**POLTAVA STATE MEDICAL UNIVERSITY**

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WITH AUTOPSY COURSE


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Навчальний посібник "Спеціальна патоморфологія" (англійською мовою) розроблений на кафедрі патологічної анатомії з секційним курсом ПДМУ професором Старченко І.І., доцентом Прилуцьким О.К., доцентом Филенко Б.М., асистентом Задворновою А.П., асистентом Ніколенко Д.Є.

У посібнику для кожного заняття представлені основні питання теми, практичні навички, які повинні бути сформовані в студентів, алгоритми опису макро- і мікропрепаратів. Кількість і варіабельний рівень наведених тестів, дозволяє використовувати їх в якості підготовки студентів до складання ліцензованого інтегрованого іспиту «КРОК-1».

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**CONTENTS**

# ATHEROSCLEROSIS AND ARTERIOSCLEROSIS. HYPERTENSION

***Arteriosclerosis*** is a group of diseases characterized by thickening of the walls of the arteries due to the growth of connective tissue and loss of their elasticity.

*Forms of arteriosclerosis*

(depending on the etiology, pathogenesis and morphological changes):

1. Atherosclerosis (metabolic arteriosclerosis)
2. Arteriosclerosis (hyalinosis of arterioles in hypertension)
3. Menkeberg's disease (sclerosis and calcification of the middle membrane of the arteries).

## Atherosclerosis

***Atherosclerosis*** (from the Greek athere – pulp and sclerosis – compaction) is a chronic disease that occurs as a result of impaired fat and protein metabolism, characterized by damage of the arteries of elastic and elastic-muscular type in the form of focal deposits of lipids, proteins and reactive growth of connective tissue in the intima with the formation of fibrous plaques.

*Epidemiology*:

- men over the age of 40 get sick more often;
- women get sick mainly after menopause;
- more common in economically developed countries;
- mortality from complications of atherosclerosis in Ukraine ranks first (3 times more common than mortality from malignant tumors).

*Etiopathogenetic factors.* Atherosclerosis - polyetiological disease:

- alimentary;
- metabolic: exo- and endogenous (hypercholesterolemia, hypertriglyceridemia, hyper-β-lipoproteinemia and hypo-α-lipoproteinemia (LD-lipoproteins);
- hormonal (diabetes, hypothyroidism, obesity);
- hemodynamic (hypertension);
- nervous (stress);
- vascular (arteritis, thrombosis, intoxication);
- hereditary and ethnic (familial hypercholesterolemia).

*Theories of atherosclerosis:*

- alimentary dyslipoproteinemia (alimentary infiltration theory of MM Anichkov, 1912);
- hyper-β-lipoproteinemia (Chazov-Anestiadi immunological theory, 1966);
- damage to the arterial wall (intima) by various factors with the formation of parietal thrombi, which "builds" atherosclerotic plaque (thrombogenic theory Rokytanskyi-Duged, 1955);
- disorders of neuroendocrine regulation of fat-protein metabolism of the vascular wall, vasomotor disorders (neuro-metabolic theory OL Myasnikov, 1960);
- age-related sclerotic changes of the arterial wall (gerontological theory of IV Davydovskyi, 1966).

*Morphogenesis of atherosclerosis* is a staged process that has macro- and microscopic manifestations.

**Accordance of macro- and microscopic changes in atherosclerosis**

| *Macroscopic changes* | *Microscopic changes* |
|---|---|
| Fat spots and streaks | Prelipid |
| | Lipoidosis |
| Fibrous plaques | Liposclerosis |
| Stage of complications | Atheromatosis |
| | Stage of complications |
| Atherocalcinosis | Atherocalcinosis |

*Prelipid stage*

- changes that characterize metabolic disorders – hypercholesterolemia, increase of LDL (low-density lipoprotein), VLDL (very low-density lipoprotein) and decrease of HDL (high-density lipoprotein), increase plasma proteins;
- damage of the vascular wall:
  - destruction of the endothelium, basal membranes of the intima, elastic and collagen fibers,
  - accumulation of acidic glycosaminoglycans with the development of mucoid swelling,
  - increasing the permeability of the vascular wall with the accumulation of fibrinogen in the internal membrane.

*Stage of lipoidosis*

*Macroscopically:* the formation of fat spots and streaks that do not rise above the surface of the intima, due to infiltration of the vascular wall with lipids, lipoproteins and proteins.

*Microscopically:* focal infiltration of the intima by lipids, which turn orange with Sudan III. Fats are captured by macrophages, which have optically empty vacuoles in the cytoplasm when stained with hematoxylin and eosin ("foam cells"), and when stained with Sudan III, the inclusion of yellow-orange color – xanthoma cells (Greek xanthos – yellow). Destruction of elastic membranes is noted.

*Consequences:* damages are reversible or irreversible (incomplete regeneration).

*Stage of liposclerosis*

*Macroscopically:* fibrous plaques – dense, oval or round, gray-white (white-yellow) formations that rise above the surface of the intima.

*Microscopically:* growth of connective tissue and thin-walled vessels associated with vasa vasorum, with areas of lipid deposition and a large number of xanthoma cells, destruction of elastic and argyrophilic membranes.

*Consequences*: irreversible changes, narrowing of the lumen of blood vessels (stenotic atherosclerosis).

*Stage of atheromatosis*

*Macroscopically:*inside the plaque there is a decay of fat-protein complexes with the formation of detritus, resembling the contents of atheroma.

*Microscopically:* the formation of an amorphous fine-grained mass consisting of cholesterol crystals, fatty acids and destroyed collagen and elastic fibers. Atheromatous detritus is delimited by mature connective tissue (plaque cover). The plaque sinks deep due to the destruction of smooth muscle fibers.

*Consequences:* the initial stage of complications.

*Stage of complications*

*Macroscopically:*

- hemorrhage inside the plaque – intramural hematoma,
- destruction of the plaque tire – ulceration,
- formation of blood clots at the site of atheromatous ulcer.

*Microscopically:* the edges of the atheromatous ulcer are eroded, uneven, the bottom is formed by a muscular layer or adventitia, the defect is covered with thrombotic layers.

*Consequences:*

- formation of an obstructive thrombus with the development of infarction,
- embolism by atheromatous masses (fat embolism),
- thromboembolism,
- aneurysm formation,
- bleeding when the vascular wall is destroyed.

*Atherocalcinosis*

*Macroscopically:* the plaque is gray-white, stony density, is cut with a crunch (petrification of the plaque), the vascular wall is sharply deformed.

*Microscopically:* deposition of calcium salts in the fibrous tissue of the plaque, atheromatous masses with the formation of dense, brittle plates.

*Localization of atherosclerotic lesions:*

- near a branch of small arteries,
- bifurcation of blood vessels,
- basal part of the vessel (proximal),
- diffuse.

*Clinical - morphological forms of atherosclerosis*:

- aortic atherosclerosis,
- cardiac (coronary heart disease),
- cerebral (cerebrovascular diseases),
- atherosclerosis of the arteries of the lower extremities,
- renal (renal arteries),
- mesenteric (intestinal arteries).

*Atherosclerosis of the aorta* is characterized by a predominant lesion of the abdominal aorta. Atherosclerosis of the aortic arch is the basis of the aortic arch syndrome, atherosclerosis of the aortic bifurcation with thrombosis is clinically manifested by Lerich's syndrome.

**Aortic aneurysm** - a protrusion of the vascular wall in the area of atherosclerotic damage.

Classification of aneurysms

- By form:
  - cylindrical
  - sack-shaped
  - wedge-shaped
  - stratifying - the channel is covered with endothelium between the middle membrane and intima
- By wall structure:
  - genuine (true) – the aneurysm wall is represented by aortic tissues

- spurious (false) – the wall is formed by adjacent organs

*Aneurysm complications:*

- rupture with massive bleeding
- atrophy of surrounding tissues (sternum, vertebral bodies).

*Atherosclerosis of the arteries of the lower extremities* (mainly femoral) is characterized by:

- muscle atrophy
- cooling of the limb
- intermittent claudication (pain when walking)
- skin atrophy, cessation of hair growth, trophic ulcers.

*Complications* - gangrene.

*Atherosclerosis of the intestinal vessels (mesenteric form)* leads to intestinal gangrene.

*Atherosclerosis of the renal arteries* most often develops at the site of discharge of the main trunk or segmental arteries. The process is often one-sided.

*Macroscopically* – atherosclerotic shrunken kidney: wedge-shaped defects on the surface of the kidney, **large-humped kidney**.

*Microscopically*: atrophy of the parenchyma with collapse of the stroma, followed by replacement of this area with connective tissue or the development of a infarction with scar formation.

*Complication:*

- symptomatic hypertension
- uremia.

## Hypertensive disease

***Arterial hypertension*** – a stable increase in blood pressure (BP): systolic above 140 mm Hg and/or diastolic above 90 mm Hg, due to increased peripheral vascular resistance (resistance).

Types of hypertension:

- essential (primary, idiopathic) arterial hypertension – hypertensive disease
- secondary (symptomatic) hypertension.

***Symptomatic hypertension*** occurs secondarily in diseases:

- of kidney
- of nervous system (tumors, injuries, inflammatory processes)
- endocrine pathology (aldosteronism, pheochromocytoma, thyrotoxicosis)
- vascular diseases (aortic arch atherosclerosis, aortic coarctation, vasculitis).

***Hypertensive disease*** – a chronic disease of unknown etiology with a hereditary predisposition, which is characterized by a stable increase in blood pressure in the absence of organic damage to organs and systems that regulate it.

*Epidemiology*

- morbidity is common in economically developed countries (increasing psycho-emotional stress – «the disease of unresponsive emotions» (GF Lang),
- in Ukraine, an average of 20-25% of the population suffers from hypertensive disease,
- gender: men get sick more often than women,
- urbanization: urban residents get sick 4-6 times more often than in rural areas,
- age: the incidence increases with age,

- mortality from hypertensive disease is associated with complications of the disease (myocardial infarction, cerebral infarction, hemorrhagic stroke, renal failure).

*Hypertensive disease risk factors:*

- genetic factors – inheritance of insufficient sodium excretion by kidneys, damage to sodium-potassium transport in myocytes (smooth muscle cells) of arterioles; change in the genes of the renin-angiotensin system;
- excessive salt intake in combination with a genetic predisposition to hypertension;
- psycho-emotional overstrain (stress);
- smoking, alcohol abuse, weight gain, hypodynamics, occupational hazards (vibration, constant noise, etc.).

*Pathogenesis of hypertensive disease.* Nervous, hormonal, renal and hereditary factors take part in the mechanism of development of hypertensive disease.

- Theory of primary increase in cardiac output: decrease of Na ion excretion → increase of circulating blood volume → increase of cardiac output → increase of peripheral vascular resistance → increase of arterial pressure in vessels of medium and large caliber.
- Theory of vasoconstriction: psychoemotional overload → prolonged excitation of the center of vascular tone regulation → activation of the sympatho-adrenal system → spasm of the renal arterioles → activation of the renin-angiotensin system → spasm of the arterioles.

*The course of hypertensive disease:*

- malignant
- benign

***Clinical and morphological signs of hypertensive disease***

<u>*Malignant hypertensive disease*</u> is characterized by a acute rise in blood pressure due to spasm of the arterioles – a **hypertensive crisis**.

*Microscopic changes in blood vessels:*

- significant narrowing of the lumen of the arterioles (spasm),
- corrugation and destruction of the basal membrane of the vascular endothelium,
- endothelium in the form of a palisade (columnar protrusion into the lumen of the vessel),
- detachment of the endothelium from the basal membrane,
- plasma impregnation or fibrinoid necrosis of the arteriole wall,
- thrombosis, sludge phenomenon.

<u>*The benign course of hypertensive disease*</u> is characterized by the development of three successive stages.

Stage I – *transient (preclinical)* - episodic increase in blood pressure.

*Vascular changes*: hypertrophy of smooth muscle cells and elastic membranes of blood vessels.

*Cardiac changes*: compensatory left ventricular hypertrophy (left ventricular thickness up to 18 mm, heart weight 400 g).

Stage II – *widespread vascular changes* – a steady constant increase in blood pressure.

*Vascular changes*: plasma impregnation of arterioles → hyalinosis of arterioles (arteriolosclerosis); elastofibrosis of arteries of elastic and muscular-elastic type (arteriosclerosis); damage of the arterial endothelium → atherosclerosis of the arteries with the formation of circular plaques.
*Heart changes*: concentric left ventricular hypertrophy (tonogenic dilatation, weight up to 800-1000 g, left ventricular wall thickness 2-3 cm) → eccentric left ventricular hypertrophy (myogenic dilatation).
Tonogenic dilatation - increase in the size of the heart due to the lengthening of the external tract to 11-13 cm
Myogenic dilatation is an increase in the size of the heart due to the lengthening of both the efferent and afferent tracts.
Stage III – *secondary changes in the organs* due to changes in blood vessels, disorders of intra-circulatory circulation:

- diffuse small focal cardiosclerosis
- arteriosclerotic nephrosclerosis (primary wrinkled kidneys)
- hemorrhages in the brain
- atherosclerotic dementia
- secondary diabetes mellitus
- degenerative adenomas and adrenal atrophy

*Clinical and morphological forms of hypertensive disease*

- cardiac form (ischemic heart disease)
- cerebral form (cerebrovascular diseases)
- renal form: acute, chronic

The acute renal form develops in the malignant course of hypertensive disease due to thromboembolism or arterial thrombosis.
*Macroscopically:* the kidneys are reduced, variegated, the surface is fine-grained.
*Microscopically:* subtotal or total fibrinoid necrosis of arterioles and capillaries of glomeruli, edema of the stroma with hemorrhage, protein dystrophy of the epithelium of the tubules, cellular reaction, sclerosis.
*Consequence:* acute renal failure.
Chronic renal form in the benign course of hypertensive disease.
*Macroscopically:* the kidneys are significantly reduced, dense with a fine-grained surface, atrophy of the cortical substance.
*Microscopically:* hyalinosis of arterioles, arteriolosclerosis, collapse of capillary loops and sclerosis of glomeruli, atrophy of nephron tubules with sclerosis.
*Consequence:* chronic renal failure (azotemic uremia).
*Complications and causes of death in hypertensive disease:*

- acute heart failure (ischemic myocardial infarction)
- chronic heart failure (cardiosclerosis)
- cerebrovascular insufficiency (hemorrhagic, ischemic stroke)

***Training macropreparations***

**Aortic atherosclerosis**. The shape of the body is preserved, the inner surface of the wall is gray, tuberous. There are gray-yellow atherosclerotic plaques on the surface of the intima, which rise above the level of unchanged intima, some plaques with ulceration in the center.

**Aortic atherosclerosis with thrombosis**. Fragment of the abdominal aorta, intima of the vessel is deformed. Fat spots and streaks, fibrous plaques are identified on the surface, some with ulceration. A thrombus of dense consistency with a rough surface measuring 10x1 cm, gray, tightly attached to one of the plaques.

**Atherosclerotic wrinkled kidney.** The kidney is slightly reduced, large- tuberous, there is an area of cicatricial involvement on the surface.

**"Beef" heart (Cor bovis)**. The heart is increased in size, the wall thickness of the left ventricle is 2.5-3.0 cm, the cavity is expanded due to the external tract, the afferent tract is not changed.

**Arteriosclerotic nephrosclerosis (primary wrinkled kidney)**. The kidney is sharply reduced in size, its surface is fine-grained, the capsule is thin.

### *Training micropreparations*

**Aortic atherosclerosis** (Sudan staining III): the lumen of the vessel is narrowed due to atherosclerotic plaque. Orange masses are determined in the center of the plaque, the plaque cover is represented by hyalinized connective tissue.

**Arteriosclerotic nephrosclerosis** (hematoxylin and eosin staining): the walls of the arterioles are sharply thickened, homogeneous, unstructured, the lumen is narrowed, obliterated in places. Collapse of glomeruli with replacement of connective tissue or masses of hyaline with the formation of "hyaline" balls. The tubules are atrophied. The amount of intermediate connective tissue is increased. Preserved nephrons are compensatory hypertrophied.

**Myocardial hypertrophy** (hematoxylin and eosin staining): muscle cells and their nuclei are sharply enlarged, round, hyperchromic.

### *Questions for self-control*

1. Atherosclerosis and arteriosclerosis: general data.
2. Morphological characteristics and stages of atherosclerosis, structure of atherosclerotic plaque.
3. Clinical and morphological forms of atherosclerosis: pathological anatomy, consequences.
4. Determination of hypertensive disease and symptomatic hypertension.
5. The course and stages of hypertensive disease.
6. Clinical and morphological manifestations of hypertensive crisis.
7. Morphological changes of arterioles in hypertensive disease.
8. Clinical and morphological forms of hypertensive disease, their consequences.

### *Examples of tests*

1. At the autopsy of a 48-year-old woman who died suddenly, yellowish areas are identified in the intima of the aorta that do not rise above its surface. Histological examination of these areas reveals cells with foamy cytoplasm, and when stained with Sudan III yellow. Determine the stage of atherosclerosis in the aorta.

