances.
Classification of pigments: 1 exogenous; 2 endogenous.
Endogenous pigments: 1 haemoglobin-derived pigments; 2 lipidogenic pigment (lipofuscin); 3 tyrosinogenic pigment (melanin)
There are normal haemoglobin-derived pigments: 1 hemosiderin; 2 bilirubin; 3 ferritin.
There are abnormal haemoglobin-derived pigments: 1 hematoidin; 2 hemomelanin; 3 hematin.
Hemosiderosis is a condition, characterized by hemosiderin deposition in many organs and tissues in systemic overload of iron.

Hemosiderin is a haemoglobin-derived granular pigment that is brown and accumulated in tissues (cells), with a local or systemic excess of iron.
Classification:
1.1 .Systemic Hemosiderosis (in diseases, accompanied by intravascular haemolysis),
1.2 . Local Hemosiderosis (accompanied by haemorrhages).
2.1. Primary Hemosiderosis (Idiopathic pulmonary hemosiderosis),
2.2 Secondary Hemosiderosis (Congestion-associated hemosiderosis).
Etiology
Increased contents of ferritin in blood and tissues caused by intravascular and extra vascular haemolysis.
Pathogenesis
Local excess of iron, and consequently hemosiderin, results from gross hemorrhage or myriad minute hemorrhages accompanying severe vascular congestion. After lysis of the erythrocytes at the site of hemorrhage, the red cell debris parts are phagocytosed by macrophages; the haemoglobin content is then catabolized by lysosomes with accumulation of the heme iron in hemosiderin. The same process is seen in the ordinary bruise. The array of colours through which the bruise passes reflects these transformations. The original red-blue colour of haemoglobin is transformed to various shades of green-blue by the local formation of biliverdin (green bile) and bilirubin (red bile) from the heme moiety; the iron ions of haemoglobin are accumulated as golden-yellow hemosiderin.
Abnormality of melanin metabolism may increase or look decrease this pigment.
Classification: 1.1 Hereditary and 1.2 Acquired; 2.1 local and 2.2 generalised; 3.1 hyper pigmentation and 3.2 hypo pigmentation.
Hyper pigmentation: pigmental Xeroderma, Addison's disease, melanodermia, lentigo, Pigmented nevus. Hypo pigmentation: Albinism, vitiligo.
PATHOLOGIC CALCIFICATION.
Definition: Pathologic calcification is referred to as abnormal precipitation of calcium salts.
Classification: There are dystrophic and metastatic calcifications.

Microsamples:
1 № 21 Brown induration of lung as Hemosiderosis of lung (Prussian blue histochemical reaction Pearl' stain) **des.**
2 № 60 Hemosiderosis of the liver (1. Prussian blue histochemical reaction Pearl's stain. H & E) **des.**
3 № 67 Liver in mechanical jaundice **des**.
4 № 63 Pigmented nevus.
5 № 7 Skeletal muscle necrosis with calcification.
6 № 155 Metastatic calcification of the lung **des.**
7 № 29 Gouty tophus.

Macrosamples:
1 Kidney in mechanical jaundice.
2 Brown induration of lungs.
3 Brown atrophy of the heart.

4 Rachitic bones.
5 Gallstones (Cholelithiasis).
6 Renal stones (Urolithiasis).
7 Pigmented liver in Malaria.
8 Cavitated intracerebral hemorrhage.

№ 21 BROUN INDURATION OF THE LUNG AS HEMOSIDEROSIS OF THE LUNG (Prussian blue histochemical reaction Pearl' stain) **des.**
Microscopically: Alveolar capillaries engorged with blood. Alveolar septal edema is also present, as well as focal minute intra-alveolar and septal hemorrhage. The septa are thickened and fibrotic, alveolar spaces contain multiple hemosiderin-laden macrophages ("heart failure cells" into the sputum), brown coloured with HE-staining. Hemosiderin is also accumulated in stroma, lymph vessels and nodes. As hemosiderin contains iron it can be unambiguously identified with the Prussian blue histochemical reaction (blue coloured) named Pearl's stain.
Grossly: the lungs are enlarged and dense, brown coloured (Brown induration of lungs).
The diseases:
Ischemic heart disease, myocarditis and chronic obstructive pulmonary diseases accompanied by chronic heart failure; hemolytic anemias, transfusions; hemochromatosis; pulmonary hypertension and vascular sclerosis (in left-to-right shunts, mitral stenosis; scleroderma and other connective tissue diseases, vasculitis; pneumoconiosis; recurrent thromboembolism); diffuse pulmonary hemorrhage syndromes (Goodpasture's syndrome, idiopathic pulmonary hemosiderosis, vasculitis-associated hemorrhage).
Outcome:
Diffuse interstitial fibrosis; pneumosclerosis.
Clinical correlations:
Diffuse interstitial fibrosis complicated lungs hemosiderosis is a morphologic basis for chronic lung or lung-heart failure. There is a gradual increase of respiratory symptoms observed in hemosiderosis of lungs: shortness of breath, cough, or vague substernal discomfort; dyspnoea, haemoptysis. The "heart failure cells" are often revealed in phlegm.

2 № 60 HEMOSIDEROSIS OF THE LIVER (1. Prussian blue histochemical reaction Pearl's stain. 2. H & E). **des**.
Microscopically: Iron becomes evident as golden-yellow and brown hemosiderin granules in the cytoplasm of periportal hepatocytes. Hemosiderin contains iron. It can be unambiguously identified with the Prussian blue histochemical reaction (blue coloured) named Pearl's stain. There is some progressive involvement of the rest of the lobule, along with
bile duct epithelium and Kupffer cell pigmentation.
Grossly: The liver is enlarged, dense and brown.
Definition: see above
Classification: this is general hemosiderosis or it may be hemochromatosis (primary and secondary)
Etiology: hemosiderosis: intravascular haemolysis (blood diseases, poisoning, infectious diseases, transfusion of incompatible blood, or increase of food iron intake)

Primary hemochromatosis: genetic defect with increasing of the intake of food iron.
Secondary hemochromatosis: iron excessive saturation of the organism (hem transfusion with iron, over dose of vitamin C, anaemia).
Pathogenesis: hemosiderosis: iron may be normal 2-6gr|L; hemochromatosis: 15gr|L.
Localisation: hemosiderosis: mononuclear phagocytes of the liver; hemochromatosis: Hepatocytes.
Outcome: Hemosiderosis does not damage the tissue; Primary hemochromatosis: cirrhosis of the liver. Secondary hemochromatosis leads to atrophy of the parenchyma, sclerosis.
*Clinical signs***:** for Hemosiderosis it is jaundic**e;** for Primary hemochromatosis they are bronzed disease, diabetes mellitus, and cardiomyopathy.

3 №63 LIVER IN MECHANICAL JAUNDICE. H & E **des.**
Microscopically elongated green-brown plugs of bile are visible in dilated bile canaliculi. Rupture of canaliculi leads to extravasation of bile, which is quickly phagocytosed by Kupffer cells. Droplets of bile pigment also accumulate within hepatocytes, which can take on a wispy appearance (foamy degeneration). Duct epithelial cells proliferation is observed as well as looping and reduplication of ducts. Associated portal tract findings include edema and periductal infiltrations of neutrophils. Prolonged obstructive cholestasis leads to focal destruction of the parenchyma, giving rise to bile lakes (pools) filled with cellular debris and pigment.
Grossly the liver is enlarged, dense, green-brown coloured.
Definition: Jaundice is yellow pigmentation of the skin, sclerae, mucous membranes and organ parenchyma with both unconjugated and conjugated bilirubin in hyperbilirubinemia (blood level of bilirubin over 1.2 mg/dl).
Classification

1. Hemolytic jaundice (subhepatic) is characterized by excessive production of bilirubin, accompanied with increased lysis of erythrocytes, and reduced hepatocellular uptake. These mechanisms produce unconjugated hyperbilirubinemia.
2. Obstructive jaundice (mechanical or infrahepatic) is characterized by impaired bile flow and decreased hepatocellular excretion, leading to conjugated hyperbilirubinemia.
3. Parenchymatous jaundice (hepatic) is associated with hepatocytes injury, which may operate due to any of the named above mechanisms and produce both unconjugated and conjugated hyperbilirubinemia.

Etiology and pathogenesis
Extrahepatic biliary obstruction leads to dilation and rupture of bile canaliculi and extravasation of bile, which accumulates in Kupffer cells and hepatocytes. Accumulation of bile leads to degeneration, injury and necrosis of hepatocytes and portal tract fibrosis, which initially extends into and subdivides the parenchyma with relative preservation of hepatic architecture. Ultimately, in the final stage bile-stained cirrhotic liver occurs.
Diseases:
Gallstone obstruction of biliary tree; carcinomas of head of pancreas, extrahepatic bile ducts, ampulla of Vater; extrahepatic biliary atresia; biliary strictures and choledochal cysts; primary sclerosing cholangitis; liver fluke infestation.

Complications and outcome:
Cholestatic condition, which result from extrahepatic biliary obstruction and leads to biliary cirrhosis and may be complicated by hepatic failure, multiple organ failure, coagulopathy, hepatic encephalopathy, hepatorenal syndrome, portal hypertension from cirrhosis, esophageal varices and risk of rupture, hepatocellular carcinoma.
Clinical correlations:
1) Conjugated hyperbilirubinemia, 2) hypoalbuminemia, 3) bilirubinuria, leading to renal tubular necrosis, 4) yellow discoloration of skin, sclerae, mucous membranes, 5) pruritus, 6) hemorrhagic syndrome.