A. * Lipoidosis
B. Atheromatosis
C. Ulceration
D. Liposclerosis
E. Atherocalcinosis

2. Microscopic examination of the coronary artery in the deceased 53 years old revealed a narrowing of the lumen of the vessel due to fibrous plaque with lipid impurities. Determine the stage of atherosclerosis.
A. * Liposclerosis
B. Lipoidosis
C. Dolipidna
D. Atheromatosis
E. Ulceration
3. A 70-year-old patient who died of heart failure was diagnosed with deformed, narrowed coronary arteries during autopsy. The inner surface of the arteries is hilly, the wall is whitish, brittle, stony density. What is the stage of atherosclerosis?
A. * Atherocalcinosis
B. Liposclerosis
C. Atheromatosis
D. Lipoidosis
E. Ulceration
4. A 67-year-old patient had been suffering from hypertension for 20 years. He died of chronic renal failure. What did the kidneys look like at the autopsy?
A. * Small, dense, fine-grained surface
B. Large with multiple thin-walled cysts
C. Big red
D. Big white
E. Large variegated
5. A patient with hypertension showed a significant increase in left ventricular myocardial mass. This is due to:
A. * Increased cardiomyocyte volume
B. Increase in the number of cardiomyocytes
C. Growth of connective tissue
D. Fatty myocardial infiltration
E. –

## CEREBROVASCULAR DISEASES

Cerebrovascular diseases are characterized by acute cerebrovascular disorders, the background for the development of which is atherosclerosis and hypertensive disease.
*Etiology:* spasm, thrombosis and thromboembolism of the precerebral and cerebral arteries, psychoemotional stress, which leads to angioneurotic disorders, increased vascular permeability or rupture.

*Classification:*

- transient ischemia of the brain
- stroke.

***Transient cerebral ischemia*** occurs due to short-term vascular disorders: spasm of arterioles, plasma impregnation of their walls, perivascular edema and isolated small hemorrhages.
*Macroscopically:* reversible focal changes in brain tissue - edema, diapedetic hemorrhage into the brain.

*Microscopically*: perivascular edema, dystrophic changes of cell groups; perivascular hemosiderin deposits can be identified at the site of former minor hemorrhages.

***Stroke*** – an acute local disorder of cerebral circulation, accompanied by damage to the substance of the brain and disorders of its function.

**Types of strokes**

| *Hemorrhagic stroke* | *Ischemic stroke (infarction)* |
|---|---|
| Hematoma | Ischemic |
| Hemorrhagic infiltration | Hemorrhagic |
| Subarachnoid hemorrhage | Mixed |

*Hematomas of the brain* are formed due to rupture of the vascular wall and occur in 85% of cases of hemorrhagic stroke.

*Macroscopically:* different sizes of cavities filled with blood clots and softened brain tissue (red softening of the brain), which are localized in the subcortical nodes of the brain, visual cortex, internal capsule and cerebellum, sometimes blood breaks into the lateral, III and IV ventricles of the brain.

*Microscopically:* blood, necrosis of brain tissue, siderophages on the periphery, glial cells, granular globes.

*Consequence:* strokes with a breakthrough in the ventricles of the brain always end in death. If the person survives, a cyst with rusty walls is formed.

*Hemorrhagic impregnation of the substance of the brain*.

*Macroscopically*: small hemorrhages that merge in the visual cortex and the pons and usually do not occur in the cerebral cortex and cerebellum.

*Microscopically:* among the blood-soaked brain substance are determined nerve cells with necrobiotic changes.

*Ischemic stroke* is formed by thrombosis of atherosclerotic altered precerebral or cerebral arteries.

*Macroscopically:* the center of the gray softening of the brain of different localization.

*Microscopically:*dead neurons among necrotic masses.

*Consequence:* formation of a cyst or glial scar (at the small sizes).

*Hemorrhagic stroke:* on the background of ischemia of brain tissue hemorrhages are formed. The area resembles a focus of hemorrhagic infiltration: most often in the cerebral cortex, less often – in the subcortical nodes of the brain.

*Mixed stroke* is characterized by the development of both ischemic and hemorrhagic stroke, always occurs in the gray matter of the brain.

***Training macropreparations***

**Diapedetic hemorrhage into the brain:** the shape of the organ is preserved, the size is not increased; brain pale yellow, marked border between white and gray matter; small inclusions of brown color up to 1 mm in diameter.

**Brain hematoma**: a large blood clot of brown color is present in brain tissue, brain structures are displaced; the brain tissue in the area of hemorrhage is destroyed.

**Ischemic cerebral infarction**: foci of irregular shape, flabby mushy consistency, grayish color (site of gray softening).

***Training micropreparations***

**Diapedetic hemorrhages in the brain**: small foci of erythrocytes are around the blood vessels, the substance of the brain is swollen.

### *Questions for self-control*

1. Definition of cerebrovascular disease.
2. Etiology, risk factors, background diseases in cerebrovascular diseases.
3. Classification of cerebrovascular diseases.
4. Causes and mechanisms of ischemic brain damage.
5. Consequences of ischemic and hemorrhagic cerebral infarct.
6. Complications, causes of death in cerebrovascular diseases.

### *Examples of tests*

1. A 69-year-old patient was hospitalized in a serious condition, lost consciousness, right-sided movement disorders in the extremities. According to relatives, the patient had episodes of cerebral circulatory disorders. With increasing symptoms of cerebral insufficiency, the patient died. At autopsy: in the left hemisphere of the brain found a center of unstructured grayish tissue, watery, with blurred borders. Your diagnosis.

A. * Ischemic stroke
B. Malignant brain tumor
C. Focal encephalitis
D. Senile encephalopathy
E. Hematoma of the brain

2. A 60-year-old man suffered from hypertension for a long time (blood pressure 220/110 mm Hg). Hospitalized with impaired movement in the right extremities. After 5 hours the patient died. At the autopsy: in the left hemisphere of the brain found a cavity with jagged edges, filled with red soft blood clots. Identify circulatory disorders in the brain?

A. * Hematoma
B. Hemorrhagic infiltration
C. Petechiae
D. Venous plethora
E. Thrombosis

3. A 68-year-old woman has long suffered from hypertension (blood pressure 220/110 mm Hg). Hospitalized with impaired movement in the right extremities. There have been complaints of headaches recently. 5 hours later the patient died. At the autopsy: in the left hemisphere of the brain found a cavity with jagged edges, filled with red soft blood clots. What background disease could cause a circulatory disorder in the brain of a sick woman?

A. * Hypertension
B. Ischemic heart disease
C. Glomerulonephritis
D. Atherosclerosis
E. Diabetes mellitus

## ISCHEMIC HEART DISEASE

**Ischemic heart disease (IHD)** is a group of heart diseases caused by absolute or relative insufficiency of coronary circulation.

*Epidemiology.*

a) morbidity:

- men:women (41-50 years) = 5: 1;
- men: women (51-60 years) = 2: 1

b) mortality: 26-30 years – 6.4%, 31-35 years – 11.4%. The mortality rate from **IHD** among cardiovascular diseases is 2/3 of cases.

*Risk factors for ischemic heart disease:*

- hypercholesterolemia, hypertriglyceridemia;
- hypertension;
- decreased glucose tolerance;
- alimentary obesity, sedentary lifestyle;
- gender – male; age – after 40 years;
- smoking, alcohol abuse.

*Diseases pathogenetically associated with ischemic heart disease:*

- atherosclerosis of the coronary arteries (96%),
- hypertensive disease.

*Classification of ischemic heart disease*

Acute form:

- Acute ischemic myocardial dystrophy,
- Myocardial infarction.

Chronic form:

- Cardiosclerosis postinfarction large focal,
- Cardiosclerosis atherosclerotic, diffuse, small focal,
- Chronic heart aneurysm.

***Acute (ischemic) myocardial dystrophy*** is a form of ischemic heart disease that occurs as a result of short-term episodes of coronary insufficiency.

*Macroscopically:* there are no changes, when using salts of tetrazolium, the sites of ischemia look light against a dark background of an unchanged myocardium.

*Microscopically:* paretic dilation of capillaries, erythrocyte stasis, interstitial edema, hemorrhage and leukodiapedesis, accumulation of leukocytes on the periphery of the ischemic zone. Necrobiosis of muscle fibers, loss of striation, glycogen.

***Myocardial infarction (MI)*** is a form of ischemic heart disease, which is characterized by the development of local myocardial necrosis due to acute mismatch of coronary circulation and myocardial oxygen demand.

*Classification of myocardial infarction*

- By time of occurrence:
  - primary (acute) lasts 28 days,
  - recurrent develops within 28 days after acute one,
  - repeated develops 28 days after acute MI.
- By localization in different parts of the heart:
  - basin of the anterior interventricular branch of the left coronary artery (most often): the apex of the heart, the anterior and lateral walls of the left ventricle, the anterior interventricular septum;
  - basin of the circumferential branch of the left coronary artery (rarely): the posterior wall of the left ventricle, the posterior interventricular septum;
  - right coronary artery (very rare): right ventricle.
- By localization in the heart muscle:
  - subendocardial (under the endocardium),

- subepicardial (under the epicardium),
- intramural (in the middle part of the muscle),
- transmural (for the entire thickness of the heart muscle).

- By prevalence:
  - small-focal,
  - large-focal,
- By the course:
  - stage of necrosis,
  - scarring stage.

*Pathomorphological changes* depend on the stage and duration of the disease.

Dynamics of morphological changes of myocardial infarction

| ***Term*** | ***Macroscopically*** | ***Microscopically*** |
|---|---|---|
| Minutes | There are no changes, dilation of the heart cavities with the presence of liquid blood, uneven myocardial blood supply. Inconsistently small hemorrhages under the epicardium and endocardium. | Paretic dilation and plethora of capillaries and veins, diapedesis of erythrocytes. Focal fragmentation of muscle fibers, increased striation of myocytes. Uneven staining of sarcoplasm. |
| 3-4 hours | The same changes. Myocardial edema.The site of infarction is indistinctly delimited, uneven blood supply, focal hemorrhages. Coronary thrombosis is possible. | The same changes. Stromal edema. Karyopyknosis and karyolysis, sarcoplasmic oxyphilia, focal edema, and areas of deep muscle fiber breakdown. Focal plasma infiltration of the intima of the coronary arteries. Plasmo- and hemorrhage in the thickness of atherosclerotic plaques. Parietal thrombi are possible. |
| 1st day | The area of the infarction with clear contours, with a hemorrhagic halo. Hemorrhages in infarction (variegation) are possible. | Common signs of necrobiosis and necrosis. Leukocyte infiltration appears in the stroma. |
| 2nd-3rd day | Infarction with clear contours, dry, dense. | The spread of leukocyte infiltration into the depth of the necrotic zone. |
| the end of 1stweek | A yellow border appears around infarction. Eventually, it turns yellow, yellowish-green with softening. | In the peripheral zone of the infarction, there is an ingrowth of granulation tissue, disintegration and resorption of muscle fibers. |
| 2ndweek | On the periphery of the infarct, dark red juicy granulation tissue, which fades by the end of 2 weeks, becomes translucent, gelatinous. | Disintegration and resorption of necrosis with its partial replacement by granulation tissue with infiltration by lymphocytes, plasma cells, eosinophils, macrophages, fibroblasts. |
| 3rd week | On the periphery of the | Simultaneously with the disintegration |

| | | |
|---|---|---|
| | granulation tissue appear whitish layers of scar tissue, | and resorption of the area of necrosis there is an increase in the number of collagen fibers in the granulation tissue. On 14-17 days, leukocytes disappear. |
| 4$^{th}$week | Juicy full-blooded scar tissue prevails. | Small areas of necrosis. Collagenization of granulation tissue with the disappearance of cellular elements and capillaries. |
| 5$^{th}$week | The area of the infarction has a whitish color. | Granulation tissue turns into young scar tissue, thin elastic fibers and thin broad-blooded sinusoidal vessels appear. |
| 2,3,5 months | The formation of white scar tissue with clear uneven contours, dense to the touch. | Mature scar tissue consisting of collagen and elastic fibers. |

*Complications of myocardial infarction:*

- pulmonary edema,
- acute heart aneurysm,
- myomalacia with rupture of the heart,
- chronic heart aneurysm,
- erosions and acute gastric and intestinal ulcers,
- thromboendocarditis (70-80%).

***Cardiosclerosis*** is a form of chronic ischemic heart disease, which is characterized by the growth of connective tissue in the myocardium.

*Classification:*

- atherosclerotic, diffuse, small focal
- postinfarction large focal.

Atherosclerotic, diffuse, small-focal cardiosclerosis occurs against the background of atherosclerosis of the coronary arteries, due to narrowing of the lumen of blood vessels by fibrous plaques and the development of ischemia of the heart muscle. Hypoxia stimulates fibroblast proliferation and connective tissue growth.

*Macroscopically*: against the background of the unaltered myocardium, multiple dense small layers of white color are determined.

*Microscopically*: the growth of mature connective tissue around blood vessels and in the intermuscular spaces.

*Consequences:*

- chronic heart failure,
- Dressler's syndrome (pericarditis, pleuritis, pneumonitis).

*Causes of death from ischemic heart disease*:

- arrhythmia - ventricular fibrillation, asystole
- cardiogenic shock
- rupture of the heart with tamponade
- aortic thromboembolism
- chronic heart failure in the stage of decompensation.

***Training macropreparations***

**Myocardial infarction.** The area of yellow-gray color with clear boundaries is defined on the anterior-apical area of the myocardium with the transition to the

septum. White infarction is surrounded by dark red hemorrhage (hemorrhagic crown). The wall thickness of the left ventricle is approximately 1.8 cm.

**Postinfarction cardiosclerosis**. In the myocardium is defined by a large field of scar connective tissue (at the site of a previous myocardial infarction), with clear, uneven contours.

**Hemopericardium**. The heart is slightly increased in size, under the pericardium are determined by the brown color of the mass – blood.

### *Training micropreparations*

**Myocardial infarction** (staining with hematoxylin and eosin): necrotic altered cardiomyocytes with karyolysis, coagulation and disintegration into clumps of myoplasm, lack of transverse striation; dilated whole blood vessels, hemorrhages (hemorrhagic corolla) and infiltration by polymorphonuclear leukocytes, macrophages, plasma cells; areas of preserved myocardium.

**Focal cardiosclerosis** (hematoxylin and eosin staining): in the myocardium there is an area of coarse fibrous scar connective tissue, muscle fibers around the scar are thickened, with large nuclei.

**Cardiosclerosis** (Van Gizon staining): Among the muscle tissue of the area of growth of coarse connective tissue (fibrous) tissue, which stains picrofuxin in yellow-red color.

### *Questions for self-control*

1. Etiology, epidemiology, classification of ischemic heart disease.
2. Macro-microscopic changes in the stages of myocardial infarction.
3. Types and pathomorphology of chronic ischemic heart disease.
4. Complications and causes of death in ischemic heart disease.

### *Examples of tests*

1. Examination of the coronary arteries of the heart revealed atherosclerotic plaques with calcification, closing the lumen by 1/3. The muscle has small multiple whitish layers of connective tissue. What process was found in the myocardium?

A. * Diffuse cardiosclerosis
B. Tiger heart
C. Postinfarction cardiosclerosis
D. Myocarditis
E. Myocardial infarction

2. At the autopsy of the deceased from pulmonary edema in the myocardium found a large focus of yellow-gray color, and in the coronary artery - a fresh clot. Clarify the diagnosis:

A. * Myocardial infarction
B. Cardiosclerosis
C. Myocarditis
D. Amyloidosis
E. Cardiomyopathy

3. A 59-year-old patient suffering from a transmural infarction of the left ventricular myocardium died of a real rupture of the heart - cardiac tamponade. What process in the area of the heart attack could have contributed to the rupture of the heart?

A. * Autolytic processes of myocardial tissue melting (myomalacia)
B. Replacement of the infarct area with connective tissue (organization)

C. Increase in pressure in a small circle of blood circulation
D. Scar formation with thinning of the left ventricular wall
E. -
4. At autopsy, a large dense area of gray, histologically composed of coarse-grained connective tissue surrounded by hypertrophied muscle fibers, was macroscopically detected in the myocardium. What changes did you find in your heart?
A. * Postinfarction large-focal cardiosclerosis
B. Small focal diffuse cardiosclerosis
C. Necrotic stage of myocardial infarction
D. Ischemic stage of myocardial infarction
E. Myocarditis

## SYSTEMIC CONNECTIVE TISSUE DISEASES: rheumatism, rheumatoid arthritis, Bechterew's disease, systemic lupus erythematosus, systemic scleroderma, dermatomyositis. Heart defects.

***Systemic connective tissue diseases*** (rheumatic diseases) are a group of diseases with a staged course, characterized by systemic progressive connective tissue damage due to impaired immunological homeostasis.
This group includes:

- Rheumatism
- Rheumatoid arthritis
- Systemic lupus erythematosus
- Systemic scleroderma
- Dermatomyositis
- Bekhterev's disease
- Sjogren's disease (syndrome)
- Nodular periarteritis (NP)

### Rheumatism

***Rheumatism (Buyo disease)*** is an infectious-allergic systemic inflammatory disease of the connective tissue with a predominant localization of the process in the cardiovascular system.
*Etiology:* β-hemolytic streptococcus group A (tonsillitis, pharyngitis), polygenic heredity.
*Risk factors:*

- female,
- age 7-15 years,
- transferred acute streptococcal infection and frequent nasopharyngeal infections,
- presence of rheumatism or diffuse connective tissue diseases in relatives.

*Pathogenesis.* Antibodies (AB) that cross-react with tissue antigens are synthesized to streptococcal antigens (AG). Tissue targets for antibodies are:

- glycoproteins of heart valves (they are similar to hyaluronate [salt of hyaluronic acid] capsules of streptococcus);
- myocardial and smooth muscle sarcolemma;
- cardiac myosin (similar to streptococcal protein M) (the main virulence factor of group A streptococci).

*Clinical and anatomical forms of rheumatism:*

1) cardiovascular,
2) visceral,
3) articular,
4) cerebral,
5) nodular,
6) erythematous.

*General morphology of rheumatism.*

Productive inflammation can be common nonspecific, less often – focal with the formation of rheumatic granulomas, in the development of which there are three stages.

1) First stage:

- mucoid swelling,
- fibrinoid swelling,
- fibrinoid necrosis, around which polymorphonuclear leukocytes, lymphocytes and macrophages accumulate.

2) Second stage – activated macrophages become larger, their cytoplasm becomes basophilic with large nuclei, in which chromatin accumulates in the central part of the nucleus ("caterpillar cells")

3) Third stage – fibrinoid is resorbed by macrophages, they die or emigrate, but their released monokines stimulate fibroblasts that produce collagen fibers. Fibroblasts are large, juicy, between them thin collagen fibers are defined, as a result the fibrous-cellular scar is formed. If the resorption of fibrinoid by macrophages has not occurred, then hyalinosis develops.

***Organ morphology of rheumatism.***

Endocarditis - inflammation of the endocardium.

*Classification*:

- parietal,
- chordal,
- valvular (65-70% – mitral, 25% – mitral and aortic, 10% – aortic).

*Types of valvular endocarditis:*

*1. Diffuse endocarditis or valvulitis* – foci of mucoid and fibrinoid swelling, the endothelium is not damaged.

*2. Acute warty endocarditis*:

- fibrinoid changes,
- damage to the valve endothelium,
- parietal thrombi (warts) are formed along the closing edge of the valve cuspids,
- diffuse lymphoid-macrophage infiltrates, rheumatic granulomas in the connective tissue of the valve.

*Consequence* is valve fibrosis.

*3. Fibroplastic endocarditis*:

- severe valve fibrosis,
- formation of joints between the valve cuspids,
- fibrosis of the chordal threads.

*4. Rotary warty endocarditis*:

- on the background of fibrosis there is damage to connective tissue (fibrinoid necrosis),
- thrombi (warts) on the valves.

As a result, hyalinosis and sclerosis of the valves and chords, develops, which leads to the development of acquired heart defects.

Myocarditis - inflammation of the myocardium.

*1. Productive (granulomatous) myocarditis* – the formation of granulomas in the perivascular connective tissue throughout the myocardium (delayed-type hypersensitivity)

*2. Diffuse intermediate exudative myocarditis* (immediate hypersensitivity).

*Macroscopically:* the heart muscle is flaccid, the cavities are dilated.

*Microscopically:* edema, connective tissue plethora, significant lymphocytic, histiocytic, neutrophilic and eosinophilic infiltration of focal or diffuse serous type.

*3. Focal intermediate exudative myocarditis* – focal infiltration of the myocardium by lymphocytes, neutrophils, histiocytes.

*Consequence* is cardiosclerosis.

Pericarditis – inflammation of the pericardium:

- serous,
- serous-fibrinous ("**hairy heart**") with the organization of exudate, obliteration of the pericardial cavity and dystrophic calcification **("armored heart").**

Vasculitis – inflammation of the vessel (arteritis, arteriolitis, capillaritis) leads to obliteration of the lumen of the vessel.

Polyarthritis is an exudative serous-fibrinous inflammation of mainly large joints.

*Feature* – articular cartilage is never affected and ankylosis does not develop (as in rheumatoid arthritis).

*Microscopically*: in the periarticular tissue edema, foci of fibrinoid with lympho-macrophage reaction, resembling rheumatic granulomas (rheumatic nodules).

Minor chorea is a neurological disorder that develops mainly in children and is characterized by involuntary, chaotic, rapid movements. The mechanism of development is not clear, the striopalidar system affected.

Glomerulonephritis is a focal lesion of the vessels of the microcirculatory tract of the glomerular apparatus of the kidney. The form of glomerulonephritis depends on the composition of immune complexes: in the presence of streptococcal antigen - acute glomerulonephritis, in the presence of tissue antigens – more often mesangioproliferative.

Pneumonia (aseptic rheumatic serous or serous-desquamative) – lesions of the perivascular and peribronchial connective tissue, interalveolar septa and capillaries.

Erythema marginatum (nodules) – red spots-papules, which rise slightly above the skin, progressively increase:

- occur in 10-60% of cases, more often in children,
- the histological structure resembles rheumatic granulomas.

*Complications* of rheumatism are more often associated with heart disease:

- heart defects;
- warty endocarditis – a source of thromboembolism of the vessels of systemic circulation. In this regard, infarctions develop in the kidneys, spleen, retina, foci of softening in the brain, gangrene of the extremities;

- bonding processes in cavities.

*Death* from rheumatism can occur during an attack of thromboembolic complications, but more often patients die from decompensated heart disease.

## Heart defects

***Heart defects*** – persistent deviations in the structure of the heart with a violation of its function.

There are:

- congenital heart defects,
- acquired heart defects.

*Acquired heart defects* are morphological (organic) changes in the valvular apparatus, atrioventricular orifices or main vessels that occur as a result of disease or injury and lead to impaired intracardiac and systemic hemodynamics.

Etiology.

- Rheumatism – the most common cause of acquired heart disease (20-25% of cases)
- Infectious endocarditis
- Systemic connective tissue diseases:
  - rheumatoid arthritis
  - systemic lupus erythematosus
  - systemic scleroderma
- Atherosclerosis
- Syphilis
- Heart injury

*Classification*

- Isolated defect
  - stenosis of the orifice
  - valve failure
- Combined defects - simultaneous damage to several valves, combination of valve insufficiency and stenosis of the orifice of one location.
- By severity:
  - compensated,
  - decompensated.

*Frequency of valve damage in rheumatism:*

- mitral stenosis – 48-68%,
- aortic stenosis – 23%,
- insufficiency of aortic valves – 14%,
- tricuspid defect – 10-39%,
- combined defects.

Left atrioventricular orifice stenosis (mitral stenosis) is a heart defect characterized by narrowing of the left atrioventricular orifice, which prevents blood flowing from the left atrium to the left ventricle.

*Mechanism of development*: thickening and fusion of the flaps, narrowing of the fibrous ring.

*Morphological changes*: the orifice takes the form of a "buttonhole".

*Hemodynamic disorders*: increased pressure in the left atrium → hypertrophy and dilatation of the left atrium → increased hydrostatic pressure in the pulmonary veins and capillaries → development of brown pulmonary induration → pulmonary artery hypertension → hypertrophy and dilatation of the right ventricle → relative insufficiency of the right atrium → blood stasis in the systemic circulation.

Mitral valve insufficiency is a heart defect characterized by incomplete closure of the mitral valve leaflets and, as a result, blood flow from the left ventricle to the left atrium (mitral regurgitation).

*Mechanism of development:* cicatricial changes of the valve leaflets (their shrinkage and shortening), cicatricial changes of the heart chords.

*Morphological changes:* The valve takes the shape of a "fish's mouth".

*Hemodynamic disorders*: regurgitation of blood in the left atrium during left ventricular systole → eccentric hypertrophy of the left atrial myocardium → eccentric hypertrophy of the left ventricular myocardium → decompensation of the left heart → blood stasis in the small circle of blood circulation → right ventricular hypertrophy → right ventricular failure.

Aortic stenosis is a heart defect characterized by narrowing of the left ventricular outflow tract in the area of the aortic valve, which impedes blood flow from the left ventricle to the aorta.

*Forms of aortic stenosis:*

- valvular,
- supravalvular,
- subvalvular.

*The mechanism of development*: the fusion of the valve leaflets together.

*Hemodynamic disorders:* impaired blood flow from the left ventricle to the aorta → concentric hypertrophy of the left ventricular myocardium → decompensation of the left ventricle with dilatation (“cor bovis”) → hypertension of the left atrium → passive retrograde venous hypertension in the lungs → left ventricular heart failure → compensatory hypertrophy of the right ventricle with its subsequent decompensation.

Aortic valve insufficiency is a heart defect characterized by incomplete closure of the valve leaflets during diastole, leading to regurgitation of blood from the aorta to the left ventricle.

*Mechanism of development*: cicatricial deformation and shrinkage of the valve leaflets with calcification.

*Hemodynamic disorders*: reverse blood flow from the aorta to the left ventricle during diastole → eccentric hypertrophy of the left ventricle ("cor bovis") → left ventricular failure with the development of hypertension in the small circulation.

Tricuspid valve insufficiency is a heart defect characterized by incomplete closure of the tricuspid valve and regurgitation of blood from the right ventricle to the right atrium.

*Mechanism of development*: cicatricial deformation and shrinkage of the valve leaflets with calcification.

*Hemodynamic disorders*: reverse blood flow from the right ventricle to the right atrium in diastole → dilatation of the right atrium → right ventricular hypertrophy

followed by dilatation → stagnation in the veins of the systemic circulation ("nutmeg liver", cyanotic induration of the kidneys and spleen).

Stenosis of the right atrioventricular orifice is a heart defect characterized by the fusion of the tricuspid valve leaflets with difficulty in blood flow from the right atrium to the right ventricle.

*Hemodynamic disorders*: compensatory hypertrophy of the right atrium → decompensation of the right atrium → venous plethora of the great circle of blood circulation.

*Complications of acquired heart defects:*

- acute left ventricular failure (dilatation, left atrial thrombosis),
- thromboembolism of the main trunk of the pulmonary artery,
- gangrene of the extremities, intestines,
- chronic left ventricular failure,
- chronic right ventricular failure.

## Systemic lupus erythematosus

***Systemic lupus erythematosus*** (SLE, Liebman-Sachs disease) is a chronic polysyndromic disease of mostly young women and girls, which develops against the background of genetically determined imperfections of immunoregulatory processes, which leads to uncontrolled production of antibodies to their own tissues and their components with the development of autoimmune and immunocomplex chronic inflammation.

*Epidemiology*. Morbidity – 48-50 cases per 100 thousand population, mortality – 5.8 per 1,000,000.

*The etiology and pathogenesis* have not been definitively established.

*Risk factors:*

- Environmental factors: excessive insolation, hypothermia, stressful situations, physical overload, etc.
- Hereditary predisposition is more common in the presence of certain types of genes HLA-DR2, DR3, B9, B18, complement deficiency C1, C2, C4.
- Hormonal factor: young women (high estrogen level).
- Some protein drugs (vaccines, D-penicillamine, hydrazine).
- Chronic viral infections (increased titers to a number of RNA / DNA viruses).
- Immune disorders: decreased number of T-suppressors, predominance of T-helper T-lymphocytes and increased activity of B-lymphocytes. Development of the immune response in relation to the component of nuclei and cytoplasm of cells – antinuclear antibodies, especially to native (double-stranded) DNA, which are found in 50-60% of patients.

*Pathomorphology*

- there is a systemic disorganization of connective tissue with a predominance of fibrinoid changes and generalized lesions of the microcirculatory tract (arteriolitis, capillaritis, venulitis);
- a feature of SLE is a pronounced pathology of cell nuclei, especially mesenchymal, which is manifested by their deformation, depletion of chromatin content, karyopyknosis, karyorexis, karyolysis. The admixture of chromatin material to fibrinoid gives it a basophilic hue when stained with hematoxylin and eosin;

- accumulation of chromatin material in the tissues and lumen of blood vessels, the formation of hematoxylin cells and "lupus" (LE – lupus erythematodes) cells (phagocytosis by neutrophilic leukocytes and macrophages of cell nuclei affected by the virus) and lupus factor (antinuclear pathogens).

*Morphological groups of SLE:*

The first group: acute dystrophic and necrotic changes of connective tissue. Chromatin grains are found in the composition of fibrinoid.

The second group: subacute interstitial inflammation in all organs and the nervous system, vascular lesions of the microcirculatory tract (arteriolitis, capillaritis, venulitis), lymphocytic, macrophage, plasma infiltration. Polyserosites.

The third group: sclerosis and new areas of connective tissue disorganization. Periarterial bulbous sclerosis.

The fourth group: changes in the immunocompetent system.

Fifth group: nuclear pathology.

*Clinical and morphological syndromes of SLE:*

- dermatitis,
- arthritis,
- polyserositis,
- glomerulonephritis,
- carditis.

Skin lesions are observed in 85-90% of patients.

*Macroscopically:* erythematous spots on the face in the area of the cheekbones and back of the nose – "butterfly", erythema of various shapes and sizes, swollen, with clear boundaries on the neck, chest, elbows, knees, dry skin, hair loss. In subacute SLE – annular erythema with telangiectasia and depigmentation in the center.

*Microscopically:* around the venules and derivates of the skin – infiltrates of lymphocytes and histiocytes, and in the vessels – proliferative-destructive vasculitis. The epidermis is thin, atrophic. In hair follicles – atrophy of the epithelium. In the dermis - disorganization of connective tissue with fibrinoid changes, single hematoxylin bodies, productive and productive-destructive changes, pronounced pathology of the nuclei in the cells of infiltrates, vascular endothelium.

Joint damage – arthritis (synovitis) (80-90% of patients).

*Localization:* small joints of hands, radiocarpal, shin.

*Clinical and morphological manifestations*:

- symmetrical polyarthritis,
- intense and prolonged pain – arthralgia,
- morning stiffness of movements,
- development of flexion contractures of fingers due to tendovaginitis,
- formation of rheumatoid hand.

*Microscopically*:

- in the synovial membrane: acute or subacute synovitis with a slight cellular reaction, pronounced pathology of the nuclei and hematoxylin bodies;
- in the articular cartilage and bone tissue of the epiphysises – changes in the tinctorial properties of the main substance, dystrophic changes in chondrocytes and osteocytes, up to necrosis, that destroys cartilage, but without active granulation tissue.

Kidney damage (lupus nephritis) – classic immunocomplex extra- and intracapillary glomerulonephritis (50% of cases) – lupus glomerulonephritis and mesangioproliferative glomerulonephritis.
*Macroscopically:* the kidneys are slightly enlarged, variegated.
*Microscopically*: hematoxylin bodies, fibrinoid deposits in the glomerular loops, hyaline thrombi, thickening and splitting of the basal membranes of the glomerular capillaries in the form of "wire loops". In tubules, especially curled, allocate various degree of a dystrophy, in a lumen – cylinders with a basophilic shade. Lymphoid and plasma cell infiltrates are in the stroma.
Lesions of the cardiovascular system (about 50% of patients):

- lupus carditis – all membranes of the heart are affected (rarely at the same time); inflammation of separate membranes or their sequential involvement in the process is usually registered.
- pericarditis – the most common sign of SLE (serous, fibrinous, mixed).
- Liebman-Sachs abacterial warty endocarditis.

*Macroscopically:* in places of endothelial damage thrombotic layers in the form of warts.
*Microscopically*: a characteristic feature is the presence of hematoxylin cells, fibrin in the foci of endothelial necrosis. In contrast to rheumatic endocarditis, mucoid and fibrinoid swelling of the connective tissue is not expressed.
Lung damage
*Macroscopically*: the lungs are compacted, the incision surface is reflecting, in the area of the roots – lung tissue is strand and reticular.
*Microscopically*: diffuse thickening of alveolar septa due to fibrinoid swelling, infiltration by lymphocytes, proliferation of septal cells. On the inner surface of the alveoli hyaline membranes (fibrin) are defined. In the microcirculatory system – destructive-productive vasculitis. The combination of changes causes the development of alveolar-capillary block and respiratory failure. Secondary infection often joins, up to the formation of abscesses.
Lesions of the CNS and peripheral nervous system in the form of alterative-exudative meningoencephalomyelitis and alterative-productive radiculitis, neuritis, plexitis are caused mainly by vasculitis in the microcirculatory system. Characteristic scattered foci of micronecrosis with localization in the subcortical nuclei.
Lesions of serous membranes (90% of patients): pleura, pericardium, rarely – peritoneum. Clinical manifestations - pain, friction noise of the pericardium, pleura, peritoneum over the spleen and liver.
Lesions of the spleen and lymph nodes – generalized lymphadenopathy, enlargement of the spleen and liver.
*Pathognomonic changes in the spleen*: atrophy of lymphoid follicles, severe plasmatization, development of concentric perivascular sclerosis (the phenomenon of "bulbous husk"), deposition of homogeneous protein precipitate, which does not give a positive reaction to amyloid.
*Complications of SLE:*

- renal failure on the background of lupus nephritis,
- purulent infections, "steroid" tuberculosis, hormonal disorders as a complication of steroid therapy.

## Rheumatoid arthritis

***Rheumatoid arthritis (RA)*** is a chronic systemic connective tissue disease with progressive lesions of predominantly peripheral joints on the type of erosive-destructive polyarthritis.

*Epidemiology*: frequency from 0.6 to 1.3%, women are more likely to get sick than men (4:1).

*Etiology and pathogenesis*.

- Viral infections, especially Epstein-Barr virus, which has the ability to disrupt the synthesis of immunoglobulins.
- Genetic factors: increased incidence of RA in relatives of patients and monozygotic twins (in patients with RA detect HLA antigens of loci D and DR).
- Damage of connective tissue (mainly joints) is the result of immunopathological processes (autoaggression): IgM, IgA, IgD (rheumatoid factors) against IgG.

*Pathomorphology*. The pathological process develops mainly in the joints and periarticular tissues. The inflammatory process in the synovial membrane becomes chronic and is accompanied by destruction of cartilage with the subsequent development of fibrous and bone ankylosis. The process is staged.

*The first (early) stage.*

*Macroscopically:* swelling and plethora of the synovial membranes, accumulation of turbid fluid in the joint cavity, articular cartilage is preserved.

*Microscopically:* edema of the villi, in their stroma – mucoid and fibrinoid swelling with the development of necrosis. Necrotic villi, floating in the synovial fluid, form molds – rice bodies. Synoviocyte proliferation is observed in some villi. Vessels of the microcirculatory tract are full-blooded, perivascular infiltration by lymphocytes, plasma cells, macrophages, neutrophils. Rheumatoid factor is determined in the cytoplasm of macrophages and plasma cells.