4 № 63 PIGMENTED NEVUS. H& E
Microscopically: Brown pigment of melanocytes can be seen, growing like nests or groups along the border of the epidermis and then derma. The cells are of oval or rounded form with rounded nuclei.
Grossly: brown- black eminence, as usual 0, 2 – 0, 5 cm diameter.
Definition: Melanin is the endogenous pigment, of proteinogenic (tyrosinogenic) nature
Pathogenesis: Tyrosine is oxygenated to DOPHA and melanin.
Localisation is the skin, eye, intestine, meninges.
Clinical sign: Pigmented nevus is benign tumour derived from the skin melanocytes.

5 № 7 SKELETAL MUSCLE NECROSIS WITH CALCIFICATION. H & E des**.**
Microscopically: the depositions of calcium salts among necrotic muscle cells. Calcification occurs as intra and extracellular basophilic deposits.
Grossly: calcium salts may be seen as fine white granules.
Definition: There is dystrophic type of pathologic calcification.
Pathogenesis: Dystrophic calcification occurs in dead or dying tissue. It occurs with normal serum levels of calcium.
See also Unit 3.

6 № 155 METASTATIC CALCIFICATION OF THE LUNG H & E **des**.
Microscopically: There are calcium deposits in the interstitial tissue of the lung as amorphous or crystalline structures.
Grossly: Extensive calcification in the lung may produce radiographs
Definition: Metastatic calcification occurs in normal tissues with hypercalcaemia.
Organs: Metastatic calcification is the pathologic calcification with deposition of calcium salts in the interstitial tissue of the vasculature, Heart, Kidneys, Lungs and gastric mucosa.
Pathogenesis: All these tissues become inadequately acid and rich in alkali contents. There are four major causes of hypercalcemi*a*: 1 increased secretion of parathyroid hormone due to primary parathyroid tumors; 2 destruction of bones due to Paget disease, immobilisation or tumours; 3 vitamin D- related disorders;
4 renal failure in which phosphate retention leads to secondary hyperparathyroidism.
Clinical sign: may be respiratory deficit.

7 № GOUTY TOPHUS H & E

Microscopically: the tophus is seen in tissues as a mass of amorphous or crystalline urates surrounded by macrophages, lymphocytes and fibroblasts. Large foreign body - type giant cells are wrapped around the urate.

Grossly: Persistent chronic inflammation leads to fibrosis and erosion of the articular cartilage. Ankylosis may be exhibited.

Classification: lots of tophi in tendons, bursae, soft tissue and, occasionally, in the heart can be revealed.

Definition: a group of disorders that produce hyperuricemia with the deposition of urates within or close to joints, tendons and cartilages creating tophi is identified.

Pathogenesis: Uric acid is the end product of purine metabolism. Hyperuricemia is characterized by a primary overproduction of uric acid with or without excessive excretion of uric acid. The cause of the overproduction is unknown.

Clinical signs: asymptomatic hyperuricemia, acute gouty arthritis, "intercritical" gout, Chronic tophaceous gout.

Unit 7 ADAPTIVE AND COMPENSATORY PROCESSES. REGENERATION.

Definition: **Hypertrophy** is an increase in the size of an organ or tissue due to enlarged size of cells.

The size of the ventricular chamber may be normal or some with constricted as concentric hypertrophy or extended:

a) in vertical size – tonogenic dilation

b) in cross (transversal) size – myogenic dilation.

Phase of compensation is characterized by Hypertrophy of the myocardium and tonogenic dilation of the chamber**. Phase of decompensation** is characterized by concentric hypertrophy of the myocardium and myogenic dilation of the chamber. In this phase myocardium is soft in consistency. Subendocardial surface shows apparent bands of yellow myocardium alternating with bands of darker, red-brown, the so-called "tiger heart." Cause is a mild hypoxia. If subendocardial surface shows apparent diffusion of yellow myocardium, the cause is severe hypoxia.

Some causes of decompensation hypertrophic heart are as follows:

1. Disparity between adequate blood supply of the hypertrophic and limiting capability of the vasculature. It leads to chronic hypoxia.
2. Progressive destruction of mitochondrions in hypertrophic myocardiocytes.
3. Increase of cytosol free calcium in myocardiocytes is due to dilation of endoplasmic reticulum.

Classification: 1.Adaptive hypertrophy

1.1. Neuro- humoral hypertrophy

1.2. Hypertrophic growth

2. Compensative hypertrophy

2.1. Working hypertrophy

2.2. Vicar hypertrophy.

Definition: **Atrophy** is adaptive response of decrease in size and function of cells, tissues, organs; shrinkage in the size of cells is due to the loss of cell substance.

Classification: Atrophy may be as follows:

1. General atrophy (cachexy)
    1.1. Alimentary cachexy
    1.2. Cancer cachexy
    1.3. Hypophysial cachexy
    1.4. Cerebral cachexy
    1.5. Chronic infection cachexy
2. Local atrophy
    2.1. Atrophy due to decreased work load
    2.2. Atrophy due to loss of innervations
    2.3. Atrophy due to inadequate nutrition
    2.4. Atrophy due to diminished blood supply
    2.5. Atrophy due to pressing
    2.6. Atrophy due involved to physical and chemical factors.

Regeneration is the form of adaptation with reconstruction structure formation and rehabilitation of the functions of cells, tissues or organs.

There are three types of regeneration: 1physiologic; 2 reparation; 3 pathological.

There are four types of healing: 1 healing with epithelization; 2 healing under a "crust"; 3 healing by first intention; 4 healing by second intention.

Microsamples:

1 № 73 Myocardial hypertrophy **des**.
2 № 157 Nodular hyperplasia of the prostate **des**.
3 № 69 Neurogenic atrophy of the skeletal muscle (Denervation atrophy) **des.**
4 № 105 Granulate tissue **des.**
5 № 67 Brown atrophy of the liver.

Macrosamples:

1. Myocardial hypertrophy
2. Fatty change in myocardium ("Tiger Heart") see above unit 4 cellular injures.
3. Nodular hyperplasia of the prostate and hypertrophy of the urinary bladder wall.
4. Hyperplasia of the thyroid (Goiter, struma).
5. Hydronephrosis.
6. Myocardial brown atrophy.
7. Retardation of wound healing.
8. Cardiosclerosis (Large foci).
9. Pathologic regeneration with polyps in the large intestine mucosa.
10. Metaplasia of the yellow medulla into red.

1 №73 MYOCARDIAL HYPERTROPHY. H & E. **des.**
Microscopically: The myocardiocytes are enlarged and contain large, hyper chromatic nuclei.
Grossly: The heart is enlarged; the weight of the heart usually exceeds 350-400gm. and over. Thickness of the left ventricular wall is over 1.2 cm (normal thickness is 0.7 to 1.2cm), the one of the right ventricular wall is over 0.5cm thick (normal thickness is 0.2-0.5 cm).
Etiology: Myocardial hypertrophy is usually working hypertrophy.
Pathogenesis: Working hypertrophy is caused by increased Functional demand (increased work load). The myocardial cells (myocardiocytes) become hypertrophic. The nuclei of myocardiocytes are enlarged, rich in chromatin. The whole intracellular structures increased in number (mitochondrions, muscular filaments, ribosomes). Endoplasmic reticulum is dilation enlarged. The myocardial stroma, nervous filaments and vessels become also hypertrophic.
With increase of hypertrophy, the metabolic requirements continue to increase but the capability of the heart to meet adequate requirements is decreased.
It leads to fatty dystrophy of the heart and decompensation.
Diseases: **1. Left ventricular hypertrophy shows:**
1.1. Essential hypertension.
1.2. Secondary hypertension.
1.3. Heart valve disease aortic stenosis and insufficiency.
1.4 Congenital malformation valve disease: coarctation of the aorta.
Diseases: **2. Right ventricular hypertrophy shows:**
2.1. Diffuse lung diseases with pulmonary hypertension (Chronic bronchitis, obstructive chronic diffuse emphysema, diffuse pneumosclerosis and others).
2.2 Rheumatic mitral valve diseases.
2.3 Congenital malformation valve diseases (tetralogy of Fallot, patent ductus arteriosus, septal defects and others).
Clinical signs: Accidental or consolidate (compensative) phase of myocardial hypertrophy may be a symptomatic. In decompensation phase of myocardial hypertrophy, clinical manifestations of heart failure occur.

2 № 157 NODULAR HYPERPLASIA OF THE PROSTATE. H & E. **des.**
Microscopically: The hyperplasic nodules are composed of varying proportions of proliferating glandular elements and fibromuscular stroma. The number of glands and number of cells in glands are increased. The glands are lined with tall, columnar epithelial cells and a peripheral layer of flattened basal cells; crowding of the proliferating epithelium results in the formation of papillary projections in some glands. The glands are surrounded by proliferating stromal elements.

Grossly: The prostate is enlarged, solid. The cut surface may contain multiple, fairly well circumscribed nodules, commonly marked in the inner (transitional and periurethral) region. The urethra is compressed by the hyperplasic nodules, often to a slit- like orifice formation.
. Hyperplasic nodules lying just under the mucosa of the proximal prostatic urethra may project into the bladder lumina as a pedunculated mass, resulting in a ball-valve type of urethra obstruction. The wall of the bladder is thickened due to hypertrophy.
Definition: Hyperplasia is enlarged of an organ or tissue due to increase in cell number or intracellular structures.
Classification: Hyperplasia of the prostate may be: 1.Glandular. 2. Stromal. 3. Mixed.
Etiology and pathogenesis: Age- related disturbances in androgens and estrogens levels are the cause of nodular hyperplasia of the prostate.
Testosterone through the action of 5-a-reductase appears to be the major hormonal stimulus for glandular and stromal proliferation.
Increases in estrogen levels in older males may contribute to the development of nodular hyperplasia as well.
Clinical signs: Since nodular hyperplasia involves portions of the prostate, its most common manifestations are those of lower urinary tract obstruction (difficulty in starting the stream of urine, intermittent interruption of the urinary stream while voiding).
Later complete urinary obstruction with resultant painful distention of the bladder and Hydronephrosis may occur. The combination of residual urine bladder and chronic obstruction increases the risk of urinary tract infections (cystitis, uretheritis, and pyelonephritis) and sepsis.

3 №69 NEUROGENIC ATROPHY OF THE SKELETAL MUSCLES (denervation atrophy).H& E. **des.**
Microscopically: The muscle fibers are substantially decreased in size, atrophic. They are surrounded by proliferation of connective tissue and adipose tissue.
Definition: Neurogenic atrophy of the skeletal muscle is local atrophy due to innervations loss.
Etiology: traumatic denervation (loss of innervations), poliomyelitis.
Results are in fatty tissue and connective tissue replacement muscles.
Clinical signs: muscle weakness.

4 №105 GRANULATIVE TISSUE H & E **des.**
Microscopically: there are a lot of newly formed vessels of microcirculatory bed, fibroblasts, granulocytes, macrophages, plasma cells and lymphocytes.
Grossly: With gray - red granules tissue can be seen.
Definition: Granulate tissue is a new connective tissue rich in vessels and cellular elements.

Pathogenesis: Granulate tissue is the specialized type of the tissue playing the basic role in the process of scaring. It is formed in wound healing, regeneration of the connective tissue and substitution.
There are six levels of granulate tissue: 1 leucocytes and necrotic zone; 2 layer of vessels loop; 3 layer of vertical vessels; 4 maturity layer; 5 layer of horizontal fibroblasts; 6 fibrous layer.
Result is in the scar
Clinical sign: Healing of the wounds.

5 №67 BROWN ATROPHY OF THE LIVER H & E

Microscopically: the hepatocytes are reduced, sinusoid spaces enlarged. Brown pigment lipofuscin is seen within hepatocytes plasma near the nuclei.
Grossly: The liver is enlarged, flabby; its front edge is shaped; the cutting surface of the parenchyma is of brown color.
Definition: Brown atrophy is the sign of cahexia with accumulation of lipofuscin within cells of the myocardium, the liver, the skeletal muscle and reduction of sizes.
Etiology: correlates with classification of general atrophy.
Pathogenesis: Decrease of protein synthesis and increase of protein catabolism. Increase of autophageous vacuoles and autolysosomes. Lipofuscin granules are named cellular debris into lysosomes without their digestion.
Diseases: Simmonds'disease; carcinoma of the stomach; senile degeneration.
Result is in sclerosis.
Clinical signs: Cachexy, decrease of the body weight, depression of the functions.

Macrosamples

Hyperplasia of the thyroid (Goiter, struma).
Grossly: The gland may be soft and smooth or dense and uneven.
Definition: Goiter is enlargement of the thyroid gland.
Etiology: The presence of goiter reflects impaired synthesis of thyroid hormone. Impairment of thyroid hormone synthesis leads to a compensatory rise in the TSH serum level.
Pathogenesis: The thyroid gland is diffusely or nodularly enlarged because of the presence of hypertrophy and hyperplasia of thyroid follicular epithelial cells.
Diseases: Endemic goiter, sporadic goiter, Graves' [Basedow's, Parry's] disease.

Hydronephrosis.
Grossly: the kidney shows marked dilatation of the pelvis and calyces and thinning of renal parenchyma.
Definition: Hydronephrosis is dilatation of the renal pelvis and calyces with accumulation of a fluid.
Etiology: the obstruction of the urinary tract.

Pathogenesis: The obstruction may occur at any level of the urinary tract leading to obstruction of the outflow of urine, with accompanying atrophy of the renal parenchyma. This is a local atrophy due to pressing.
Diseases: Congenital atresia of the urethra; calculi; tumors; spinal cord damage with paralysis of the bladder.
Result is in sclerosis of parenchyma.
Complication: pyelonephritis; pyonephrosis.
Clinical signs: Unilateral Hydronephrosis may remain completely silent for long periods; it may be revealed with ultrasound examination.
Bilateral Hydronephrosis leads to chronic renal failure.

Myocardial brown atrophy
Grossly: the heart is smaller then normal with convoluted vessels and brown myocardium with lipofuscin.
This is morphologic sign of general atrophy.

Wound healing retardation
Grossly: wound shows pale grey bottom and solid, hang over edges.
Etiology: radioactive emanation
Pathogenesis: phases of wound healing: inflammation, granulation tissue and wound contraction with collagen accumulation may be impaired. Wound healing may ultimately be reduced.
Result may be in squamous carcinoma.

Cardiac sclerosis (Large foci).
Grossly: there is an area of myocardial sclerosis (fibrosis) with firm whitish scaring.
Etiology: Transmural myocardial infarction.
Pathogenesis: Formed in 7-8 weeks. The process shows formation of granulate tissue and its growth from edge of infarct tissue.
Result is in dilatation of all cardiac chambers and compensatory perifocal myocardial hypertrophy.
Disease: Chronic ischemic heart disease.
Clinical signs: progressive congestive heart failure.

Pathologic regeneration with polyps in the large intestine mucosa.
Grossly: Nipple-like, hemispherical, smooth, slightly lobulated protrusion of the mucosa, single or multiple.
Definition: a polyp is non-neoplastic mass that protrudes into the lumen of the gut.
Etiology: Inflammation; hamartomatous polyp; hyperplastic polyp.
Pathogenesis: They occur sporadically and frequently increase with age.
Result is in precursor of colorectal carcinoma.
Disease: Chronic inflammation non-specific and specific.
Clinical signs: slight anemia, melena.

Metaplasia of the yellow medulla of a tubular bone into red.
Grossly: Red bone marrow is revealed.
Definition: Metaplasia is a transformation of one adult tissue type in to another, usually of the same embryonic tissue.
Etiology: leukemia, myelofibrosis.

Unit 8 EXUDATIVE INFLAMMATION.

Definition: Inflammation is the complex local cyclic vascular mesenchimal reaction of the organism developed during process of evolution. This is a response to lesion, leading to elimination of causality agent with regeneration of the tissue as a completion phase.
Classifications of inflammation:

1.1. Acute
1.2. Subacute
1.3. Chronic

2.1. Exudative
2.2. Productive

Etiology: of inflammation:

1. Infectional (viral, bacterial, fungal, parasitic, rickettsiae, protozoan);
2. Noninfectional factors (chemical and physical factors, foreign body);
3. Immune factors.
4. Unknown factors.

PATHOGENESIS of inflammation may by of three- component phases:

- Alteration
- Exudation
- cells proliferations.

The inflammatory response includes 1 circulating cells, plasma proteins, vascular wall cells, cells and extracellular matrix of the surrounding connective tissue.
Nomenclature: stomatitis- inflammation of the mouth; *amygdalitis (angina, tonsillitis*)- inflammation of the palatine tonsil; *laryngitis*- inflammation of the larynx; *pneumonia*- the inflammation of the lung; myositis- the inflammation of the muscles; hepatitis- the inflammation of the liver; *nephritis*- the inflammation of the kidney; *leptomeningitis*- the inflammation of the pia mater of the brain; pachymeningitis- dura mater of brain, *pancarditis*- the inflammation of all membranes of the heart;

"**Pery**" means inflammation of the serous membrane or vascular adventitia (pericarditis; periflebitis). "**Para**" means inflammation of fatty tissues surrounding an organ (paranephritis).

Definition of exudative inflammation:
Exudative inflammation is the type of inflammation, characterized by predominance of exudation over alteration and proliferation.
Classification: The types of exudative inflammation are as follows:
1. Serous, 2. Fibrinous, 3. Purulent. 4. Hemorrhaged, 5. Putrid, 6. Catarrhal, 7. Mixed.

OUTCOME of exudative inflammation:

1. Complete resolution.
2. Scarring (fibrosis).
3. Progression to other types of inflammation.

Fibrinous inflammation

Definition: Fibrinous inflammation is the type of exudative inflammation, characterized by a fibrin rich exudation.

Classification: there are two types of fibrinous inflammation of the mucous membranes 1croupous; 2 diphtheritic.

Purulent (suppurative) inflammation

Definition: Purulent (suppurative) inflammation is characterized by a purulent exudate (pus), consisting of neutrophils, parenchymal cell debris, neutrophils debris and micro organisms.

Classification: of purulent inflammation: 1 Phlegmonon; 2 Abscess; 3 Empyema.

Phlegmonon is diffuse purulent exudative inflammation of friable connective tissue.

Abscess is the local purulent inflammation with degradation of the tissue and the formation of a cavity enclosed by a pyogenic membrane.

Empyema is the purulent (suppurative) inflammation of the anatomic cavity walls with the accumulation of pus in the anatomic cavity.

Etiology: 1.Pyogenic microorganisms (staphylococcus, streptococcus, gonococcus, meningococcus, E. coli and other).

2. Some chemical factors (turpentic, mustard) as Aseptic purulent Inflammation.

Microsamples:

N 79 Serous dermatitis **des**
N 81 Fibrinous pericarditis **des**
N 83 Croupous tracheitis **des**
N 93 Phlegmon of the subcutaneous fat **des**
N 223 a Local Pneumonia with formation of multiple abscesses **des.**

Macrosamples:

1 Fibrinous pericarditis ("Hair heart").
2 Croupous laryngothrachitis.
3 Diphtheritic colitis
4 Phlegmonous appendicitis. Empyema of the appendix.
5 Abscess of the liver (brain, lung).
6 Appostematous nephritis (Metastatic abscesses in the kidney).
7 Postpartum purulent endometritis.
8 Purulent meningitis (or hemorrhagic meningitis).
9 Gangrenous amygdalitis.