*The second stage.*

*Macroscopically*: dryness, granularity, yellowing of the cartilage surface, ulceration, sometimes complete destruction of the articular surfaces.

*Microscopically*: the growth of granulation tissue in the subsynovial layer rich in blood vessels, lymphoid and plasma cells, which crawls on the cartilage and synovial membrane in the form of a panus; focal, more often perivascular, arrangement of the lymphocytes forming lymphoid follicles with the light centers and plasma cellular reaction on periphery; destruction of cartilage with the formation of patterns, cracks and sequesters, immersed in the subchondral bone.

*Consequences*: dislocations and subdislocations of the interphalangeal and metacarpophalangeal joints of the hands and feet to the ulnar side (ulnar deviation) with the formation of the hands in the form of "walrus fins".

*The third (final) stage* is characterized by:

- growth of fibrous tissue on the surface of damaged joints,
- narrowing of joint spaces,
- formation of fibrous adhesions,
- simultaneous growth of bone beams with their transition from one end of the joint to the other – the formation of fibro-bone ankylosis.

Extra-articular lesions

Skin: rheumatoid nodules around the joint – limited or merged foci of fibrinoid necrosis, surrounded by histiocytes with pyroninophilic cytoplasm; sometimes there are impurities of giant multinucleated cells. On the periphery of the nodule are lymphoid and plasma cells, fibroblasts, neutrophils. A fibrous capsule with newly formed vessels is formed around the nodule. Nodule formation ends in sclerosis, often with the deposition of calcium salts.
Vasculitis in RA has a generalized nature and polymorphism: from moderate endothelial proliferation and infiltration of the outer shell to necrosis of the middle membrane of the vessel. Vessels of all calibers are affected, but more often small vessels of skin, skeletal muscles, internal organs. The most common productive vasculitis and thrombovasculitis.
Cardiac lesions (rheumatoid carditis) – rheumatoid nodules at the base of the mitral valve: in the connective tissue – foci of fibrinoid, with nonspecific exudative-proliferative reactions (histiocytes, lymphocytes, plasma cells) and the development of sclerosis.
Kidneys (60% of cases):

- amyloidosis,
- glomerulonephritis (membranous or membranous-proliferative),
- nephroangiosclerosis,
- chronic interstitial nephritis,
- acute and subacute pyelitis, angiitis.

Amyloidosis can also affect the liver, gastrointestinal tract and other internal organs.
*Complications of rheumatoid arthritis*.

- subluxations and dislocations of small joints
- fibrous and bone ankylosis
- osteoporosis
- renal amyloidosis with the development of renal failure.

## Bekhterev's disease

***Bekhterev's disease*** (ankylosing spondylitis) is a chronic disease of unknown etiology with a predominant lesion of the articular ligament of the spine with the development of axial ankylosis.
*The etiology* is unknown. Of great importance is hereditary predisposition; men get sick more often.
*Pathogenesis.* The histocompatibility antigen HLA-B27 (found in all patients) is linked to the weak immune response gene, which is manifested by insufficient response to viral or bacterial antigens with the development of chronic immune inflammation in the spine with osteoplastic transformation of its tissues and chronic inflammation with sclerosis.
*Pathomorphology*. Inflammatory enthesopathies (inflammation of the tendon attachment sites, ligaments, fibrous part of the intervertebral discs, joint capsules), inflammation of the bones that form the joint (ostitis) and synovitis (type of rheumatoid arthritis). Later, fibrous and bone ankylosis, ossification of the spinal ligament (columnar spine) develop.
*Complications*: renal amyloidosis.

## Systemic scleroderma

***Systemic scleroderma*** is a systemic disease of connective tissue and small vessels, characterized by widespread fibro-sclerotic changes of skin, stroma of internal organs and symptoms of obliterative endarteritis in the form of widespread Raynaud's syndrome.

*Epidemiology.* Women get sick 3-7 times more often than men, age peak – 30-60 years.

*The etiology* is unknown. It is assumed that the value is:

- viral infection (Coxsackie virus, shingles, rubella),
- heredity.

*Provoking factors*: hypothermia, vibration, trauma, contact with certain chemicals, neuroendocrine disorders, allergies.

*Pathogenesis:*

- unrestrained uncontrolled collagen formation due to damage of DNA and RNA of fibroblasts – abnormal neofibriliogenesis;
- immune disorders (decrease in the level of T-suppressors with a normal number of B-lymphocytes in the blood, the appearance of antibodies to collagen);
- lesions of the microcirculatory tract (endothelium damage by cytotoxic lymphocytes, accompanied by adhesion and aggregation of platelets, activation of coagulation, release of inflammatory mediators, increased permeability of the vascular wall with plasmorrhagia and fibrin deposition, followed by vasoconstriction);
- secretion by lymphocytes, monocytes and platelets of monokines and tissue growth factors that cause hyperproduction of collagen and macromolecules of the main substance with the subsequent development of focal fibrosis.

*Pathomorphology.*

Skin. Skin lesions are the leading sign of the disease.

Localization:

- limited form – lesions of the face and hands;
- diffuse form – lesions of the skin of hands, feet, face, torso.

*Macroscopic changes:*

1. Stage of induration: dense, symmetrical, painful swelling in the hands – "sausage fingers". Facial skin is dense, folds and wrinkles are smoothed, the disappearance of facial expressions – "mask-like face"; alternation of areas of pigmentation and depigmentation, telangiectasias appear.
2. Stage of atrophy: the skin of the fingers and hands is compacted, there are flexion contractures, sclerodactyly, acrosclerosis, shortening of the fingers due to osteolysis of separate phalanges. Trophic disorders: hair loss, nail deformity, ulceration. The skin of the face is stretched with an unnatural glow, the nose is sharpened ("bird's beak"), purse-like folds appear around the mouth, and it is difficult to open the mouth.

Joints. Variants of the joint syndrome:

- polyarthralgia;
- scleroderma polyarthritis with exudative-proliferative or fibro-indurative changes;

- periarthritis – the development of contractures due to fibrous changes in periarticular tissue without destructive changes in the joints.

Heart (in 2/3 of patients): scleroderma heart with the development of cardiovascular insufficiency.

*Macroscopically:* hypertrophy (round heart), thickening and whitishness of the parietal endocardium, marginal sclerosis of the valves, mainly mitral; in the myocardium – small-focal cardiosclerosis (whitish strands, subendocardial scars); on the epicardium whitish foci of compaction, resembling glaze (hyalinosis).

*Microscopically*: mucoid and fibrinoid swelling mainly in the endocardium, weak cellular reaction similar to proliferative inflammation.

Lungs: the main manifestation – pneumosclerosis, which occupies mainly the basal parts of the lungs and is accompanied by the development of bronchiectasis and emphysema.

Types of scleroderma pneumosclerosis:

- cystic (with the formation of subpleural cavities),
- compact (large fields of sclerosis and hyalinosis).

Kidneys – scleroderma kidney (acute nephropathy): generalized lesion of the renal arterioles with their thrombosis, the development of cortical necrosis and sclerosis, which leads to renal failure.

Digestive organs. Esophagitis is the most common lesion, which is manifested by dysphagia due to diffuse dilation of the esophagus with narrowing of its lower third, weakening of peristalsis and rigidity of the walls.

Nervous system – polyneuropathy, rarely – encephalitis.

*Complications*: insufficiency of those organs or systems in which sclerotic changes are most developed, cachexia.

## Dermatomyositis

***Dermatomyositis*** is a diffuse progressive connective tissue disease with predominant lesions of the striated and smooth muscles, skin, and internal organs.

In 30% of cases there is no skin impression, in which case the disease is called *polymyositis*.

*The etiology* is unknown. Possible factors: viral infection (paramyxoviruses, Coxsackie viruses), genetic predisposition. Starting factors are hypothermia, stress, hyperinsolation, vaccination, drug allergies.

*Pathogenesis*: the appearance of cross-antibodies (antigenic mimicry) to muscle antigens and persistent viral infection. The development of autoimmune mechanisms is facilitated by the imbalance of T- and B-lymphocytes with a decrease in the function of T-suppressors. Myositis-specific antibodies, forming immune complexes, cause the development of immunoinflammatory process in muscles and skin.

*Classification*.

- By origin:
  - idiopathic (primary),
  - paraneoplastic occurs on the background of malignant tumors of the lungs, stomach, ovaries, breast.
- By the course:
  - sharp,
  - subacute,

- chronic.

• By periods of development:
  - prodromal,
  - manifest with skin and muscle syndrome,
  - terminal (cachectic, period of complications).

*Pathomorphology.*

*Localization*: skeletal muscles, pharyngeal muscles, larynx, diaphragm, eyes.

*Macroscopically*: muscles swollen, pale yellow, with areas of calcification.

*Microscopically*: dystrophy of muscle fibers (disappearance of streaks and reduction of glycogen), necrosis of some muscle fibers, areas of calcification, stroma infiltration by lymphocytes, plasma cells, macrophages; proliferation and desquamation of the endothelium of the microcirculatory tract with obliteration.

*Complications*: lesions of the gastrointestinal tract, heart, lungs.

### *Training macropreparations*

**Acute warty endocarditis.** The heart is normal in size, the mitral valve cuspids are dull, the chords are thin, on the free edge of the cuspids on the surface facing the atrium, you can see different sizes of gray-red corrugated thrombotic layers in the form of warts.

**Relapsing warty endocarditis**. The heart is increased in size and weight, the mitral valve cuspids are thickened, sclerosed, represented by dense opaque hyalinized tissue, fused together, the chords are shortened and thickened, the left atrioventricular orifice is narrowed; along the edge of the sclerosed valve, on the surface facing the atrium, small fresh thrombotic layers - warts are visible.

**Fibroplastic endocarditis.** Mitral valve cuspids are thickened, shortened, opaque, inelastic.

**Lupus nephritis**. The kidney is of normal size with a smooth surface, trout (areas of hemorrhage alternate with unchanged tissue).

### *Training micropreparations*

**Rheumatic granuloma** (staining with hematoxylin and eosin): in the interstitium of the myocardium - Ashof-Talalayev granuloma, consisting of fibrinoid necrosis, surrounded by large mononuclear cells, lymphocytes, plasma cells; muscle fibers are hypertrophied.

**Relapsing warty endocarditis** (hematoxylin and eosin staining): the valve cuspids is thickened due to sclerosis and hyalinosis; on the periphery of the cuspid - mucoid swelling and fibrinoid necrosis, near the necrosis zone the endothelium is destroyed with an attached mixed thrombus; in the thickness of the valve - diffuse lymphomacrophage infiltrate, newly formed vessels of capillary type.

**Lupus nephritis** (hematoxylin and eosin staining): glomeruli are enlarged, capillary walls thicken and mesangium cells proliferate.

### *Questions for self-control*

1. Rheumatism: definitions, general data (epidemiology, risk factors).
2. Clinical and morphological forms of rheumatism. Morphological changes in endocarditis. Complications of rheumatism.
3. Extracardiac forms of rheumatism.
4. Definition and classification of acquired heart defects. Hemodynamic disorders in various heart defects.

5. Rheumatoid arthritis. Morphogenesis, morphology of joint manifestations (stages of progression of rheumatoid arthritis, complications and consequences).
6. Systemic lupus erythematosus: pathological anatomy, morphological changes in the skin, blood vessels, heart, kidneys. Complications, causes of death.
7. Systemic scleroderma: pathological anatomy, visceral manifestations, complications, causes of death.
8. Dermatomyositis, ankylosing spondylitis: pathological anatomy, clinical and anatomical forms. Complications, causes of death.

***Examples of tests***

1. Histological examination of the mitral valve cuspids revealed: mucoid swelling, endothelial damage, the formation of fibrin clots on the closing edge. What form of rheumatic endocarditis is observed?
A. * Acute warty endocarditis
B. Diffuse endocarditis
C. Fibroplastic endocarditis
D. Rotary warty endocarditis
E. Polyposis-ulcerative endocarditis
2. During the autopsy of a 45-year-old woman who died of chronic renal failure, the following were found: sclerosis and hyalinosis of the dermis, focal necrosis of the cortical layer of the kidneys and nephrosclerosis, focal cardiosclerosis and basal pneumosclerosis. Your diagnosis.
A. * Systemic scleroderma
B. Nodular periarteritis
C. Dermatomyositis
D. Systemic lupus erythematosus
E. Rheumatism
3. In a patient with a high titer of antinuclear antibodies, death occurred from progressive renal failure. Pathological and anatomical examination revealed mesangioproliferative glomerulonephritis, abacterial warty endocarditis, periarterial bulbar sclerosis in the spleen, and productive proliferative vasculitis in the skin. Your diagnosis.
A. * Systemic lupus erythematosus
B. Nephrotic syndrome
C. Rheumatism
D. Dermatomyositis
E. Nodular periarteritis
4. A 70-year-old patient died of acute coronary insufficiency. During his life there was swelling, deformity and pain in the knee joints. Pathomorphological examination of deformed joints and synovial membranes revealed: hyperemia of membranes with multiple peri-vascular inflammatory infiltrates of lymphocytes, plasma cells, macrophages. The accumulation of fibrin, which is organized, covers areas of the synovial membrane and is determined in the joint fluid in the form of rice grains. Your diagnosis.
A. * Rheumatoid arthritis
B. Nodular periarteritis
C. Ankylosing spondylitis

D. Tuberculous arthritis
E. Deforming arthrosis
5. A 50-year-old patient had rheumatic heart disease for many years. With exacerbation of the disease developed hemiplegia and death. Histologically, the mitral valve revealed severe sclerosis, focal cellular infiltrates, small thrombotic layers. Determine the form of endocarditis.
A. * Relapsing warty
B. Acute warty
C. Diffuse
D. Fibroplastic
E. Ulcerative-polypoid

## VASCULITES

***Vasculitis*** – diseases characterized by inflammation and necrosis of the vascular wall.

Types:

***Local vasculitis*** – the spread of the process to the vascular wall from adjacent areas (purulent-necrotic vasculitis in phlegmon).

***Systemic vasculitis*** is a heterogeneous group of diseases, the main morphological feature of which is inflammation of the vascular wall, and the range of clinical manifestations depends on the type, size and location of the affected vessels and the severity of concomitant inflammatory disorders.

In systemic vasculitis, vascular inflammation is the essence of the pathological process, in contrast to other rheumatic diseases, in which vasculitis is only a component of the disease, such as rheumatoid arthritis, diffuse connective tissue diseases, rheumatism etc. Systemic vasculitis is characterized by widespread vascular damage, ischemia, and dysfunction of the affected area or organ system.

*Classification*

Primary (nosologically independent systemic vasculitis).

1. Necrotizing panvasculitis:
    1.1. Nodular periarteritis (classic) – (Kusmaul-Meyer disease)
    1.2. Asthmatic nodular periarteritis (necrotizing angiitis with granulomatosis – Cherzha-Strauss syndrome)
2. Granulomatous vasculitis:
    2.1. Wegener's granulomatosis
    2.2. Middle facial granuloma
    2.3. Lymphomatoid granulomatosis
3. Hemorrhagic vasculitis (Shenlein-Henoch disease).
4. Giant cell vasculitis:
    4.1. Nonspecific aortoarteritis (Takayasu's disease)
    4.2. Temporal arteritis (Horton's disease)
    4.3. Rheumatic polymyalgia.
5. Obliterating thromboangiitis (Burger's disease).
6. Other forms of vasculitis:
    6.1. Behcet's disease
    6.2. Kawasaki disease (mucocutaneous-glandular syndrome)

6.3. Thrombotic thrombocytopenic purpura.

Secondary:

1. With infections:
    1.1. Bacterial (sepsis, infectious endocarditis)
    1.2. Viral (chronic hepatitis)
    1.3. Rickettsial.
2. With drug-induced disease.
3. In malignant tumors (hairy cell leukemia, lymphoma, etc.).
4. In systemic connective tissue diseases.
5. In parasitic diseases.
6. In occupational diseases (beryllium, silicosis, arsenic intoxication).

*Etiology:*

- medications (especially antibiotics, vaccines, serums, anti-TB drugs, sulfonamides, etc.);
- viruses (hepatitis B viruses, herpes, cytomegaloviruses, retroviruses, parvovirus);
- bacterial infection (tuberculosis, streptococci, yersinia, chlamydia, salmonella, etc.);
- allergic diseases (medicinal, food, cold, hay fever);
- chronic focal infection (especially nasopharyngeal);
- genetically determined defect of the immune response.

*Pathogenesis.*

- production of autoantibodies (antibodies to components of neutrophil cytoplasm, vascular endothelium, to phospholipids);
- formation of immune complexes, including cryoglobulins;
- violation of the mechanisms of apoptosis of endothelial cells and the interaction between them and leukocytes;
- loss of endothelial function to regulate blood clotting;
- platelet synthesis of various inflammatory mediators that have vasoactive, chemotactic, thrombogenic and proteolytic properties, which causes the activation of complement.

## Nodular periarteritis

***Nodular periarteritis*** (Kusmaul-Meier disease) is a rheumatic disease in the form of systemic necrotizing vasculitis by the type of segmental lesion of small and medium-sized arteries with the formation of aneurysms.

*Epidemiology*.

- morbidity – 2-3 cases per 1 million population per year,
- mostly young men get sick.

*The etiology* is unknown.

*Risk factors:*

- suffered acute respiratory (including streptococcal) infections,
- injection of vaccines and serums, drug intolerance, etc.,
- hepatitis B virus (30% of patients have a high titer of HBs antigens and antibodies to it),
- tumor antigens.

*Pathogenesis:*

- alteration → immunocomplex inflammation of the artery wall → fibrinoid necrosis,
- pronounced hemorheological disorders with the development of DIC syndrome.