1 № 79 SEROUS DERMATITIS H & E **des**

Microscopically: Epidermis is separated from the derma by a local collection of serous effusion. Derma is edematous with inflammatory hyperemia and some cellular infiltrate.

Grossly: Formation skin blister is evident

Definition:

Serous dermatitis is the type of exudative inflammation, characterized by a watery, relatively poor fluid protein (effusion).

Etiology of serous inflammation: 1. Burn. 2. Viral infection. 3. Streptococcus.
The diseases: 1.Chicken pox. 2. Natural small pox. 3. Erysipelas. 4 Herpetic fevers.
Outcome of the serous inflammation: 1. Resolution with complete recovery of structure.
2. Progression to fibrinous or purulent inflammation.
Clinical signs: Pain, reddening, swelling, dysfunction.
Additionally: Serous inflammation may be in: peritoneal, pleural, pericardial cavities, meninges, periferal nerves, parenchymal organs (lung, liver, kidney, heart).

2 № 81 FIBRINOUS PERYCARDITIS H & E **des**
Microscopically: Pink masses of fibrin exudate lie over the pericardial surface. Neutrophil infiltration and inflammatory hyperemia are seen in the thick epicardium.
Grossly: The thick epicardium covered with friable gray masses with hair- like spongeous form,. Figurative name is "Hair heart".
Definition: Fibrinous inflammation is the type of exudative inflammation, characterized by a fibrin rich exudate.
Etiology: 1. Toxic factors. 2. Bacterial infection.
Pathogenesis: This occurs as a consequence of severe injuries, with resultant greater vascular permeability to allow larger molecules (specifically fibrinogen) to pass the endothelial barrier.
The diseases: 1. Uremia. 2. Rheumatism. 3. Complication of Tuberculosis. 4. Fibrinous lobar pneumonia. 5. Complication of Transmural or subepicardial myocardial infarcts.
Outcome: 1. Resolution of the exudate with restoration of the normal tissue structure.
2. Organization of the exudate to form focal scar tissue and lead to the development of fibrous strands bridging the pericardial space.
3. Organization of the exudate with obliteration of the pericardial space.
4. Calcification of the pericardium the so-called "Shell heart".
Clinical signs: acute and chronic heart failure.

3 №83 CROUPOUSE TRACHEITIS H & E **des**
Microscopically: Friable fibrinous films can be seen as eosinophilic mesh work of threads or amorphous coagulum on the erosion mucous membrane.
Grossly: Gray friable films lie on the erosion mucous surface of the trachea.
Definition: ***Croupouse*** is the fibrinous inflammation of the mucous membrane covered with cuboid or column epithelium laying on thin solid base connective tissue. The fibrinous film is friable, easily removed. Organs: trachea, bronchi, alveoli.
Diseases: diphtheria; uraemia.
Pathogenesis: the most severe injuries may be the causes of fibrinous inflammation with great vascular permeability allowing large molecules (specifically, fibrinogen) to pass in the endothelial barrier.
Outcome: 1film flakes away easily; 2 resolution with the degradation by fibrinolysis and debris accumulation with macrophages, resulting in restoration of the normal tissue structure.

Clinical sign: friable film asphyxia (true croup).

4 № 93 PHLEGMON OF THE SUBCUTANEOUS FAT H & E **des**
Microscopically: Diffuse neutrophil infiltration and inflammatory hyperemia are seen in the subcutaneous fat.
See Definition, classification and etiology above.
The diseases: 1. Trauma. 2. Wound formation. 3. Typhoid Fever. 4 Sepsis.
Complications: Dissemination of the purulent inflammation may lead to fistula or leakage.
Outcome: 1. Resolution of the exudate with restoration of the normal tissue structure. 2. Scarring.
Additionally: Phlegmonous inflammation may occur also in the appendix, in the bile cyst and other organs.

5 №223 PNEUMONIA WITH MULTIPLE ABSCESSES FORMATION OF H & E
Microscopically: there is local suppurative exudate that fills the bronchi, bronchioles and adjacent alveolar spaces with foci of destruction; necrosis may lead to abscesses formation.
Grossly: The lungs are enlarged with severe hyperemia. On a cut there are a lot of foci of inflammatory consolidation. They are distributed in patches throughout one or several lobes, most frequently bilateral and basil. Well-developed lesions up to 3 or 4 cm in dia are slightly elevated and are grey-red to yellow abscesses. Their are multiple small liquid foci of yellow or gray color within the lung.
See Definition above.
Classification: 1acute abscess; 2 chronic abscess.
Acute abscess consists of two layers: 1 pus; 2 pyogenic membrane
Chronic abscess consists of three layers: 1 pus, 2 granulate tissue, 3 fibrous tissue.
Outcome: spontaneous emptying and pus outcome into the pleural cavity with formation of the fistula; 2 organization; 3 petrification.
Clinical signs: intoxication; respiratory failure.

MACROSAMPLES
Diphtheritic colitis.
Diphtheritic inflammation is the fibrinous inflammation of the mucous membrane covered with Squamous, transverse epithelium on thick friable basic connective tissue. The fibrinous film is solid, deep, hard revealed defect. There are very deep ulcers formed after removal of the film.
Organs: the pharynx, the oesophagus, the uterus, the vagina, the intestine, the stomach, the bladder.
Grossly: Mucous membrane of large intestine is swollen, hyperemic, covered with gray brown film taken off with difficulty.
Definition: It is diphtheritic inflammation – the variety of fibrinous inflammation, accompanied by the deep necrosis of tissues and formation of fibrinous films connected intimately with adjacent tissue.
Disease: Dysentery.

Outcome: 1. complete resolution. 2. scarring after film rejection with ulceration of intestine.
Complications: 1. Melena. 2. Ulcer. 3 Perforation of the intestine wall with peritonitis. 4. Paraproctitis. 5. Progression to the phlegmonon of intestine.

Postpartum purulent endometritis.
Grossly: The uterus is enlarged to a marked degree. Its wall is thickened, the cavity is widened. Mucous membrane is saturated with yellow green exudate and films are with drawn away with difficulty. There are ulcers in the sites of film withdrawal.
Etiology: postpartum pyogenic infection.
Complication: Sepsis.

Phlegmonous appendicitis. Empyema of the appendix.
Grossly: the appendix is red, swollen, and covered with a fibrinous exudate. The wall may be very thin with pus into a lumen of the appendix.
Etiology: pyogenic infection with obstruction;
Complication: it may be rupted by pus due to suppurative peritonitis.
Clinical signs: It needs appendectomy.

Abscess of the liver (brain, lung).
Grossly: It may occur as solitary or multiple lesion ranging from millimeters to many centimeters in dia. The cavity occurs with pus surrounding purulent membrane.
Etiology: 1 parasitic infections (amebic; echinococcal; other protozoal and helminthic organisms); 2 bacterial or fungal infections.
Outcome: hepatic abscess may extend into the thoracic cavity to produce empyema or a lung abscess.

6 Appostematous nephritis (Metastatic abscesses in the kidney).
Grossly: the cortical surface is studded with multiple focal abscesses.
Etiology: staphylococcus, streptococcus.
Diseases: sepsis, acute pyelonephritis.
Complications: purulent paranephritis; pyonephrosis.
Outcome: sclerosis (scarring)
Clinical signs: bacteriuria, pyuria, pain in the low back.

Unit 9 PRODUCTIVE INFLAMMATION

Definition: Productive inflammation is the type of inflammation, characterized by predominance of proliferation over alteration and exudation.
Classification: 1 INTERSTITIAL (MEDIATE), 2 GRANULOMATOUS
3 INFLAMMATIONS WITH POLYP FORMATION.
GRANULOMA may be:
1. according to etiology:
   1.1. Infectional,
   1.2. Unintentional,
   1.3. Unknown.

2. according to morphological structure
   2.1. Specific
   2.2. Nonspecific.

SPECIFIC GRANULOMA is the granuloma whose morphological structure is specified only with this disease and contains microorganisms.

Etiology: 1. Infections
1.1 Viruses (coxsackievirus, ECHO, influenza),
1.2 Chlamydia,
1.3 Rickettsia (typhus fever),
1.4 Bacteria (Diphtheria, scarlet fever),
1.5 Fungi (Candida).
2. Immune – Mediated reactions (rheumatic fever, systemic lupus erythematosus, and drag hypersensitivity).
3 Physical and chemical agents

Microsamples:

N 172 Productive interstitial myocarditis **des.**
N 97 Trichinosis of the skeletal muscle. (Productive myositis) **des.**
N 244 Tuberculous granulomas. (Millet tuberculosis of the lung) **des.**
N 305 Normal thymus of new-borns.
N 306 Incidental involution (transformation) of the thymus **des.**
N 309 Thymus of severe combined immunodeficiency (SKID)

Macrosamples:

1. Echinococcosis.
2. Millet tuberculosis of the lung (spleen).
3. Solitary gumma of the liver (brain, testis).
4. Syphilitic mesaortitis with the aneurism.
5. Chronic appendicitis.