*Course*: acute, subacute, chronic.

*Localization and frequency of lesions:*

- renal arteries – 90-100%,
- coronary arteries – 88-90%,
- mesenteric arteries – 57-60%,
- arteries of the liver, brain – 46%,
- less often – arteries of striped muscles, stomach, pancreas, adrenal glands, peripheral nerves.

*Pathomorphology*: vasculitis with the development of successive phases in the vascular wall: alteration (fibrinoid necrosis of the mesangium), exudation and proliferation in the adventitia.

Depending on the predominance of the phase there are:

- destructive vasculitis
- destructive-proliferative vasculitis
- proliferative vasculitis.

As a result of inflammation, nodular thickenings of the vascular wall are formed due to sclerosis.

Renal vascular lesions:

- glomerulonephritis (acute and chronic mesangial),
- stenosis of the renal vessels,
- renal infarction,
- ruptures of renal vascular aneurysms with the formation of paranephric hematomas.

Heart lesion:

- coronary heart disease with the development of angina, myocardial infarction,
- cardiosclerosis,
- exudative pericarditis in small blood vessels,
- hemopericardium (rare) due to rupture of the aneurysm.

Abdominal syndrome – lesions of the mesenteric arteries:

- acute abdominal pain (associated with pathology of the mesenteric arteries, ischemia, which causes the development of intestinal necrosis),
- acute appendicitis, cholecystitis, pancreatitis,
- perforation of the intestine,
- peritonitis.

Eye lesion:

- aneurysms of the fundus arteries,
- perivascular infiltrates, thrombosis of the central retinal artery.

*Consequences*: saddle-shaped deformity of the nose, vascular obliteration and the development of infarctions in the tissue of organs.

## Nonspecific aortoarteritis

***Nonspecific aortoarteritis*** (Takayasu's disease) – an inflammatory disease of the arteries of the elastic type (aorta and proximal parts of its main branches, pulmonary trunk) with the development of occlusions.

*The etiology* is unknown. There is a connection with infectious diseases, intoxications (pesticides, lead compounds).
*Anatomical types.*
Type I (brachiocephalic) - isolated lesion of the aortic arch and its branches.
Type II - isolated lesions of the thoracic and abdominal aorta and its branches.
Type III - combined lesion of the aortic arch and its branches with changes in the thoracic and abdominal parts.
Type IV - lesions of the pulmonary trunk and its branches, a possible combination with I, II and III options.
*Macroscopically*: lesions can be segmental or diffuse; the walls of the arteries are white, thickened, dense. From the intima there are thickenings with parietal thrombi, narrowing the lumen; sclerotic changes of adventitia, aneurysms meet.
*Macroscopic options*: aneurysmal, stenotic, deforming.
*Microscopically* – panarteritis with a gradual change in the inflammatory response:

- early stage (acute): destruction of the outer elastic membrane; infiltration of all layers of the vascular wall by lymphocytes and plasma cells; endothelial proliferation with the formation of parietal thrombi;
- late stage (subacute) – the formation of giant cell granulomas;
- final stage (sclerotic): sclerosis of the vascular wall with vascularization of the middle membrane; organization of blood clots.

*Consequences*: stenosis and obliteration of the lumen of the vessel.

## Wegener's granulomatosis

***Wegener's granulomatosis*** is a granulomatous-necrotizing systemic vasculitis with predominant lesions of small and medium-sized vessels (arteries, arterioles, capillaries, venules) with combined ulcerative-necrotic lesions of the upper respiratory tract.
*The etiology* is unknown, associated with bacterial and viral infections, medications.
*Provoking factors*: hypothermia, insolation, vaccination.
*Pathomorphology.*
Systemic necrotizing vasculitis with granulomatosis is characterized by the development of successive phases of alteration, exudation and proliferation. Endarteritis occurs in muscular arteries, panarteritis in small caliber arteries, destructive and destructive-proliferative arteriolitis, venulitis, capillaries are observed. Granulomas, sclerosis and hyalinosis of vessels with narrowing (obliteration) of a lumen or formation of aneurysms are formed.
Necrotizing granulomatosis of the upper respiratory tract is characterized by purulent nasopharyngitis, sinusitis, stomatitis, laryngitis, otitis, sore throat with ulceration and bleeding (localized form). The spread of the process to the trachea, bronchi and lungs with ulcerative-necrotic changes - a generalized form.
Glomerulonephritis is mesangioproliferative or mesangiocapillary.
*Complications*: pneumonia, renal failure.

## Thromboangiitis obliterans

***Thromboangiitis obliterans*** is a chronic inflammatory disease of the arteries of medium and small caliber, veins and nerve fibers with a predominant distal lesion with a gradual spread of the pathological process to the proximal vessels of the upper and lower extremities.

*The etiology* is not sufficiently studied. The disease mainly affects men over the age of 30 who smoke for a long time.
*Macroscopically:* vessels in the form of thick fibrous bands with segmental wall thickening.
*Microscopically.*
Acute stage – alternative-productive thrombovasculitis: against the background of alternative changes develops polymorphocellular leukocyte infiltration with the destruction of the inner elastic membrane and the formation of microabscesses.
Subacute stage (productive): lymphohistiocytic infiltration of the vascular wall, vascularization and thrombus organization. Formation of granulomas in the mesangium around the areas of necrosis and in blood clots.
Chronic stage – the predominant processes of thrombus organization with vascularization and calcification.
*Complications:* gangrene of the extremities.

### *Questions for self-control*

1. Definition, classification and pathogenesis of vasculitis.
2. Nodular periarteritis, morphological characteristics.
3. Nonspecific aortoarteritis, morphological characteristics.
4. Wegener's granulomatosis, morphological characteristics.
5. Obliterating thromboangiitis, morphological characteristics.

### *Examples of tests*

1. At the autopsy of a 27-year-old woman who died of chronic renal failure, scars and infarctions were found in the spleen and kidneys. Microscopically: sclerotic changes in arteries of medium and small caliber with endothelial proliferation and lymphohistiocytic infiltration around. Your diagnosis.
A. * Nodular periarteritis
B. Atherosclerosis
C. Hypertensive disease
D. Marfan's disease
E. Visceral syphilis
2. A 15-year-old high school student became acutely ill after a nose injury. Complaints of nosebleeds that recur frequently; cough with sputum; subfebrile temperature; weakness. On examination, the deformation of the nasal membrane, in the nasal passages loose juicy granulations. The mucous membrane of the mouth, nasopharynx, larynx is full-blooded with numerous petechiae. In the study of the respiratory organs - the mucous membrane of the throat and upper respiratory tract - with ulcerative-necrotic changes. Histological examination of the nasal mucosa revealed destructive vasculitis, as well as polymorphic granulation tissue with large foci of necrosis. Your diagnosis.
A. * Wegener's granulomatosis
B. Acute purulent nasopharyngitis
C. Diphtheria of the oropharynx
D. Hematogenous tuberculosis
E. Thrombocytopenia

3. A 25-year-old woman was found to have a thickening of the aortic wall in the area of the arch, narrowing of the lumen with a large number of parietal thrombi. Microscopically detected panarteritis with giant cell infiltration. Your diagnosis.
A. * Takayasu's disease
B. Visceral syphilis
C. Rheumatic arteritis
D. Aortic atherosclerosis
E. Aortic aneurysm
4. The autopsy of a 45-year-old man, who often suffered from angina, sinusitis and otitis, revealed severe destructive stomatitis, ulcerative-necrotic processes in the trachea and bronchi, bilateral granulomatous inflammation of the lungs and kidneys. Microscopically revealed destructive-productive pan-arteritis, a large number of granulomas in the lungs and kidneys with necrosis in the center. Your diagnosis.
A. * Wegener's granulomatosis
B. Hematogenous tuberculosis
C. Sarcoidosis of the lungs
D. Sepsis, septicopia
E. Focal pneumonia
5. A 30-year-old man was diagnosed with productive panarteritis of the lower extremities (vessels in the form of thick bands with segmental wall thickening). Clinical diagnosis - obliterating thromboangiitis. Histological examination of the artery wall revealed its infiltration by segmental leukocytes with the formation of microabscesses. Name the stage of the disease.
A. * Acute
B. The final
C. Initial
D. Subacute
E. Chronic

## KIDNEY DISEASES

Guided by the structural and functional principle, two main groups of kidney diseases allocate:

1. Glomerulopathy
2. Tubulopathy

By the reason, they are classified as congenital (including inherited or hereditary) and acquired.

Glomerulopathies, or kidney diseases with primary and predominant lesions of the glomerular apparatus, are based on glomerular filtration disorders.

Acquired glomerulopathies:

- Glomerulonephritis
- Idiopathic nephrotic syndrome
- Amyloidosis of the kidneys
- Diabetic and hepatic glomerulosclerosis

Congenital glomerulopathies:

- Hereditary nephritis with deafness (Alport syndrome)

- Congenital nephrotic syndrome
- Familial nephropathic amyloidosis.

Tubulopathies, or kidney diseases with primary leading tubular lesions, are characterized by impaired concentration, reabsorption and secretory functions of the tubules.

Acquired tubulopathies include:

- Necrotic nephrosis, which is the basis of acute renal failure
- "Myeloma kidney"
- "Gout kidney"

Congenital tubulopathies include various forms of tubular enzymopathy.

The group of kidney diseases with a predominant lesion of the interstitium (intermediate tissue) include:

- Interstitial (intermediate) nephritis
- Pyelonephritis
- Nephrosclerosis.

Diseases of heterogeneous nature with damage to all parts of the kidney:

- Kidney stone disease
- Polycystosis
- Kidney tumors.

Depending on the cause the kidney disease are divided into:

1. Immune-inflammatory (glomerulonephritis: primary and secondary)
2. Infectious and inflammatory (pyelonephritis)
3. Metabolic disorders (gout, diabetes)
4. Vascular (arterial hypertension of various genesis)
5. Ischemic injuries (atherosclerosis of the renal arteries)
6. Tumors
7. Congenital anomalies (polycystosis).

## Glomerulonephritis

***Glomerulonephritis*** is a disease of infectious-allergic or unidentified nature, which is based on bilateral diffuse or focal non-purulent inflammation of the glomerular apparatus of the kidneys (glomerulitis) with characteristic renal and extrarenal symptoms.

| *Renal symptoms:* | *Extrarenal symptoms:* |
|---|---|
| oliguria,<br>proteinuria,<br>hematuria,<br>cylindruria | - hypertension and compensatory left ventricular hypertrophy,<br>- dysproteinemia, edema, hyperazotemia,<br>- uremia |

Clinical forms of glomerulonephritis:

- hematuric,
- nephrotic,
- hypertensive,
- mixed.

*Etiology* of glomerulonephritis: infectious and non-infectious factors.

*Infectious agents:*

- nephritogenic forms of β-hemolytic streptococcus

- staphylococcus, pneumococcus, viruses, plasmodium falciparum, pale treponema, etc.

Infections of the upper respiratory tract caused by streptococcus (pharyngitis, tonsillitis, scarlet fever) and viruses (adenovirus, influenza, etc.) play a leading role in the development of the disease.

*Non-infectious agents:*

- ethanol (alcoholic glomerulonephritis),
- heredity (Alport syndrome), etc.

*Classification of glomerulonephritis*

By localization of the process:

- intracapillary (development of a pathological process in the glomerular vessels),
- extracapillary (the process develops in the cavity of the glomerular capsule).

By the nature of inflammation:

- exudative,
- proliferative,
- mixed.

By the course

- acute,
- subacute
- chronic

Morphological changes in the kidneys in addition to the glomeruli also develop in the tubules, stroma and blood vessels. Therefore, there are glomerulonephritis with tubular, interstitial and vascular components.

## ***Acute glomerulonephritis***

*Pathogenesis.* Acute diffuse glomerulonephritis is an immunoinflammatory disease that has the following pathogenetic variants:

- immunocomplex (the most common option),
- "low immune" (pauci-immune),
- due to the appearance of antibodies to the glomerular basal membrane,
- caused by antigenic mimicry.

Poststreptococcal glomerulonephritis is the most common variant of acute glomerulonephritis. Antibodies bind to streptococcal antigens (streptolysin, streptokinase, hyaluronidase) and settle on the basal membranes of glomerular capillaries, causing activation of the complement system.

Activation of complement leads to damage of the basal membrane of glomerular capillaries, involvement of neutrophils and monocytes in the glomerular zone, degranulation of basophils and labrocytes with the release of inflammatory mediators (histamine, leukotrienes), stimulation of platelet production by thromboxane and serotoxin.

Thus, the glomeruli of the kidneys develop immune inflammation, which reflects the immediate type of hypersensitivity reaction.

*Pathomorphology.*

*Macroscopically*: the kidneys are enlarged, swollen; pyramids are dark red, the cortex is grayish-brown with small hemorrhages on the surface and section or with gray translucent dots – "motley kidney".

*Microscopically*: 80-100% of the glomeruli are affected, which is accompanied by pronounced exudative-proliferative changes. In the initial stage of the disease there is hyperemia, enlargement of the glomeruli, pronounced edema of the mesangium with its infiltration by neutrophils and monocytes. Exudative processes are replaced by pronounced proliferation of endothelial cells of capillaries and mesangiocytes.
Phases of acute glomerulonephritis (depending on the severity of the inflammatory reaction):

- exudative – with a predominance in the glomeruli of leukocytes,
- exudative-proliferative – in combination of leukocyte infiltration with cell proliferation,
- proliferative – in the proliferation of endothelial cells and mesangiocytes.

*Consequences*:

- recovery (70%),
- transition to a chronic form (29%),
- death from acute renal failure (1%).

## ***Rapidly progressive glomerulonephritis***

Rapidly progressive glomerulonephritis (subacute, malignant, crescentic) is characterized by a rapid course, severe clinical manifestations, peculiar morphological manifestations and rapidly increasing renal failure.
*Etiology:*

- primary rapidly progressing glomerulonephritis,
- secondary - associated with various infectious and tumor diseases,
- idiopathic (determine the cause of the disease is not possible),
- rarely, the disease is associated with a streptococcal infection,
- may be associated with systemic diseases: SLE, systemic scleroderma, systemic vasculitis, etc.

*Pathogenesis*: the formation of antibodies to the basal membrane and the formation of antibodies against the cytoplasm of neutrophils and lysosomes of monocytes.
*Macroscopically*: the kidneys are enlarged, flaccid; the cortical layer is wide, swollen, yellow-gray, dull, with a red spot and well separated from the dark red medullar substance – "large motley kidney", or red and combined with full-blooded pyramids - "large red kidney".
*Microscopically*: proliferation of capsule epithelial cells and podocytes with the formation in most glomeruli of multiple crescents of Gianuzzi with total or segmental obliteration of Bowman's spaces. Characteristic fibrinoid necrosis of the glomeruli, ruptures of basal membranes, the release of erythrocytes and fibrin polymer in the Bowman space. The impression of tubules and interstitium is also noted. Fibroplastic changes, hyalinosis develop in glomeruli, their death occurs. Infiltration by inflammatory cells of various types with the subsequent development of fibrosis is noted.

## ***Chronic glomerulonephritis***

Chronic glomerulonephritis is a heterogeneous group of diseases by origin and pathomorphology, characterized by immunoinflammatory lesions of the glomeruli, tubules and interstitium of both kidneys and a progressive course, resulting in the development of nephrosclerosis and chronic renal failure.

*Etiology and pathogenesis*. In 80-90% of cases, the development of chronic glomerulonephritis is associated with circulating immune complexes with the formation of an immune response by the mechanism of delayed-type hypersensitivity. Due to damage to the basal membrane, its antigens are released into the blood and immune complexes in the bloodstream are formed with their deposition on the basal membrane and activation of the complement system, neutrophils, macrophages. Thus, the formation of immune complexes is a secondary mechanism that is formed at the final stage. In the end, with attenuation of glomerular cell proliferation, there is activation of fibroblasts and the development of fibrosis.

*Morphological classification of chronic glomerulonephritis*

1. Membrane-proliferative (mesangiocapillary) glomerulonephritis
   a) type I - subendothelial deposits
   b) type II - dense intramembrane deposits (dense deposit disease)
2. Diffuse mesangioproliferative glomerulonephritis
   a) with mesangial IgA deposits
   b) without mesangial IgA deposits
3. Sclerosing (fibroplastic) glomerulonephritis

*Clinical and morphological characteristics of chronic glomerulonephritis forms*

*Mesangiocapillary glomerulonephritis* (membranous-proliferative glomerulonephritis) is characterized by a pronounced proliferation of mesangial cells and uneven thickening of the capillary walls.

The disease mainly affects young women under 30 years. Membranous-proliferative glomerulonephritis is 10-25% of all forms of chronic glomerulonephritis.

*Clinically*: severe nephrotic syndrome with the development of edema up to anasarca, hypertension, macrohematuria.

Types of mesangiocapillary glomerulonephritis:

*Type 1* is characterized by a normal basal membrane, subendothelial and mesangial deposits, significant mesangial edema and deposits of IgG, IgM, IgA, components of complement $C_3$, $C_4$. The deposits cause thickening of the capillary wall, separate the basal membrane from the penetrating mesangium and create the effect of a "double contour of the capillary wall".

*Type 2* - the disease of "dense deposits", characterized by the presence of intramembrane and subendothelial deposits (bumps), which form a tape-like electron-dense layer in the basal membranes of glomeruli, tubules, Bowman's capsule, moderate edema of the mesangia and detection of $C_3$ component of complement.

*Mesangioproliferative glomerulonephritis* is characterized by diffuse proliferation of mesangial cells and mesangial matrix, due to focal deposition of immune complexes containing IgA, IgG, rarely IgM.