DEMONSTRATIVE MICROSAMPLES:

1. Leproma (lepromatous granulomas) H-E.
2. Leproma Sudan black stain.
3. Leproma Ziehl – Neelsen stain.

The types of productive inflammation are as follows:

1 №172 PRODUCTIVE INTERSTITIAL MYOCARDITIS H & E **des.**

Microscopically: Diffuse inflammatory cellular infiltrates are seen in myocardial stroma. They consist of lymphoid cells, histiocytes, plasma cells, macrophages and fibroblasts.
Definition: Interstitial inflammation is the type of productive inflammation, characterized by diffuse inflammatory cellular infiltrates in the organs stroma.
Grossly: The heart is enlarged, myocardium is of soft consistency.
Outcome: Diffuse cardiosclerosis.
Clinical signs: Heart failure.

2 № 97 TRICHINOSIS OF THE SKELETAL MUSCLE (PRODUCTIVE MYOSITIS) H& E **des.**

Microscopically: Trichinella spiralis cysts are seen within the skeletal muscle. They are encapsulated. The cysts are calcified. Productive inflammatory reactions of adjacent cysts are revealed

Etiology: Trichinella spiralis.

Pathogenesis: Trichinosis is a disease caused by the ingestion infected with Trichinella spiralis cysts.

Infected meat is most often pork, although other animal products may also "harbor" the parasite. When infected meat is ingested by humans, the cysts wall is digested, and the Trichinella larva attaches to the wall of the duodenum or jejunum and migrates from the gut into the general circulation flow.

Once in the bloodstream, the parasites may spread to a number of different sites, including the lungs, central nervous system, heart and ultimately skeletal muscle.

Outcome: sclerosis.

Clinical signs: Muscle pain and weakness.

3№ 244 TUBERCULOUS GRANULOMAS. (Millet tuberculosis of the lung) H& E **Des.**

Microscopically: Multiple tuberculosis granulomas in the lung are exhibited. Granulomas consist of caseous necrosis in the center, surrounded by a layer of epithelioid cells, giant polynuclear Pirogov and Langhans' sells and lymphoid cells outside.

Grossly: Lung is inflated being, "fluffy". Pleura and lung tissue consist of multiple millet like gray-yellow hillocks.

Definition: Granulomas reveal a local productive inflammation with a knot or hillock appearance.

Granulomas consist of aggregations of activated macrophages: epithelioid and Pirogov & Langhans' cells.

Epithelioid cell is a cell of nonepithelium nature, like a squamous epithelium cell with pale pink cytoplasm and indistinct cell boundaries.

Pirogov & Langhans' cell is a giant cell with multiple nuclei characterized by peripheral location of oval nuclei, typical of tuberculosis granulomas.

Tuberculosis granulomas are infectional specific granulomas.

Millet tuberculosis of the lung is manifestation of:

1. Hematogenic tuberculosis form:
   1.1. Generalized hematogenic tuberculosis,
   1.2. Hematogenic tuberculosis with principal defect of the lung.
2. Hematogenic dynamics of primary tuberculosis.

Outcome: 1. Total necrosis of the granulomas,
2. Sclerosis,
3. Encapsulation,
4. Calcification.

4 № 305& №306 ACCIDENTAL INVOLUTION OF THE INFANCY THYMUS AND NORMAL THYMUS H & E **des**.

Microscopically: Volume of the lobules is decreased in the normal thymus at the expense of decrease of the lymphocytes from of the cortical zone. Note the inversion of the thymus s. Cellular medullar layer is seen clearer than the cortical one. Within some lobules are seen wiping of boundary between layers. There are Hassall's corpuscles as the whorls of the epithelial cells; some of them are like cysts. There can be seen enlarged cortical zone. All of these changes occur as the stereotype response of the central organ of the immune system to antigene stimulations.
Grossly: Mass of the thymus is decreased; it is of soft consistency.
Cause: antigene stimuli of various etiologies.
Result: if the etiological agent is removed, the process of accidental involution is reversible. If the process is irreversible, atrophy of the thymus comes about occurs.
Clinical significance: The process is adaptation of the organism to antigene action.

5 № 309 THYMUS WITH SEVERE COMBINATIVE IMMUNE DEFICIT (Neseloff's syndrome) H & E.
Microscopically: The thymus is decreased in size. Dysplasia is noted with formation of the glandular structures and total absence of Hassall's corpuscle and strongly marked decrease of the lymphocytes amount are revealed.
Cause is the hereditary immune deficit (Neseloff's syndrome). It is inherited recessive type coupled with X-chromosome.
Clinical significance is characterized by expressed defect of the cellular and humoral immunity. It is complicated by infection diseases with extremely severe clinical course and they are the causes of death. The survival rate for Children does not exceed 1-2 years.

Unit 10 NEOPLASIA. MESENCHYMAL DERIVED TUMORS.
Definition: A neoplasm is pathologic process with loss of response to normal growth and differentiated monitoring. In routine medical practice, a neoplasm is often referred to as *a tumor*. The science study Tumors is called *oncology.*
Neoplasms demonstrate atypisms: biologic; morphologic; biochemical; genetic.
Biologic atypism includes: 1 autonomic growth; 2 infiltrative growths; 3 progressive growth; 4 metastasis capability; 5 transfer from one animal to another
Forms of tumor growth: 1 infiltrative; 2 expansive; 3 unicentric; 4 multicentric; 5 endophytic; 6 exophytic.
The tumors are divided *into benign and malignant* based on a judgment of tumor potential clinical behavior.
Metastases spread malignant tumor to remote sites.
Malignant tumors show metastases along pathways: 1 lymphogenic, 2 hematogenic, 3 contact, 4 nervous fibrils.
All tumors have basic components: the parenchyma (made up of transformed or neoplastic cells) and non-neoplastic stroma (connective tissue and vessels).
Nomenclature of Tumors of mesenchimal origin
Benign tumor is designated by attaching the suffix *–oma*
Malignant tumor is designated by attaching *–sarcoma*

Sarcoma is malignant tumor derived from mesenchimal tissue. . Sarcoma leads to metastases along hematogenic pathway.

Tumors of mesenchimal origin	*benign*	*malignant*
Connective tissue	Fibroma	Fibrosarcoma
Fatty tissue	Lipoma	Liposarcoma
Cartilage	Chondroma	Chondrosarcoma
Bone	Osteoma	Osteosarcoma
Blood vessels	Hemangeoma	Hemangiosarcoma
Lymph vessels	Lymphangeoma	Lymphangiosarcoma
Muscle		
Smooth	Leiomyoma	Leiomyosarcoma
Striated	Rhabdomyoma	Rhabdomyosarcoma

Scheme of description:
1 Microscopic description
2 Macroscopic (Gross) description
3 What tissue is the tumor derived from?
4 Define maturity of the tumor
5 Determine benign or malignant the tumor is.
6 What kind of atypism does the tumor present?
7 Does the tumor give metastases? Where does it spread to primarily?
8 Does the tumor give recidivation?
9 Name its malignant analogue.

Microsamples:
1 № 108 Leiomyoma of the uterus **des**.
2 № 119 Polymorphic cellular (myogenic) sarcoma **des.**
3 № 120 Fibrosarcoma
4 № 151 Cavernous hemangeoma **des.**
5 № 150 Capillary hemangeoma of the skin.

Macrosamples:
1 Numerous nodes of leiomyoma within the uterus.
2 metastatic nodes of sarcoma within the lung

1 № 108 LEIOMYOMA OF THE UTERUS H & E **des**.
Microscopically and definition:
Leiomyoma is the benign tumor derived from smooth muscle cells and formed with well demarcated nodes.
Grossly: there are multiple nodes within the uterus wall. All of them are very solid, well demarcated, round, of white grey colour and fibril like structure.
Classification: Leiomyoma within the uterus may by: 1 submucous; 2 intramural; 3 subserous.
Leiomyoma is mature, well differentiated, non-invasive, nonmetastatic, nonrecidival tumor with only tissue atypism. Leiomyoma may be within other organs: the stomach, the vessels. Its malignant analogue is named leiomyosarcoma.

Consequences: 1 haemorrhage within nodes; 2 edema of the nodes; 3 hyalinosis.

2 № 119 POLYMORPHIC CELLULAR (MYOGENIC) SARCOMA H & E **des.**
This is malignant tumor derived from the muscles.
Microscopically it consists of multiple polymorphic cells with polymorphic nuclei, including bizarre neoplastic giant cells.
Grossly: it may be soft, of gelatinous masses, poorly demarcated, rapidly growing, and locally invasive. It may be "fish flashy"- like.
Nomenclature: sarcoma is a malignant tumor derived from mesenchimal, muscle and vascular tissues. Rabdomyosarcoma is a malignant tumor derived from skeletal muscles.
Localisation: may be within the retroperitoneal area, head, neck, lower genitourinary tract.
The tumor has cellular and tissue atypisms, it is an immature tumor.
Sarcoma gives hematogenic metastases and first of all, it spreads to the lungs.
Consequences: 1 necrosis; 2 haemorrhage; 3 thromboses; 4 thromboembolism; 5 fistula between organs where the tumor grows; 6 intoxication; 7 cachexy.
Causes of death: Consequences may occur.

3 № 120 FIBROSARCOMA H & E
Fibrosarcoma is a malignant tumor derived from the connective tissue.
Microscopically: it is composed of atypical interlacing fascicles of fibroblasts, sometimes arrayed in a "herringbone" pattern. Nuclear atypia and mitotic activity are present.
Grossly: It is a solitary lesion with infiltrative growth or of circumscribed. The tumor has solid consistency, of grey-white colour and be like "flashy fish".
Localisation: may be within deep tissues of the thigh, knee, and retroperitoneal area.
The tumor has cellular and tissue atypisms, it is an immature tumor.
Sarcoma gives hematogenic metastases and first of all, it spreads to the lungs.
Consequences: 1 necrosis; 2 haemorrhage; 3 thromboses; 4 thromboembolism; 5 fistula between organs where the tumor grows; 6 intoxication; 7 cachexy.
Causes of death: unfavourable consequences may occur.

4 № 151 CAVERNOUS HEMANGEOMA H & E **des.**
Hemangeoma is a benign tumor derived from blood capillaries.
Microscopically: the tumor consists of multiple large, cavernous vascular spaces, partly filled with blood separated by a scant connective tissue stroma. Thrombi are seen may within vascular spaces.
Grossly: The tumor is usually a red-blue, soft spongy mass, 1-2 cm dia or rarely may be a giant form.
Localization: subcutaneous areas of the face, extremities, the liver or other organs.
The tumor is mature, with tissue atypia, gives no metastasis, no recidives, well differentiated. Its malignant analogue is named hemangiosarcoma.
Consequences: pressure symptoms and rupture with haemorrhage.
Causes of death: haemorrhage may occur.

5 № 150 CAPILLARY HEMANGEOMA OF THE SKIN H & E.
Microscopically: It is usually lobulated, unencapsulated, aggregated in closely- packed, thin-walled capillaries; blood filled and lined with a flattened endothelium, may be of several levels. The vessels are separated by scant connective tissue stroma. There are thrombi; some of them may be organized, into the lumina.
Grossly: Varying in size from 1mm up to several cm in dia. It may be bright red or blue and surface level of the skin is slightly elevated.
Localization: The skin of the neck or head, liver, spleen, kidney and other organs.
Capillary hemangeoma is a benign tumor derived from blood capillary vessels. It is mature tumor with tissue atypia and infiltrative growth. It gives no metastases, no recidives.
Consequences: may be ulcerous, with inflammation and haemorrhage.

Unit 11 EPITHELIAL DERIVED TUMORS**.** CARCINOMAS OF THE ORGANS**.**
Nomenclature:

Tumors of epithelial origin	*benign*	*malignant*
Stratified squamous	Squamous cell papilloma	Squamous cell carcinoma or epidermoid carcinoma
Basal cells of skin		Basal cell carcinoma
Transitional	Transitional cell papilloma	Transitional cell carcinoma
Epithelial lining of glands or ducts	Adenoma	Adenocarcinoma
	Papilloma	Papillary carcinomas
	Cystadenoma	Cystadenocarcinoma

Carcinoma is malignant tumor derived from the epithelium. It gives metastases lymphogenic and hematogenic pathways.

Microsamples:
1 № 129 Fibroadenoma of the breast **des.**
2 № 123 Papilloma of the skin **des**
3 № 137 Adenocarcinoma of the stomach **des.**
4 № 138 Scirrh of the stomach.
5 № 125 Squamous cell carcinoma (epidermal) with keratosis of the oesophagus **des.**
6 № 148 Metastases of carcinoma within the liver.

Macrosamples:
1 Polyp-like carcinoma of the stomach.
2 Diffuse carcinoma of the stomach
3 Carcinoma of the breast
4 Carcinoma of the lung
5 Carcinoma of the oesophagus.
6 Metastases of the carcinoma within the liver and lymph nodes.
7 Carcinoma of the cervix.

1 № 129 FIBROADENOMA OF THE BREAST H & E **des.**
Microscopically: There is a loose fibroblastic stroma containing duct like epithelium with lined spaces of various forms and sizes.
Classification: there are two types of Fibroadenoma: 1 pericanalicular and 2 intracanalicular. Pericanalicular Fibroadenoma contains open, round to oval, fairly regular ductal spaces. Intracanalicular Fibroadenoma contains ductal spaces compressed by extensive proliferation of the stroma, on cross-section there appear slits or irregular, star-shaped structures.
Grossly: It is discrete, solitary, freely movable nodule of 1 to 10 cm in dia, easily "shelled out". The tumor is firm, of white tan color on cut surface.
Definition: Fibroadenoma is a benign epithelial tumor derived from the ducts of the breast rich fibrous stroma. It is mature with single tissue atypia; its growth is named expansive; it has no metastases, no recidives. Its malignant analogue is named adenocarcinoma.
An absolute or relative increase in estrogen activity plays some role in its development.

2 № 123 PAPILLOMA OF THE SKIN H & E **des**
Microscopically: The tumor is formed by symmetric zones of papillary epidermal proliferation rather than radiates symmetrically like the rays of a crown.
Grossly: It looks like cauliflower masses, soft, tan grey and may be single (unicentric growth) or multiple (multicentric growth).
Definition: Papilloma is a benign tumor derived from squamous or transitional epithelium.
Organs: It may be on the skin, the bladder mucous membrane, the mucous membrane of the larynx.
There is a mature tumor with tissue atypia, has got no metastases, no recidives.
Its malignant analogue is named squamous or transitional cell carcinoma.
Complications: ulceration, hemorrhage, inflammation, necrosis.

3 № 137 ADENOCARCINOMA OF THE STOMACH H & E **des.**
Microscopically: Malignant cells are formed neoplastic glands, well or poorly differentiated.
Classification of microscopical forms: 1 adenocarcinoma; 2 "signet-rings" cells carcinoma; 3) scirrh; 4) solid carcinoma.
Grossly: There are five macroscopical forms: 1 polyp-like; 2 fungal like, 3 diffuse or linitis plastica; 4 flat or depressed; 5 excavated (ulcer-like). The tumor is solid or soft, white-grey, may grow through the wall of the stomach. Adenocarcinoma may grow into adjacent organs: the liver, colon, pancreas, spleen.
Definition: Adenocarcinoma is a malignant tumor derived from glandular epithelium.
Organs: Adenocarcinoma is nonspecific tumor and may occur within other organs: the large intestine, uterus, pancreas, liver etc.
It is an immature tumor, with cellular and tissue atypia, of invasive growth.
Its growth may be into lumina of the hollow organ named exophytic growth and into the organ wall named endophytic.
The background diseases are: chronic gastritis; adenomas; peptic ulcer.

Precancer is named dysplasia and large intestinal metaplasia of the gastric glandular cells. The tumor within only mucous membrane is named early gastric cancer.
Carcinoma of the stomach gives lymph metastases; first of all it spreads to lymph nodes in minor and major curvatures. It first hematogenic metastasis is within the liver.
There are three retrograde metastases of the gastric carcinoma: 1 Krukenberg tumor designates metastases into the ovary; 2 Shnitsler metastases designate metastases gastric carcinoma into the lymph nodes of pararectal adipose tissue; 3 Virchow's node designates metastasis into left supraclavicular lymph node.
Complications: 1 hemorrhage as melena; 2 perforation; 3 peritonitis; 4 penetration with contact metastases; 5 stenosis of the pyloric part of the stomach; 6 intoxication; 7 cachexy.
Causes of death are complications.

4 № 138 SCIRRH OF THE STOMACH H & E
Microscopically: The tumor is composed of gastric type mucous cells to form Small clusters within rich fibrous stroma.
Grossly: The wall is extensively infiltrated by malignancy with rigid and thickened stomach as diffuse macroform.
Definition see above
Organs see above
Complications: see above, but initially 1 stenosis of the pyloric part of the stomach may occur; 2 intoxication; 3 cachexy.
Causes of death are complications.

5 № 125 SQUAMOUS CELL (EPIDERMAL) CARCINOMA WITH KERATOSIS OF THE OESOPHAGUS H & E **des.**
Microscopically: there are multiple nest- like structures consisting of atypical polygonal cells with keratinization in the structural centers named keratin pearls.
Grossly: there are three forms: 1 Polyp like; 2 diffuse infiltrative as entophytic; 3 ulcerous. Grey-white plaque-like initial overt lesion thickens with elevation of mucosa. Thickening and rigidity of the wall combined with carcinoma growth into the respiratory tree, aorta can be revealed.
The background diseases are chronic esophagitis due to tobacco and alcoholic abuse; gastric-esophagus reflux. *Precancer* is named dysplasia and leukoplakia. The onset form is named carcinoma in situ.
Definition: Squamous cell carcinoma is a malignant tumor derived from squamous cells. The tumor may be keratinous as well-differentiated squamous cell carcinomas and non keratinous as poorly differentiated one.
It has cellular and tissue atypia, it is immature with infiltrative growth. The tumor localizations are according to anatomic luminal narrowing: 1 proximal at the cricoid cartilage; 2 downwards direction the anterior crossing of the left main bronchus; 3 distal where esophagus penetrates the diaphragm. The carcinoma spreads to paraesophageal lymph nodes.
The tumor in the upper and middle part of thoracic esophagus spreads along hematogenous pathway to the lungs; the low part of esophagus carcinoma spreads to the liver.

Organs: Squamous cell carcinoma is a nonspecific tumor and may occur within the cervix of the uterus, lung, skin, larynx, rectum etc.
Complications: fistula between the esophagus and trachea may be revealed when the tumor grows and aspiration pneumonia; may occur cachexy; intoxication, stenosis with alimentary cachexy, hematemesis.
Causes of death are complications.