There are 2 subgroups: with IgA deposits and without IgA deposits.

*1) IgA nephropathy (Berge's disease)* – a variant of mesangioproliferative glomerulonephritis, characterized by the deposition of IgA in the mesangium of the glomeruli. The incidence in Europe is 10-12%, men get sick 6 times more often than women. Nephrotic syndrome, hypertension; edema rarely develop.

*Microscopically:* focal (in part of the glomeruli), segmental or in all loops of the glomeruli proliferation of mesangial cells and enlargement of the mesangial matrix is detected. Hyalinosis of glomeruli can be defined.

*The prognosis* is relatively favorable, but the disease gradually progresses and after 10-15 years, in 20-30% develops renal failure.

*2) Mesangioproliferative glomerulonephritis with IgM renal deposition* is characterized by a severe course with the development of severe nephrotic syndrome (edema, hypoproteinemia, hypercholesterolemia, severe proteinuria – more than 4-5 g/day). Men get sick more often.

*The prognosis* is unfavorable, constant recurrences lead to CRF.

*Sclerosing (fibroplastic) glomerulonephritis* is a heterogeneous group that includes the above-described morphological forms of chronic glomerulonephritis with the development of characteristic histological features: sclerosis and desolation of the glomeruli, tubulo-interstitial fibrosis. Often at this stage it is no longer possible to morphologically distinguish the initial morphological variant of chronic glomerulonephritis.

## Interstitial nephritis

***Interstitial nephritis*** (tubulointerstitial nephritis) – inflammatory kidney disease with localization of the pathological process in the intermediate (interstitial) tissue, lesions of the tubules, blood and lymphatic vessels of the renal stroma.

*Classification*

By development:

- primary interstitial nephritis - develops without any previous disease;
- secondary interstitial nephritis - develops on the background of another kidney disease or against the background of diseases such as myeloma, leukemia, diabetes, gout and others.

By duration (course):

- acute;
- chronic.

### *Acute interstitial nephritis*

*Etiology.* Depending on the etiological factors, there are 4 groups of acute interstitial nephritis:

1. Medicatious (antibiotics, sulfonamides, NSAIDs, analgesics, immunosuppressants, diuretics, captopril, etc., intoxication with ethanol, ethylene glycol, heavy metal salts, treatment with vaccines, serums, protein drugs).
2. Infectious interstitial nephritis is caused by viruses (Epstein-Barr virus, measles, cytomegalovirus), bacteria (streptococcus, pneumococcus, mycoplasma), spirochetes (pale treponema), protozoa (toxoplasma), rickettsiae.
3. Associated with systemic diseases.
4. Idiopathic.

*Pathogenesis*. Under the influence of etiological factors there is damage of the basal membranes of the tubules. Due to the interaction of foreign substances with the protein particles of the basal membranes, complete antigens are formed. The same antigens are formed in the interstitial tissue. Subsequently, the reaction of the interaction of antigens with antibodies, with the formation of immune complexes, which are deposited on the basal membranes of the tubules and in the interstitium, complement is activated and immune inflammation develops. T-lymphocytes cause damage to the interstitial tissue of the kidneys through lymphokines and by contact

cytolysis. Cytokines activate macrophages and fibroblasts, enhance the synthesis of collagen types 3 and 5.

*Microscopically* there are 3 pathomorphological stages:

1. Edematous – there is a pronounced swelling of the interstitium.
2. Cellular infiltration – pronounced infiltration of the interstitium by lymphocytes, macrophages, neutrophils, rarely – epithelioid and plasma cells.

Depending on the predominance of the cellular composition of the infiltrate, there are different variants of interstitial nephritis:

a. lymphohistiocytic,
b. plasma cell,
c. eosinophilic,
d. granulomatous.

The cells that make up the infiltrate produce cytokines (IL-1 – IL-7, interferons, tumor necrosis factor, fibroblast growth factor, etc.).

3. Tubulo-necrotic stage – the development of necrosis, rarely nephrocyte dystrophy, under the action of cytokines.

## ***Chronic interstitial nephritis***

*Etiological factors*:

1. May be the result of acute interstitial nephritis.
2. Prolonged use of drugs (analgesics, caffeine, codeine, etc.).
3. Intoxication with heavy metal salts.
4. Radiation exposure (irradiation of the kidneys during radiation therapy of the tumor).
5. Metabolic disorders (gout, hypercalcemia).
6. Chronic intoxication with household and industrial substances.
7. Extrarenal tumors.
8. Sjogren's syndrome.
9. Idiopathic chronic interstitial nephritis (21% of cases).
10. Balkan endemic nephropathy – interstitial nephritis of unknown etiology, which develops in the inhabitants of the areas adjacent to the Danube.

*Pathogenesis*

1. Damage of the tubular apparatus of the nephrons.
2. Inhibition of enzymatic activity of the epithelium of the tubules, which contributes to the development of metabolic disorders and hypoxia of the interstitium with persistent changes in the structure and function of the tubular apparatus.
3. Renal ischemia as a result of vasoconstriction (under the influence of analgesics and nonsteroidal anti-inflammatory drugs inhibits the synthesis of prostaglandins, which lower blood pressure).
4. Development of papillary necrosis.
5. Development of immune inflammation with the formation of inflammatory infiltrate with the production of cytokines similar to acute interstitial nephritis.

*Microscopically*: dystrophy and necrosis of the epithelium of the tubules, lymphohistiocytic infiltration by lymphocytes, monocytes, neutrophils. In the future - the proliferation of fibroblasts with the subsequent development of nephrosclerosis.

## Pyelonephritis

***Pyelonephritis*** is an infectious-inflammatory disease with predominant and primary lesions of the interstitial tissue, pelvic system and renal tubules.

*Classification*

By origin:

- primary,
- secondary.

By localization:

- one-sided,
- bilateral.

By duration:

- acute,
- chronic,
- recurrent.

*Etiology:* different types of infection.

I. Gram-negative flora – a leading role in the development of pyelonephritis: Escherichia coli (34-35%), Proteus (14-26%), Pseudomonas aeruginosa (4-12%), enterococci (6%).
II. Gram-positive flora: staphylococcus (6-14%), streptococcus (rare).
III. L-forms of bacteria are found in the urine of 8.9% of patients with pyelonephritis.
IV. Mycoplasmas are the cause of chronic pyelonephritis in 25% of patients
V. Viruses and fungi are rare.
VI. Associations of pathogens – in 15% of patients.

Depending on the route of infection, there are:

- ascending path – urogenital,
- descending way: hematogenous, lymphogenic.

Contributing factors to the development of pyelonephritis may be:

- urological manipulations, retrograde pyelography;
- hypothermia;
- disorders of urodynamics - disorders of urine outflow of various genesis (stones, tumors of the urinary tract, benign prostatic hyperplasia, etc.)
- pregnancy;
- diabetes;
- chronic infections of the ORL organs, oral cavity;
- genetic predisposition.

### ***Acute pyelonephritis***

*Macroscopically*: the kidneys are enlarged, swollen, full-blooded, in the section with the presence of small abscesses. The cavities of the pelvis are dilated, filled with turbid urine of yellow-green color, the mucous membrane is dull, with areas of hemorrhage.

*Microscopically*: hyperemia and leukocyte infiltration of pelvis and renal calyces with deposition of fibrin threads on the mucous membrane, foci of necrosis. The interstitium is swollen, infiltrated with leukocytes, miliary abscesses and hemorrhages are often formed. The epithelium of the tubules in a state of dystrophy. In the lumen of the tubules epithelial and leukocyte cylinders.

## ***Chronic pyelonephritis***

It is characterized by the development of the inflammatory process initially in the segment of the upper or lower pole. Over time, the whole kidney is involved in the process and chronic pyelonephritis ends with its shrinkage.

The sequence of damage of the kidney structures in chronic pyelonephritis is as follows:

- tubules (epithelial cells),
- interstitial vessels (blood, lymph),
- interstitial nerves,
- glomeruli.

*4 stages of pathomorphological changes in chronic pyelonephritis*:

1. Inflammatory infiltration of the mucous membrane of the calyces and pelvis with the development of metaplasia of the transitional epithelium into a multilayered squamous, possible formation of polyps, glomeruli preserved, even atrophy of the tubules, diffuse lymphoplasmocytic infiltration of connective tissue.
2. Hyalinosis of some glomeruli, significant atrophy and fibrosis of the tubules, reduction of inflammatory infiltration.
3. Hyalinosis of a large number of glomeruli, tubules are filled with protein colloidal masses, while the microscopic structure of the kidney resembles the thyroid gland - "thyroid kidney", the desolation of the vessels of the interstitium.
4. Shrinkage of the kidney, pronounced fibrosis, replacement of tubules with connective tissue.

*Complications* of pyelonephritis.

- Carbuncle of the kidney - the progression of the purulent process with the merging of abscesses.
- Pyonephrosis - connection of purulent cavities with the renal pelvis.
- Perinephritis - involvement in the inflammatory process of the fibrous capsule of the kidney.
- Paranephritis - inflammation of the adrenal glands.
- Papillonecrosis - necrosis of the papillae of the pyramids.
- Sepsis.
- Chronic abscesses.
- Neurogenic hypertension.
- Chronic renal failure.

## Renal amyloidosis

***Renal amyloidosis*** – deposition in all structural elements of renal tissue (glomeruli, tubules, interstitium, vessels) of a specific insoluble fibrillar protein - amyloid, which leads to renal dysfunction with the development of chronic renal failure.

*Etiology:*

- primary (idiopathic) amyloidosis,
- hereditary amyloidosis
- secondary amyloidosis.

*Clinical and morphological stages of renal amyloidosis*

1) latent,
2) proteinuric,

3) nephrotic,
4) azotemic.

*Latent stage.*

*Macroscopically*: the appearance of the kidneys is not changed.
*Microscopically:* sclerosis and amyloidosis of vessels and collecting tubules develop in pyramids. In glomeruli – thickening and double-contour of capillary membranes with aneurysmal expansions of the capillary lumen. In the cytoplasm of the epithelium of the tubules and their lumens are protein granules.

*Proteinuric stage*.

*Macroscopically*: the kidneys are enlarged, dense with a pale gray or yellow-gray surface. In section, the cortical layer is wide, matte, the medullar substance is gray-pink with a "greasy" sheen – **a large "greasy" kidney**.
*Microscopically:* amyloid appears in the glomeruli in the form of small deposits in the mesangium and some capillary loops and walls of arterioles. Sclerosis and amyloidosis of the pyramids contribute to the atrophy of deep nephrons, reduction of juxtamedullary blood flow and lymph outflow in the renal medulla. The epithelium of the tubules of the main parts in the state of hyaline-droplet and hydropic dystrophy, cylinders are found in the tubules.

*Nephrotic stage.*

*Macroscopically*: the kidneys are large, dense, waxy – **a large white amyloid kidney**.
*Microscopically*: amyloid is found in the capillary loops of the glomeruli, arterioles and arteries, along the own membrane of the tubules. In the pyramids and the intermediate zone, sclerosis and amyloidosis become diffuse. Channels are expanded, filled with cylinders. In the epithelium of the tubules and the stroma - cholesterol accumulation.

*Azotemic stage*.

*Macroscopically*: the kidneys are moderately reduced, dense, with scars in the cortical layer – **amyloid-shrunken kidneys.**
*Microscopically*: diffuse amyloid deposition and sclerosis. Death, atrophy and replacement of nephrons with connective tissue.
*Complication:*

- infectious
- hypertension
- acute renal failure
- chronic renal failure

## Acute renal failure

***Acute renal failure (ARF)*** is an acute violation of the filtration, excretory and secretory function of both kidneys or a single kidney due to the impact on the renal parenchyma of various pathological exogenous and endogenous factors, leading to oliguria, hyperazotemia, water-electrolyte and acid-base balance.
*Etiology.*There are 4 etiological forms of ARF.
1. Prerenal ARF:

- shock of various genesis (traumatic, anaphylactic, hemolytic, cardiogenic, infectious-toxic, etc.),

- exposure to nephrotoxic substances (drugs, ethylene glycol, methanol, heavy metal salts, acetic acid, etc.)

2. Renal ARF:
   - kidney disease (acute glomerulonephritis, pyelonephritis, interstitial nephritis),
   - systemic diseases with kidney damage (SLE, nodular periarteritis, Wegener's granulomatosis, etc.),
   - thrombosis and embolism of the renal arteries (veins).
3. Postrenal ARF:
   - obstruction of the urinary tract with stones, blood clots, tumor, enlarged lymph nodes
   - retroperitoneal fibrosis
   - acute urinary retention with prostate enlargement
4. Arenal form – a rare form that develops in patients after removal of both or a single kidney.

*Stages of acute renal failure:*

- The initial (shock) stage or period of action of the etiological factor
- Oligoanuric stage
- Stage of recovery of diuresis
- Stage of recovery of renal function

*In the initial stage*, venous hyperemia of the intermediate zone and pyramids is observed with focal ischemia of the cortical layer, where the capillaries of the glomeruli collapse. Edema of the interstitium is accompanied by lymphostasis. In the epithelium of the tubules hyaline-drop, hydropic and fatty dystrophy are found, in the lumen of the tubules – cylinders, crystals of myoglobin.

*In the period of oligoanuria* – necrotic changes in the tubules of the main parts, accompanied by destruction of the basal membranes of the distal tubules – tubulorexis. The cylinders block the lumens of the tubules at different levels, which leads to stagnation of the glomerular ultrafiltrate in the capsule cavity. Edema of the interstitium is accompanied by leukocyte infiltration and hemorrhage, pronounced venous stasis with venous thrombosis. The described changes correspond to the so-called necrotic nephrosis.

*In the stage of recovery of diuresis*, edema and cellular infiltration are reduced, in the tubules there are islets-regenerates, which consist of light epithelial cells. Necrotized tubules with preserved basal membranes regenerate completely, sclerosis foci are formed at the site of destroyed nephrons.

*Consequences:*

- recovery
- segmental or total necrosis of the cortical layer of the kidneys
- chronic renal failure
- death due to uremia.

## Chronic renal failure

***Chronic renal failure (CRF)*** is a pathological symptom complex caused by a sharp decrease in the number of functioning nephrons, which leads to impaired excretory and incretory function of the kidneys, homeostasis, metabolic disorders, acid-base balance, activity of all organs and systems.

*Etiology:*

1. Chronic glomerulonephritis, subacute glomerulonephritis, chronic interstitial nephritis, chronic pyelonephritis, tuberculosis and renal amyloidosis.
2. Congenital kidney diseases: polycystosis, hypoplasia, Alport's syndrome, Fanconi's syndrome (nephropathy of degenerative-dysplastic type with polydipsia, polyuria, hypoisostenuria, physical retardation and gradually progressive renal failure), etc.
3. Systemic diseases: SLE, systemic scleroderma, rheumatoid arthritis, dermatomyositis, systemic vasculitis, etc.
4. Endocrine diseases with metabolic disorders (diabetes, hyperparathyroidism, gout).
5. Cardiovascular diseases: hypertension, renal artery stenosis (atherosclerotic, intramural, fibromuscular).
6. Obstructive diseases of the upper (stones, tumors) and lower (abnormalities of the bladder, urethra, adenoma and prostate cancer) urinary tract with the accession of chronic pyelonephritis.

*Pathogenesis.* Under the influence of etiological factors the number of functioning nephrons and glomerular filtration decreases, fibroplastic processes with replacement of nephrons by connective tissue develop. In the preserved nephrons compensatory hyperfiltration is noted, which contributes to their progressive damage. A sharp decrease in the mass of active nephrons in CRF causes the development of major pathogenetic factors:

1. Impaired renal excretory function and retention in the body of products of nitrogen metabolism – urea, creatinine, uric acid, phenol, indole, guanidine and its derivatives.
2. Disorders of water metabolism – impaired ability of the kidneys to concentrate urine, develops polyuria, nocturia, isostenuria, hypostenuria. In the polyuric stage, dehydration develops. In the terminal period, the amount of urine decreases with the development of hyperhydration.
3. Electrolyte imbalance.
4. Violation of acid-base balance. At decrease in glomerular filtration less than 25% the metabolic acidosis which is caused by decrease in excretion with urine of acid valencies, loss of bicarbonates, decrease in secretion of hydrogen ions develops.
5. The development of anemia is due to a decrease in the production of erythropoietin, an increase in the production of erythropoietin inhibitor, increased hemolysis of erythrocytes, impaired absorption of iron vitamins B12, B6, folic acid, proteins.
6. Dysfunction of the renal pressor-depressor system – increased renin production and decreased prostaglandin production contributes to the development of hypertension.

*Pathomorphology*. CRF is characterized by a gradual shrinkage and reduction of kidney size, mosaic morphological changes, ie a combination of sclerosed glomeruli and tubules with glomerular hypertrophy and dilated tubules with foci of intermediate tissue fibrosis. Glomerular sclerosis is accompanied by the desolation of the corresponding tubules, the epithelium of which atrophies. Hypertrophied tubules and small cysts are found along with atrophied tubules. The interstitial tissue of the

kidney is enlarged, there is an overgrowth of connective tissue with the formation of scars. Development of hyalinosis and lipoidosis of the walls of arterioles, obliteration of small branches.

*Consequences* – the development of uremic coma, death.

## Urolithiasis

***Urolithiasis*** is a disease characterized by the formation of stones in the urinary tract, which are formed from the components of urine.

Urolithiasis accounts for 30-45% of all urological diseases.

*Etiology and pathogenesis*. Polyetiological disease: congenital anomalies, climatic conditions, deficiency of vitamins and microelements, hormonal disorders, changes in urine pH, inflammatory processes, etc.

*Chemical composition of stones.* Every stone has an organic matrix. Most often it is impregnated and covered with calcium salts.

1. Calcium oxalate stones (calcium salts of oxalic acid) – the most common. Dark brown, branched shape, resulting injury of the mucous membrane of the renal pelvis, ureter. Calcium oxalates precipitate at normal urine pH.
2. Phosphate stones (phosphates) contain calcium salts of phosphoric acid: round, soft, brittle, grayish. They are formed in an alkaline environment.
3. Carbonate stones (carbonates) - calcium salts of carbonic acid: homogeneous, white, brittle.
4. Urates - stones from uric acid salts: hard, smooth, yellow-brick color.
5. Cystine stones (rare): yellow, round, soft texture with a smooth surface.
6. Cholesterol (very rare): soft, brittle, black.
7. Protein stones generally consist of fibrin with impurities of salts and bacteria, white, soft, flat. These stones are X-ray negative, so before surgery they are diagnosed as urate.

*Pathomorphology*. Changes in the kidneys in urolithiasis depend on their complications – chronic pyelonephritis, hydronephrotic transformation (hydronephrosis).

Prolonged stay of stones in the kidney and ureter, in addition to pyelonephritis, pyeloectasia, hydronephrosis, ureterohydronephrosis, can cause wrinkling and fatty degeneration of the kidney, pedunculitis, apostematous pyelonephritis, carbuncle of the kidney, senescence, pyonephrosis periureteritis, perforation of the kidney into the intestine with the formation of renal fistula, etc.

Short-term stay of a stone in a renal pelvis and an ureter is followed by insignificant changes in their mucous membrane.

## Hydronephrosis

***Hydronephrosis*** (Greek hydro – water and nephros – kidney) – a disease associated with impaired urine outflow from the kidney, increasing its size and the gradual atrophy of its parenchyma.

Impaired urine outflow due to obstruction of the ureteral lumen by a stone and pathological changes in its wall cause morphological changes in the kidney. At first (after disturbance of outflow of urine in the middle or lower third of an ureter) in aseptic conditions there is an expansion only of an ureter, and then a renal pelvis and calyces.

Due to the accession of the infection, aseptic ureterohydronephrosis is transformed into pyonephrosis. Ureteritis, periureteritis develop, the ureter becomes sclerosed and becomes immobile. At the site of obstruction (obturation) of the ureter with a stone often formed narrowing, bedsores and even perforation of its wall.

## Polycystic kidney disease

***Polycystic kidney disease*** is an inherited kidney disease with bilateral cystosis of a relatively developed parenchyma – canalicules and collecting tubules.

*Etiology:* hereditary disease – a violation of embryogenesis in the first weeks, accompanied by the formation of glomerular, tubular and excretory cysts.

*Macroscopically*: the appearance of the kidneys in polycystosis resembles a bunch of grapes. Kidney tissue consists of many cysts of different sizes and shapes, filled with light fluid, colloidal (semi-liquid) masses of chocolate color.

*Microscopically*: the cyst wall is covered with cubic, flattened epithelium; sometimes a shrunken vascular glomerulus is found in it. Renal tissue between the cysts is atrophied. Polycystic kidney disease is often combined with polycystic liver, ovary, lung and pancreas.

*Consequence* – progressive renal failure.

### *Training macropreparations*

**Rapidly progressing glomerulonephritis ("large motley kidney").** The kidneys are sharply enlarged (weighing up to 300-500 g, normally 120-150 g), flabby, the cortical layer is thickened, swollen, dull, with red dots and is well separated from the dark red medullar substance of the kidney.

**Chronic glomerulonephritis with wrinkles (secondary shrunken kidneys).** The kidney is reduced in size, dense, fine-grained surface, due to the alternation of areas of sclerosis and hyalinosis of the glomeruli with areas of hypertrophied glomeruli; in section the cortical and cerebral substance is thinned.

**Renal amyloidosis**. Kidney white-gray, in section with sebaceous luster, the edges of the section are sharp, fragile.

**Polycystic kidney disease**. The kidney is significantly increased in size, the parenchyma of the organ is replaced by multiple cysts of different sizes containing colloidal masses.

**Hydronephrosis.** The kidney is sharply increased in the sizes, its cortical and layers are thinned with the erased borders, pelvis and cups are stretched, in a cavity of a pelvis the coral stone is visible.

### *Training micropreparations*

**Mesangiocapillary glomerulonephritis** (hematoxylin and eosin staining): diffuse thickening of glomerular capillary walls, moderate mesangiocyte proliferation, with partial hyalinosis and glomerular lobules. In the epithelium of the convoluted tubules granularity and hydropic dystrophy, in the lumen of the tubules - hyaline cylinders.

**Extracapillary productive glomerulonephritis** (hematoxylin and eosin staining): the inflammatory process is localized mainly extracapillary and is represented by proliferation of podocytes and nephrothelia with the formation of characteristic of this type of nephritis "crescents". There is damage (microperforation) of the basal membranes of capillaries, deposition of fibrin in the glomerulus, foci of fibrinoid necrosis and sclerosis, synechiae with capsule. The epithelium of the proximal and

distal tubules in the state of hydropic dystrophy, the renal stroma is diffusely sclerosed, focially infiltrated with lymphohistiocytic elements.

**Secondary-shrunken kidney due to chronic glomerulonephritis** (staining with hematoxylin and eosin): in some areas there is atrophy of the glomeruli and tubules, their replacement by connective tissue. The glomeruli look like scars or hyaline balls; in other areas the glomeruli are preserved, sometimes hypertrophied, capillary loops are sclerosed, the lumen of the tubules is expanded, the epithelium is thickened; arterioles are sclerosed and hyalinized.

**Renal amyloidosis** (Congo-red color): the presence of amyloid between the loops of capillaries in the glomerulus; along the basal membranes of the tubules and in the stroma.

**Necrotic nephrosis** (hematoxylin and eosin staining): necrosis captures the epithelium of the proximal and distal tubules and is focal. Expressed edema, leukocyte infiltration of the stroma, hemorrhage. These changes are characteristic of the oligoanuric stage of the disease.

## Questions for self-control

1. Classification of kidney diseases.
2. Definition, etiology and pathogenesis of glomerulonephritis; renal and extrarenal symptoms of glomerulonephritis;
3. Classification, macro- and microscopic features of acute, subacute and chronic glomerulonephritis.
4. Amyloidosis of the kidneys: definition, etiology, pathogenesis, pathological anatomy of amyloidosis by stages; complications, causes of death.
5. Acute and chronic tubulopathies: definition, etiology, pathogenesis, pathological anatomy, complications, causes of death.
6. Urolithiasis: definition, etiology, pathogenesis, pathological anatomy, complications, causes of death.
7. Interstitial nephritis: definition, etiology, pathogenesis, pathological anatomy, complications, causes of death.
8. Pyelonephritis: definition, etiology, pathogenesis, pathological anatomy, complications, causes of death.
9. Acute and chronic renal failure: definition, etiology, pathological anatomy, consequences.

## *Examples of tests*

1. At the autopsy of a 67-year-old man, a coral-shaped stone was found, which fills the entire pelvis of the right kidney. The kidney is enlarged, full-blooded, the capsule is difficult to remove, the cavities of the pelvis and calyces are dilated, filled with turbid greenish-yellow viscous fluid, their mucous membrane is dull, with foci of hemorrhage. In section, the kidney tissue is variegated, with yellow areas up to 1 cm in diameter. Identify the complications of urolithiasis.

A. * Chronic pyelonephritis with exacerbation
B. Tumor
C. Post-infectious glomerulonephritis
D. Primary amyloidosis
E. Rapidly progressing glomerulonephritis

2. The young man developed fatal renal failure during the year. At autopsy, large variegated buds with small red drops in the yellow-gray cortical layer were found. Histologically, "crescents" of proliferating nephrothelia were found in the glomeruli. Your diagnosis.
A. * Rapidly progressing glomerulonephritis
B. Amyloidosis
C. Hemorrhage in the kidneys
D. Purulent nephritis
E. Kidney cancer
3. A patient with bleeding developed acute renal failure that resulted in death. At autopsy macroscopically: the kidneys are enlarged with a wide pale pink cork layer, sharply separated from the dark red pyramids. Microscopically: the absence of epithelial nuclei of the convoluted tubules, tubulorexis, venous stasis, nuclei of vascular glomeruli and straight tubules are preserved. Your diagnosis.
A. * Necronephrosis
B. Infarction
C. Glomerulonephritis
D. Pyelonephritis
E. Nephrosis
4. A 33-year-old man died of uremia. At autopsy - enlarged buds resemble a bunch of grapes, weighing 500g each, consisting of many cavities with a diameter of 0.5-2cm, filled with light yellow clear liquid. Bowls and ureters without features. What is the kidney disease that caused the uremia?
A. * Bilateral polycystic kidney disease
B. Chronic pyelonephritis
C. Kidney tumor
D. Tuberculosis of the kidneys
E. Rapidly progressing glomerulonephritis
5. A 21-year-old man underwent nephrobiopsy. Revealed: proliferation of mesangial cells, swelling and proliferation of endothelial cells, enlargement of the mesangial matrix, diffuse thickening and bifurcation of the glomerular basal membrane, moderate tubulo-interstitial component. Electron microscopic examination revealed interposition of the mesangium, diffuse and uneven thickening of the glomerular basal membrane. Determine the form of glomerulonephritis.
A. * Mesangioproliferative glomerulonephritis
B. Rapidly progressing glomerulonephritis.
C. Membranous glomerulonephritis.
D. Mesangiocapillary glomerulo-nephritis
E. Post-infectious glomerulonephritis.

## DISEASES OF THE ESOPHAGUS AND STOMACH. GASTRITIS. TUMORS OF THE ESOPHAGUS AND STOMACH. ULCEROUS DISEASE OF THE STOMACH AND DUODENUM

Diseases of the esophagus are divided into:

- inflammatory,

- strictures,
- diverticula,
- tumors.

## Esophagitis

*Esophagitis* – inflammation of the mucous membrane of the esophagus.

*Classification:*

By etiology:
- primary (rare),
- secondary (more often).

By duration:
- acute,
- chronic.

*Acute esophagitis*

Types: catarrhal, fibrinous, phlegmonous, ulcerative-gangrenous.

*Macroscopically*:
- catarrhal esophagitis – the mucous membrane is swollen, hyperemic, the folds are smoothed;
- fibrinous esophagitis – a whitish-gray pellicle appears on the mucous membrane;
- destructive forms (phlegmonous, ulcerative-gangrenous): purulent melting of the esophageal wall or the appearance of necrotic ulcers of varying depth.

*Microscopically:* wall infiltration by lymphocytes, plasma cells, neutrophils.

*Consequences:*
- most often – complete epithelialization of the mucous membrane of the esophagus;
- sometimes with deep destructive changes (due to chemical burns) there are scar strictures of the esophagus.

*Chronic esophagitis*

Occurs due to chronic irritation of the esophagus:
- smoking, alcohol, hot and spicy foods;
- on the background of circulatory disorders in the esophageal wall, etc.

*Macroscopically:* the mucosa is swollen, hyperemic, with areas of epithelial destruction. With reflux esophagitis, erosions and ulcers appear on the mucosa.

*Microscopically:* leukoplakia and sclerosis of the mucous membrane may be observed; at specific inflammations there is a corresponding morphological picture.

*Consequences*: leukoplakia (facultative precancer).

## Esophageal strictures

*Esophageal strictures* – narrowing of the esophagus (clinically – esophageal stenosis).

*By reason*, there are:
- congenital;
- post-infectious (actinomycosis, tuberculosis, diphtheria, etc.);
- caused by endogenous (gastric juice) and exogenous (salts, acids, radiation) stimuli;
- tumors;
- external compression and pathological formations of the mediastinum.

## Esophageal diverticulum

*Esophageal diverticulum* is a limited blind protrusion of the wall.
*Types*: true and muscular.
A true diverticulum consists of all the layers of the esophagus.
The muscular diverticulum consists of mucous and submucosal layers, protruding through the slits in the muscular layer.
*Etiology* of diverticula:

- hereditary defects of the connective tissue and muscle wall;
- acquired (inflammation, sclerosis, strictures, high pressure in the esophagus).

*By localization:* pharyngo-esophageal, bifurcation, epiphrenal, multiple.
*By reason*: relaxative, connective.
*Complications* – diverticulitis.

## Esophageal cancer

*Risk factors:*

- features of food: very hot food; concentrated alcohol; frozen, dry, overcooked meat, fish;
- bad habits: smoking, chewing gum;
- geological and mineralogical features of the soil;
- lack of vitamins, iron, etc.

*Background diseases:*

- ulcerative esophagitis;
- long-term esophageal spasm;
- genetic predisposition.

*Precancerous processes*:

- moderate and severe squamous cell dysplasia;
- parakeratosis, hyperkeratosis of the mucous membrane of the esophagus;
- leukoplakia;
- papillomatosis;
- congenital dyskeratosis.

*Localization:* middle / lower / upper third of the esophagus (9/3/1).
*Type of growth and shape of the tumor*:

- exophytic;
- endophytic;
- unicentric, multicentric;
- annular dense;
- ulcerative.

*Histological classification:*

- squamous cell carcinoma with or without keratinization;
- adenocarcinoma;
- undifferentiated cancer: fibrous cancer; medullary cancer.

*Lymphogenic metastases depending on the location of the tumor*.

- In cancer of the upper third of the esophagus: paratracheal, paraesophageal, supraclavicular lymph nodes.
- With cancer of the middle third of the esophagus: paraesophageal, bifurcation, basal, paracardial lymph nodes.

- In cancer of the lower third of the esophagus: in the closest to the tumor paraesophageal, paracardial lymph nodes and along the abdominal area.

*Consequences*:

- narrowing of the esophageal lumen, swallowing disorder (difficulty);
- nutritional depletion;
- compression of surrounding organs (trachea, bronchi, mediastinum, pleura, etc.);
- the formation of fistulas between the esophagus and respiratory tract;
- abscess and lung gangrene;
- aspiration pneumonia;
- pleural empyema, purulent mediastinitis.

## Gastritis

*Gastritis* is an inflammatory disease of the gastric mucosa.

Types: acute and chronic gastritis.

### ***Acute gastritis***

*Etiology and pathogenesis*:

- nutritional factor – spicy, cold, hot, rough food;
- the effect of alcohol;
- drug factor – corticosteroids, salicylates, sulfonamides, etc.;
- chemical exposure – occupational hazards, acids, alkalis;
- infectious factor – salmonella, staphylococci, etc.;
- toxic substances and products of metabolic disorders.

There are:

- exogenous gastritis, when the pathological factor directly affects the gastric mucosa (alcohol, drugs, etc.);
- endogenous gastritis, when the pathological effect occurs indirectly and is realized through vascular, neuro-humoral or immune mechanisms (allergic gastritis, gastritis with uremia, etc.).

*By the prevalence of the process*:

- focal gastritis (fundal, antral, pyloroantral and pyloroduodenal);
- diffuse gastritis.

*Forms of acute gastritis*:

- catarrhal (simple),
- fibrinous,
- purulent (phlegmonous),
- necrotic.

*Macroscopically:*

- catarrhal gastritis: the mucous membrane is thickened, hyperemic, the folds are smoothed;
- fibrinous gastritis: a whitish-gray pellicles appears on the mucous membrane;
- destructive forms: visually revealed purulent melting of the stomach wall or the appearance of necrotic ulcers of varying depth.

*Microscopically*: infiltration by lymphocytes, plasma cells, neutrophils.

*Consequences*:

- complete recovery of the mucous membrane (catarrhal gastritis);
- chronicity (with frequent recurrences);

- atrophy of the mucous membrane with subsequent sclerotic deformation of the gastric wall (destructive forms).

## ***Chronic gastritis***

*Etiology*.

Exogenous factors:

- non-compliance with the diet and rhythm of nutrition;
- alcohol abuse;
- action of chemical, thermal and mechanical agents;
- the effect of occupational hazards.

Endogenous factors:

- Helycobacter pylory;
- chronic autointoxication;
- allergic reactions;
- circulatory disorders in the gastric mucosa;
- neuroendocrine disorders;
- gastroduodenal reflux.

*Classification* (forms) of chronic gastritis:

- superficial;
- atrophic with remodeling and without remodeling of the mucous membrane;
- peculiar forms: giant hypertrophic gastritis (Menetrie's disease), eosinophilic gastritis.

*Modified Sydney classification:*

- Autoimmune (type A);
- Helicobacter-associated (type B);
- Reflux gastritis (type C).

*Chronic superficial gastritis*:

- dystrophic changes of the superficial fossular epithelium, change in the shape of epitheliocytes;
- reduction of secretory action of main and parietal cells;
- lamina propria is swollen and infiltrated by lymphocytes, plasma cells, single neutrophils.

*Chronic atrophic gastritis*

*Macroscopically*: the mucous membrane is thinned, the folds are smoothed.

*Microscopically*: the number of glands decreases. Preserved glands are placed in groups, their ducts are dilated. The secretion of pepsin and hydrochloric acid is disturbed. The mucous membrane is infiltrated by lymphocytes, plasma cells, single neutrophils. Epithelial metaplasia occurs. Gastric platens, resembling the villi of the small intestine, covered with fringed epitheliocytes, appear goblet cells and Panet cells (rearrangement of the intestinal mucosa). The secretory cells of the stomach (main, parietal, mucous) disappear, cubic cells appear, which are characteristic of the pyloric glands. Later, along with metaplasia, dysplasia develops. There are moderate and severe atrophic gastritis.

*Consequences:*

- chronic anemia,
- stomach cancer.