6 № 148 METASTASES OF CARCINOMA WITHIN THE LIVER H & E.
Microscopically: there are multiple metastatic carcinoma nodules with structures of primary carcinoma.
Grossly: There are structures well defined, soft or firm, tumor nodules of grey – white color.
Definition: Hematogenic metastases spread from malignant tumor into other organs.
Complications: the parenchymal jaundice.
Cause of death intoxication, cahexia,

Macrosamples
Carcinoma of the breast
Grossly: The lesion may be stony-hard on palpation with white color. It is retracted or elevated of the skin or nipple, infiltrated into surrounding breast tissues. It may be localized with limphedema as the cause of the so-called orange peel skin.
There are gross forms of breast carcinoma: 1 nodal; 2 diffuse; 3 mixed.
Microscopical forms: 1noninvasive lobular; 2 noninvasive ductal carcinoma; 3 invasive lobular; 4 invasive ductal carcinoma; 5 Paget disease of the nipple.
Noninfiltrative (in situ) and infiltrative Growth. It has cellular and tissue atypisms.
Metastases: Carcinoma spreads to the axillary lymph nodes, supra and infraclavicular lymph nodes; parasternal nodes, extrasternal nodes via lymphogenic pathway.
It spreads to the lungs and bones via hematogenic pathway.
Phone lesions: non proliferative, simple cyst mastopathy.
Precancerous lesions: 1 proliferative hyperplasia (with and without atypia);
2 sclerosing adenosis.
Complications: 1 cahexia; 2 intoxication. There may lead to fatal outcome.
Cause of death: cahexia, intoxication.

Carcinoma of the cervix
Grossly: Conspicuous tumor has node-like with barrel-like form of the cervix. It may be solid or soft of white- grey color with yellow and red colored sites. The tumor may be endophytic, exophytic and mixed.
Microscopically: 1 squamous cell carcinoma; 2 adenocarcinoma; 3 adenosquamous carcinoma; 4 nondifferential.
Etiology: Human papillovirus 16, 18, 31, 33
Metastases: It spreads to pelvic and para-aortic lymph nodes. Hematogenic metastases may occur within the liver, the lung, and the bones.
Phone lesions: Chronic cervicitis, condylomas, endocervicosis.
Precancerous lesions: CIN 1 Mild dysplasia; CIN2 moderate dysplasia; CIN 3 severe

Dysplasia. Then may be carcinoma in situ.
Etiology: Human papillovirus 16, 18, 31, 33
Complications: 1 cahexia; 2 intoxication; 3 cervix-bladder fistula; 4 cervix-rectums fistula. Causes of death may be cahexia; intoxication.

Carcinoma of the lung
Grossly: There is a large white central (hilar) mass with white bulky masses pushing into adjacent lung parenchyma. This lesion is severe due to obstruction of bronchial lumen.
The tumor may be: 1 multibranch; 2 nodular-multibranch; 3 polyp-like; 4 diffusive.
Microscopically: 1 Squamous cell carcinoma; 2adenocarcinoma; 3 bronchioloalveolar carcinoma; 4 large cell undifferentiated carcinoma; 5 small cell carcinoma; 6 combined carcinoma.
Cause is smoking
Metastases are in local hilar lymph nodes.
Phone lesion is chronic bronchitis.
Precancerous lesions are squamous metaplasia; dysplasia.
Complications are cahexia, intoxication, hemorrhage, pneumonia, and pleuritis.
Causes of death are cahexia, intoxication, hemorrhage, respiratory failure.

Unit 12 TUMORS OF THE NERVOUS SYSTEM, THE MENINGES, MELANIN FORMING TISSUE. TUMORS OF INFANCY AND CHILDHOOD.
Tumors of the brain:
The distinction between benign and malignant tumors is less than in other parts of the body. The malignant tumors very rarely give metastases outside the CNS.
Nomenclature: Gliomas are tumors of the glial cells include: 1 benign tumor as astrocytoma, oligodendroglioma, ependimoma; 2 malignant tumors as glioblastoma multiform. Neuronal tumors contain mature neurons (ganglion cells):
1 benign tumors: gangliocytoma; 2 malignant tumor is named neuroblastoma.
Poorly differentiated tumor is named medulloblastoma.
Tumors are derived from the meningothelial cells of the arachnoid named meningeoma with its verity psammoma and malignant meningeoma.
Tumors of the peripheral nervous system: benign forms are schvannomas (neuromas) and neurofibromas and malignant are named malignant peripheral nerve sheath tumors. The multicentric growth of neurofibroma is named von Recklinghausen disease.
Pigmental tumors: 1 nevus; 2 melanocarcinoma.
Tumors of infancy and childhood have characteristic properties: 1inversion (ability of malignant immature tumor to turn into benign mature tumor); 2 benign tumors predominate under malignant tumors; 3 in malignant tumors, sarcomas are more common; 4 embryonic tumors predominate.
Hemangiomas are the most common tumors of infancy, sacrococcygeal teratomas are the most common germ cell tumors of childhood.

Microsamples
1 109 Neurofibroma

2 111 Schwannoma (Neuroma) **des**
3 115 Glioblastoma multiforme **des**
4 114 Meningeoma **des**
5 114a Psammoma
6 144 Melanoma
7 145 Teratoma of the anterior mediastimun

Macrosamples
1 Meningeoma
2 Schwannoma (Neuroma)
3 Neurofibroma (Neurofibromatosis)
4 Glioblastoma
5 Ependymoma
6 Melanoma

1 № 111 SCHVANNOMA (NEUROLEMMOMA) H & E **des.**
Microscopically: Schwannoma contains areas termed Antoni A tissue intermixed with looser, myxoid regions termed Antoni B tissue. In the denser areas cell nuclei may form orderly palisades, termed "Verocay bodies".
Grossly: Schwannoma presents as well circumscribed gray- white masses attached to peripheral nerve, cranial nerve or spinal nerve root as well.
Definition: Schwannoma is benign tumor derived from Schwann cells of the peripheral nerve sheath.
It is mature tumor with tissue atypism and expansive growth.
It gives no metastasis, no recidives.
Malignant analogue is named neurosarcoma.
Organs: the eighth cranial nerve, the skin.
Clinical signs: it may be as asymptomatic mass or induce neurological deficit and pain.

2 №115 GLIOBLASTOMA MULTIFORME H & E **des**
Microscopically: It presets in a serpentine pattern occurring in areas of hypercellularity with high anaplastic cells crowded along the edges of the necrotic regions producing the so-called pseudopalisading.
Grossly: Glioblastoma multiforme is an irregular medium enhancing lesion associated with considerable edema. It is infiltrative with irregular areas of hemorrhage, necrosis and cystic change.
Definition: Glioblastoma multiform is malignant tumor derived from glial cells.
It is immature tumor with cellular and tissue atypisms and infiltrative growth. Very rare metastasizes outside CNS.
Organs: The medium regions of the brain.
Clinical signs: Headache with increasing intracranial pressure or seizures.
Treatment involves surgical resection followed by radiation therapy and/or chemotherapy.

3 №114 MENINGEOMA H & E **des.**

Microscopically: Some recapitulation of the compact cellular whorls seen in the normal arachnoid mater.
Grossly: Meningeoma presents firm lobulated white- gray lesion attached to the dura mater. A sharp boundary is usually present between the tumor and the adjacent brain or spinal cord.
Definition: Meningeoma is benign tumor derived from the meningothelial cells to the arachnoid mater.
It is mature tumor with tissue atypism and expansive growth.
It gives no metastases, no recidives.
Common histological types include syncythial, fibroblastic and Psammoma.
Malignant analogue is named memingosarcoma or malignant meningeoma.

4 **№**114a PSAMMOMA H & E
Microscopically: It demonstrates calcification. Calcification takes the form of concentrically laminated, calcified granules termed Psammoma bodies.
Grossly: Psammoma is a variant of Meningeoma.
Clinical signs: Increasing of intracranial pressure accompanied by marked and focal neurological deficits is noted.

5 №144 MELANOCARCINOMA (MELANOMA, MALIGNANT MELANOMA) H & E
Microscopically: It contains large cells with large nuclei with irregular contours having chromatin characteristically clumped at the periphery of the nuclear membrane and marked red (eosinophilic) nucleoli. Spindle and epithelioid cells can be seen. Cells grow in poorly formed nests. The nature and extent of the vertical growth phase determine the biologic behavior of malignant melanoma.
Grossly: Melanoma is the pigmentation occurring in shades of black, brown, red, dark blue and gray. The boundaries are irregular and often “notched”.
Definition: Melanoma is malignant tumor derived from melanocytes.
It is immature tumor with cellular and tissue atypisms and infiltrative growth.
It spreads in hematogenic and lymphogenic pathways and gives recidives.
Organs: the skin, the oral and anogenital mucosal surfaces, the esophagus, the meninges, the eye.
Etiology: sun-exposed skin, preexisting nevus (a dysplastic nevus), hereditary factors, exposure to certain carcinogens.
Clinical signs: Melanoma is usually asymptomatic. The most important sign is a change in color or size in a pigmented lesion. Pain and itching may accompany it.

6 №145 TERATOMA OF THE ANTERIOR MEDIASTINUM H&E
Microscopically: The totipotential cells are differentiated along various germ layers producing tissues: the skin, muscle, fat, gut epithelium, tooth structures.
Grossly: The node may be soft or solid with structures containing hair and cheesy sebaceous material, of grey –white and yellow color.

Definition: Teratoma is benign tumor made up of a variety of parenchymal cell types representative more then one germ layer, usually all the three. They arise from totipotential cells.
It is mature tumor with tissue atypism and expansive growth.
It gives no metastases, no recidives.
Malignant analogue is named malignant teratoma (teratoblastoma).
Clinical signs: Benign teratomas are encountered in younger infants (about four months). In adult ages teratoma may be seen in ovaries.

Unit 13 TUMORS OF THE HEMATOPOIETIC AND LYMPHOID SYSTEMS (HEMOBLASTOSIS). RADIATION SICKNES

Definitions: Hemoblastosis is a total term to designate tumors of the hematopoietic and lymphoid systems.
1 ***Leukemias*** (syn. Leucosis) are the systemic neoplasms to arise in the bone marrow and circulate in the peripheral blood.

Leukemias are classified as follows:

I. In accordance with the state of maturity of the leukemic cells:

1 Acute Leukemias are characterized with replacement of the bone marrow with **immature cells** (called "**blasts**" Leukemias).

2 Chronic Leukemias-are characterized with replacement of the bone marrow with **mature** cells (called "**cytics**" leukemias).

II. Of the **cell type** involved (according to the cytogenesis):

Acute	Chronic:
1 **Lymphoblastic** leukemia	1.**Lymphocytic** leukemia
2 **Myeloblastic** leukemia	2.**Myelocytic** leukemia
3 **Monoblastic** leukemia	3.**Monocytic** leukemia
4 **undifferentiated cell** leukemia (immature cells without cytochemical identification).	4.**Erythremia** (polycythemia vera).

Etiology: 1.Ionizing radiations.
2. Chemicals.
3. Viruses (HTLV-1 and EBV).

*Pathogenesis***: Leukemias** are primary disorders of the bone marrow. There is initiation of neoplastic proliferation of white blood cells. Bone marrow becomes pyoid. The leukemic cells spread from bone marrow into the blood, in large amounts. These cells also infiltrate the liver, spleen, lymph nodes and other tissues throughout the body, causing enlargement of these organs.
As the leukemic cells accumulate in the marrow, they suppress normal hematopoietic stem cells development.
Leukemic infiltrate- is local metastasis with the growth of leukemic cells.
Complications: The patients have anemia, thrombocytopenia, infection complications (pneumonia, sepsis), bleeding (petechiae, ecchymoses, epi-

staxis, gum bleeding and others), and necrotic complications (ulcer, necrotic tonsillitis and others). These complications may be the cause of death.

Clinical features and Signs:

1 Philadelphia chromosome is found within leukemic cells.

2 Blood test shows increase of leukocytes anemia, cases of thrombocytopenia.

3 Bone marrow becomes pyoid.

4 Spleen is enlarged mass up to 4-5 kg with myelocytic leukemic infiltration. Lymphoid cells are atrophic. There may be ischemic infarction and scar area within the spleen.

5 Lymph nodes are enlarged as well. There is myeloid leukemic infiltration within lymph nodes. Lymphoid cells are atrophic.

2 ***Lymphomas*** are tumor masses within either lymph nodes or other organs.

Definition: Lymphoma is a regional tumor disease of the peripheral lymphoreticular tissue, particularly in lymph nodes.

Classification Lymphomas are classified as follows:

1 Non-Hodgkin's lymphomas
- -small lymphocytic lymphomas
- -large cell lymphomas
- -Lymphoblastic lymphomas
- -Burkitt's lymphoma.

2 Hodgkin's disease (Lymphogranulomatosis).

Radiation sickness is injury produced by **ionizing** radiation.

Classification: a) acute; b) chronic.

All types of radiation exert their effects on cells causing alterations of the cells. The most important direct or indirect targets are DNA, lipids (membranes) and proteins (enzymes).

Biological effect depends on the physical properties of the radiation factors 1) type of radiation; 2) absorbed dose; 3) direct or indirect action; 4) time of action.

Biological effect depends on the cellular properties: 1) mitotic phase; 2) type of the cell; 3) water concentration; 4) cumulative effect of the cell.

Microsamples:

№256 Liver with myeloid leukemia (leucosis) **des**.

№258.Liver with lymphocyte leukemia (leucosis) **des.**

№259.Lymph node (or spleen №260) designates metastases with lymphogranulomatosis. (Hodgkin's disease) **des.**

№295.Palatine tonsil with radiation injury.

№297.Lung with radiation injury.

Macrosamples:

1. The set of organs with leukemia.

2. Gangrenous amygdalitis.
3. Hemorrhagic diatheses (hemorrhage within the brain, within the epicardium, within the kidney pelvis).
4. Metaplasia of the yellow bone marrow into red.
5.”Porphyric” spleen.
6. The organs with generate atrophy (heart, spleen).
7. Anencephaly.
8. Wound healing retardation.

1 №256 LIVER WITH MYELOID LEUKEMIA (LEUCOSIS) H and E **des**.
(chronic myelocytic leukemia).
Microscopically: Leukemic infiltrations mainly of promyelocytes and myelocytes are localized in hepatic lobules between hepatic bulks. Hepatocytes suffer compression due to leukemic infiltrations with hypoxia. The process of Fatty degeneration (dystrophy) occurs.
Grossly: The liver is considerably enlarged, (mass may be to 4 kg. and over) with smooth surface and of grey-brown color.
Definition Chronic myeloid leukemia is a system malignant tumor disease of hematopoietic tissue, characterized by diffuse replacement of the bone marrow by mature neoplastic cells of the myeloid stem (promyelocytes, myelocytes and metamyelocytes).
Consequences: blast crisis, decreased immunity to diseases.
Complications: hemorrhage, necrotic and purulent processes.
Causes of death: blast crisis and complications.

2 №258 LIVER WITH LYMPHATIC LEUKEMIA (chronic lymphocytic leukemia) H and E. **des.**
Microscopically: Leukemic infiltrations mainly of prolymphocytes and lymphocytes are localized in the portal tract, periportal connective tissue and in the stroma between lobules. Leukemic infiltrations with small, mature-like lymphocytes manifest lymphomas.
Grossly: The liver is enlarged, of gray-brown color.
Definition: chronic lymphocytic leukemia (CLL) is a systemic malignant tumor disease of hematopoietic tissue, characterized by diffuse replacement of the bone marrow by mature neoplastic cells of the lymphoid stem (prolymphocytes and lymphocytes).
Clinical Sings:
1 CLL typically affects individuals over 50.
2 In more than 95% of cases, CLL is a neoplasm of B cells and only 5% - are tumors of T –cells.
3 The leukemic B cells fail to respond to antigene stimulation. Patients have hypogammaglobulinemia and they show increased susceptibility to bacterial infections.

4 15% of patients have antibodies against red cells, giving rise to an auto-immune hemolytic anemia.
5 The patients have generalized lymphadenopathy and heptosplenomegaly.

3№259 LYMPH NODE (OR SPLEEN №260) WITH LYMPHOGRANULOMATOSIS (OR HODGKIN'S DISEASE) H & E. **des.**
Microscopically-The lymphoid tissue is depleted. The tumor is composed of atypical binucleate Reed - Sternberg – Berezovsky cells surrounded by multiple cell types, including atypical histiocytes – Hodgkin's cells, eosinophies, lymphocytes, plasma cells, benign histiocytes. The Foci of the necrosis and sclerosis may be seen in lymph node.
It is lymphogranulomatosis, mixed cellular type.
Grossly: lymph nodes are enlarged, painless, rich, of grey-pink color and may be joined in conglomerates (packets).
the spleen with lymphogranulomatosis is the so-called "Porphyric" spleen. There are small splenic enlargements with grey sites of necrosis and sclerosis between red spleen tissues.
Definition: Lymphogranulomatosis is a malignant tumor of lymphoid tissue with lesion of lymph nodes and organs, characterized by growth of the giant cells called **Reed-Sternberg – Beresovsky** cells, large and small atypical histiocytes (Hodgkin's cells) and inflammatory infiltration.
The lymphoid tissue is depleted due to the development of necrosis and sclerosis.
Etiology: EBV infection.
Classification: Lymphogranulomatosis may be:
1. **Local** lymphogranulomatosis, involving a single node or chain of nodes in one group of lymph nodes (usually neck nodes).
2. **Generalized** lymphogranulomatosis, characterized by spreading of pathological process to other groups of lymph nodes and organs (spleen).
Histological variants of the lymphogranulomatosis.
1 With lymphocyte predominance.
2 Nodular scleroses.
3 Mixed cellularity.
4 With lymphocyte depletion.
Clinical significance: 3 and 4 variants are characterized by unfavorable prognosis.

№297 LUNG WITH RADIATION INJURY H & E.
*Microscopically***:** A variety of degenerative changes occur, including endothelial cell swelling and vacuolation, or even dissolution with total necrosis of the walls of small vessels with rupture or thrombosis.
Etiology: X-rays and Gamma rays; Alpha and Beta particles and protons.
Pathogenesis: May occur acute respiratory distress syndrome (ARDS), edema and interstitial fibrosis.
Result is in hemorrhage and edema.

Clinical sing: respiratory failure

1 The set of organs with leukemia.
The set of organs contents: liver, spleen, lymph nodes, kidney, heart, large and small intestine.
-liver is enlarged with smooth surface, of grey-brown color on cut section.
-spleen is substantially enlarged, grey-red color, with gray-white areas of the ischemic in farts and scar.
-lymph nodes are greatly enlarged as well, rich, of grey- pink color.
-solitary and group lymph follicles (Peyer's patches) of the large and small intestine are above massively enlarged one. Some of these lymph Follicles may occur with local ulceration.
-kidney is enlarged too, of grey color.
-heart is of soft consistency, yellow color or may present "tiger heart" picture.
In the subendocardial surface of the heart and in the mucous membrane of the renal pelvis hemorrhage may occur (looks like petechiae).
Enlargement of all of these organs are result of the leukemic infiltration.
2 *Gangrenous amygdalitis.*
Grossly: Nasopharyngeal glands (palate lymphoid structures and glands) are of black color, disintegrated of soft consistency. This disease may be the complication of leukemia.
3 Anencephaly.
Grossly: the orbital bones are of nearly normal size, despite of absence of the brain and cranial bones.
This congenital malformation is the most common and severe of cranial neural tube defects.
Causes: Ionizing radiation with DNA damage of fetus with destruction of neurons and glial cells.