## Stomach cancer

*Risk factors:*

- alimentary (spicy and hot food; concentrated alcohol; irregular diet);
- carcinogens;
- radiation from building materials;
- genetic predisposition;
- gender: men/women – 2/1.

*Background diseases:*

- chronic gastritis (hypoacid, achilles),
- polyposis of the stomach,
- callous gastric ulcer,
- pernicious anemia,
- atrophic gastritis after gastrectomy.

*Precancerous processes:*

- dysplasia of the glandular epithelium I-III degree,
- intestinal metaplasia of the epithelium,
- combination of dysplasia with intestinal metaplasia,
- atrophy of the mucous membrane,
- malignancy of polyps.

*Cancer localization:*

- antral and pyloric parts of the stomach – 65%;
- cardiac part – 20%;
- proximal, subcardiac part – 15%;
- total defeat;
- multiple lesions.

*Type of tumor growth:*

- exophytic,
- endophytic,
- exo-endophytic.

*By number of nodes:*

- unicentric,
- multicentric.

*Forms of tumor growth.*

Cancer with predominantly endophytic growth:

- ulcerative-infiltrative (50%),
- diffuse (20-25%).

Cancer with predominantly exophytic growth:

- fungal (mushroom-shaped) (10%);
- polypoid (5%);
- plaque-like (1-5%);
- saucer-shaped (1-5%);
- ulcer-cancer (1-5%).

Cancer with exo-endophytic growth: transitional forms.

*Histological classification:*

- adenocarcinoma (tubular, papillary, mucinous, poorly differentiated, intestinal and diffuse cancers);

- squamous cell carcinoma;
- glandular squamous cell carcinoma;
- undifferentiated cancer (skirr, solid, ring-cell).

*Metastasis.*

1. Lymphogenic spread:
   - in regional lymph nodes (orthograde),
   - in distant lymph nodes (orthograde, retrograde),
   - retrograde metastases
     - in the left supraclavicular lymph nodes ("Virchow metastases");
     - in parameterium and pararectal lymph nodes ("Schnitzler's metastases");
     - in the ovaries ("Krukenberg's cancer").
2. Implantation (contact) spread – into the pleura, peritoneum (peritoneal carcinomatosis), greater omentum, rectal-vesical fold (in men), rectal-vaginal fold (in women).
3. Hematogenous spread: 50% in the liver (portal vein), lungs, pancreas, bones, kidneys, adrenal glands.

*Complication:*

- secondary necrotic and inflammatory changes of the tumor (perforation, bleeding, peritumorous inflammation, gastric phlegmon);
- tumor growth in neighboring organs (jaundice, portal hypertension, ascites, intestinal obstruction, portal stenosis, etc.);
- cancerous cachexia.

## Peptic ulcer

***Peptic ulcer*** – a chronic disease with cyclic course, the main morphological manifestation of which is recurrent gastric or duodenal ulcer (ulcus ventriculi, ulcus duodeni).

Symptomatic ulcers of the stomach and duodenumoccur when:

- endocrine diseases – endocrine ulcers;
- circulatory disorders – dyscirculatory-hypoxic ulcers;
- exogenous and endogenous intoxications – toxic ulcers;
- allergies – allergic ulcers;
- specific inflammation – tuberculous or syphilitic ulcers;
- drug treatment – drug ulcers.

Depending on the location of the ulcer and the pathogenesis of the disease, there are ulcers in the pyloroduodenal area and in the body of the stomach.

*Epidemiology:*

- incidence rate – 10-12%;
- age: 30-40 years;
- sex: male/female ratio, as 6/1 in gastric ulcer and 5/1 in duodenal ulcer;
- localization: in 70% of cases – duodenum, in 30% - gastric ulcer;
- the predominance of duodenal ulcer: at a young age, and gastric ulcer – in adulthood and old age.

*Risk factors:*

- chronic gastritis;
- endocrine diseases: parathyroidism, thyrotoxicosis;
- dyscirculatory-hypoxic disorders (coronary heart disease, hypertension);

- toxic: in exogenous and endogenous intoxications (salts of heavy metals);
- tuberculosis, syphilis;
- operations on the stomach and intestines;
- medicinal: in the treatment of corticosteroids, salicylates, etc.;
- allergic;
- bad habits – smoking, alcohol.

*Etiology:*

- the causative agent Campylobacter pyloridis (Helycobacter pylory), which has a high hydrolysis activity and has a direct destructive effect on the gastric mucosa (Marshall's infection theory);
- vascular disorders (Virchow's theory);
- change in the composition of gastric juice (Aschoff peptic theory);
- stress, psycho-emotional overstrain (cortico-visceral theory of Bykov-Kurtsin);
- disorder of the hypothalamic-pituitary-adrenal system (hormonal theory).

*Pathological anatomy:* The morphological substrate of peptic ulcer disease is a chronic recurrent ulcer, which during its formation goes through several stages:

- erosion,
- acute ulcer,
- chronic ulcer.

Erosion is a superficial defect of the gastric mucosa that does not penetrate the muscular plate of the gastric mucosa.

Acute ulcer – irregularly rounded or oval tissue defects (in the amount of 5 or more) are deep, with clearly defined sharp edges. The bottom is formed by a muscular (serous) layer of a stomach of black or dirty-gray color. In most cases, localization on the small curvature, in the antral and pyloric parts of the stomach and in the area of the bulb of the duodenum.

Chronic (peptic) ulcer is usually single, rarely 2-3 ulcers.

*Macroscopically* acute and chronic ulcers have different appearance.

**Differential diagnosis of acute and chronic ulcers**

| *Sign* | *Acute ulcer* | *Chronic ulcer* |
|---|---|---|
| Localization | • small curvature of the stomach;<br>• in the antrum;<br>• the pyloric part;<br>• in the area of the bulb of the duodenum. | • small curvature of the stomach;<br>• stomach gate;<br>• anterior wall of the antrum of the stomach;<br>• bottom of the stomach;<br>• large curvature of the stomach;<br>• body of the stomach;<br>• anterior or posterior walls of the bulb of the duodenum. |
| Shapes | • funnel-shaped: the base faces the mucous membrane, and the apex to the peritoneum;<br>• rounded;<br>• oval;<br>• slit-like. | • round;<br>• oval;<br>• in the form of a "butterfly" with wings open on the front and back wall of the stomach;<br>• polygonal; |
| Size | small (from 0.1 mm to 20 mm) | large (from 2 cm to 15 cm). |

| | | |
|---|---|---|
| Margins | • sharp, "stamped" | • dense;<br>• raised (roller-shaped);<br>• cardiac edge deep, steep, slightly undermined (in the form of a visor);<br>• pyloric edge is flat (terraced). |
| Bottom | • formed by the submucosal layer;<br>• formed by the muscular layer;<br>• colored dark brown (hematin hydrochloric acid). | • dense, smooth;<br>• raised, rough;<br>• granular with vascular thrombosis;<br>• with a hole (perforation);<br>• painted dark brown due to hematin hydrochloric acid;<br>• reaches the muscular layer;<br>• reaches the peritoneum. |

*Microscopically depending on the period.*

During the period of exacerbation in the bottom and edges of the ulcer are three main areas:

- area of fibrinoid necrosis, the surface of which is covered with fibrinous-purulent or purulent exudate;
- area of granulation tissue with a large number of eosinophilic leukocytes;
- area of coarse fibrous connective tissue with signs of mucoid and fibrinoid swelling; fibrinoid changes in the walls of blood vessels, sometimes with thrombosis.

In the period of remission in the edges of the ulcer is scar tissue; the mucous membrane around the ulcer is thickened with hyperplasia. Scarring of the muscular layer is observed in the area of the bottom. Scar tissue is characterized by a large number of blood vessels with thickened walls and narrowed lumen. Nerve fibers and ganglion cells are in the stage of dystrophy and decay.

*Clinical and morphological complications of peptic ulcer.*

- Destructive complications:
  - arosive bleeding – haemorrhagia per diabrosin (12%);
  - perforation (breakthrough) of the organ wall (18%);
  - penetration – the spread of ulcers to neighboring organs.
- Inflammatory:
  - gastritis;
  - duodenitis;
  - perigastritis;
  - periduodenitis.
- Ulcerative scar: pylorostenosis.
- Malignancy of the ulcer.
- Combined complications

*Causes of death:*

- profuse gastrointestinal bleeding;
- diffuse fibrinous-purulent peritonitis.

### *Training macropreparations*

**Chronic atrophic gastritis**. The mucous membrane in the area of pathology is smoothed, there are no folds, atrophy of the mucous membrane.

**Fungal cancer of the stomach**. On the mucous membrane of significant size protrusion into the stomach cavity, which resembles a mushroom, the consistency is dense, the surface is uneven, the growth is exophytic, unicentric.

**Diffuse gastric cancer**. A significant part of the stomach wall is sharply thickened due to the growth of dense whitish tissue, which has no clear boundaries; mucous membrane with smoothed folds, rigid.

**Plate-like gastric cancer**. On the small curvature of the stomach is determined by a large plate-shaped node with raised uneven edges and lowered ulcerative bottom. The tissue of the node is white-gray, dense, germinates all layers of the stomach wall, has no clear boundaries.

**Gastric polyp**. There is a small exophytic formation that protrudes into the lumen of the stomach on a broad basis with a papillary surface.

**Chronic gastric ulcer**. On the small curvature of the stomach in the pyloric department is located a significant deepening in the stomach wall 2x3.5 cm; the surrounding surface is devoid of characteristic folds. The folds converge to the limits of formation. The bottom of the ulcer is smooth, formed by a serous membrane, the edges are rolled up, dense, have a different configuration: the edge facing the goalkeeper, sloping.

**Hemorrhagic erosions of the stomach**. Gastric mucosa with numerous formations of dense consistency, black (due to hematin hydrochloric acid).

### *Training micropreparations*

**Gastric adenocarcinoma** (hematoxylin and eosin staining): the tumor is represented by glandular complexes of various shapes and sizes, which are formed by atypical epithelial cells with hyperchromic nuclei, figures of pathological mitoses.

**Chronic atrophic gastritis with remodeling of the mucous membrane** (staining with hematoxylin and eosin): the mucous membrane of the fundus of the stomach is sharply thinned, the glands are reduced, are located in groups. The ducts of the glands are dilated. There are foci of intestinal metaplasia of goblet cells. Diffuse lymphoplasmacytic infiltrate, sclerosis in the own plate of the mucous membrane.

**Acute necrotic gastritis** (staining with hematoxylin and eosin): in the superficial parts of the mucous membrane there are alternative changes, in the deep parts - inflammatory infiltration, hemorrhage.

**Chronic gastric ulcer with exacerbation** (hematoxylin and eosin staining): a zone of fibrinoid necrosis is observed in the area of the bottom and edges of the ulcer. On the surface of necrotic masses - fibrinous-purulent exudate. The area of necrosis is separated by granulation tissue with a large number of thin-walled vessels and cells, many of which are eosinophils. Deeper behind the granulation tissue is coarse fibrous connective tissue

### *Questions for self-control*

1. Pathomorphology of esophagitis and tumors of the esophagus.
2. Definition, etiology, classification and pathomorphology of acute gastritis.
3. Definition, etiology, classification and pathomorphology of chronic gastritis.
4. Gastric cancer: definition, etiology, precancerous conditions and processes.

5. Macroscopic forms and microscopic types of gastric cancer.
6. Definition of peptic ulcer disease and symptomatic ulcers.
7. Localization and macroscopic characteristics of acute and chronic gastric and duodenal ulcers.
8. Pathomorphological characteristics and complications of peptic ulcer disease.

***Examples of tests***

1. At a gastrobiopsy at the patient the intestinal metaplasia of a superficial epithelium of a mucous membrane is established. At the same time sclerosis at the site of mucous glands and lymphohistiocytic infiltration are observed. Your diagnosis.
A. * Chronic atrophic gastritis
B. Corrosive gastritis
C. Chronic gastritis with glandular lesions without atrophy
D. Erosive gastritis
E. Superficial chronic gastritis
2. Histological examination of biopsies taken from the thickened edges of gastric ulcers revealed nest clusters of sharply atypical hyperchromic small epithelial cells located among a very developed stroma. Your diagnosis:
A. * Skin undifferentiated cancer
B. Medullary cancer
C. Adenocarcinoma
D. Undifferentiated sarcoma
E. Adenoma
3. A 54-year-old patient died of acute heart failure (myocardial infarction). An autopsy in the stomach wall revealed 5 deep oval defects measuring 1 × 2 cm with smooth soft edges and a rough soft bottom. Your diagnosis.
A. * Acute ulcer
B. Chronic gastritis
C. Chronic ulcer
D. Gastric cancer
E. Acute fibrinous gastritis
4. Morphological examination of the stomach revealed a deep defect of the wall with damage to the muscular membrane, the proximal edge of which is undermined, the distal - sloping. Microscopic examination: at the bottom of the defect, a zone of necrosis is found, under which granulation tissue is located and a massive area of scar tissue at the site of the muscle layer. Your diagnosis.
A. * Chronic ulcer in the acute stage
B. Chronic ulcer with malignancy
C. Acute ulcer
D. Erosion
E. Cancer-ulcer

## HEPATITIS. HEPATOSIS

*Classification of liver diseases:*

By origin:

- hereditary,

- acquired,
- primary (own liver disease),
- secondary (liver damage in other diseases).

By duration:

- acute,
- chronic.

By etiology:

- infectious,
- toxic (endogenous and exogenous toxins),
- due to circulatory disorders,
- due to eating disorders (lack of protein, vitamins),
- due to metabolic disorders.

***Classification of liver diseases depending on the predominance of pathological processes***

| *Liver disease* | *Characteristic processes* |
|---|---|
| Hepatosis | dystrophy, necrosis of hepatocytes |
| Hepatitis | inflammation |
| Cirrhosis | • dysregenerative processes;<br>• multiple sclerosis;<br>• restructuring of liver tissue. |

## Hepatosis

*Hepatosis* – liver disease with a predominance of dystrophy and necrosis of hepatocytes.

*Classification:*

By etiology:

- hereditary,
- acquired.

By duration:

- acute – toxic dystrophy or progressive massive liver necrosis;
- chronic – fatty hepatosis.

*Toxic liver dystrophy*
*(progressive massive liver necrosis)*

*Etiology:*

- exogenous toxic substances: poisonous mushrooms, phosphorus, arsenic;
- endogenous intoxications: toxicosis of pregnant women (gestosis), thyrotoxicosis.

*Stages:*

1. Stage of yellow dystrophy (up to 2 weeks).

*Macroscopically:* the liver is enlarged, flaccid, yellow.

*Microscopically:*

- in hepatocytes parenchymal fatty dystrophy;
- necrosis, autolytic decay of hepatocytes.

2. Stage of red dystrophy (from the 3rd week).

*Macroscopically:* a sharp decrease in the volume of the liver, it becomes red.

*Microscopically:*

- massive necrosis of hepatocytes;

- fat-protein detritus is eliminated by macrophages;
- absence of hepatocytes around the sinusoid, exposure of the reticular stroma with a sharp dilation of blood vessels, which give a red color.

*Consequences:*

- acute liver failure;
- postnecrotic cirrhosis of the liver.

*Fatty hepatosis*

*Fatty hepatosis* (fatty liver disease, hepatic obesity, hepatic steatosis) is a chronic disease characterized by increased accumulation of fat in hepatocytes.

*Etiology:*

- Toxic substances
  - alcohol,
  - insecticides,
  - some medicines.
- Endocrine and metabolic disorders
  - diabetes,
  - general obesity.
- Hypoxia – cardiovascular, pulmonary insufficiency, etc.
- Abuse of fatty and carbohydrate foods.

*Macroscopically:* the liver is enlarged, its surface is smooth, yellow or reddish-brown ("clay", "goose" liver).

*Microscopically:* fatty vacuoles are found in hepatocytes.

Depending on the size of fat inclusions in hepatocytes there are:

- dusty obesity;
- small drip obesity;
- large-drip obesity ("ring-shaped" cells).

Depending on the prevalence of the process there are:

- disseminated obesity (single hepatocytes in the stage of obesity);
- zonal obesity (obesity in groups of hepatocytes);
- diffuse obesity (obesity of the entire parenchyma).

Stages of fatty hepatosis:

1. Simple obesity – no destruction of hepatocytes and mesenchymal cell reaction.
2. Obesity with hepatocyte necrobiosis and mesenchymal cell reaction.
3. Obesity with the initial restructuring of the lobular structure of the liver.

*Consequences*: at 1 and 2 stages – favorable; stage 3 – the formation of liver cirrhosis.

## Hepatitis

*Hepatitis* is a liver disease that is accompanied by inflammatory processes.

*Classification* by origin and etiology:

| Primary hepatitis | Secondary hepatitis |
|---|---|
| Hepatotropic viruses (viral hepatitis A, B, C, D, E, F, G) | Infectious diseases (yellow fever, typhoid fever, dysentery, sepsis, tuberculosis) |
| Alcohol abuse (alcoholic hepatitis) | Intoxications (thyrotoxicosis, metabolic products) |
| Drug abuse (drug-induced hepatitis), etc. | Systemic connective tissue diseases |
| Cholestasis, subhepatic jaundice | Gastrointestinal damage |

By the course hepatitis are divide into acute and chronic.

## ***Acute hepatitis***

*Macroscopically*: the appearance depends on the nature of the inflammatory process.
*Microscopically:*

1. Exudative:
   - serous hepatitis – serous exudate permeates the stroma of the liver;
   - purulent hepatitis – impregnation of portal tracts with purulent exudates.

2. Productive: dystrophy, necrosis of lobular hepatocytes and proliferation of reticuloendothelial structures. As a result, diffuse infiltrates of Kupffer cells, endothelium and hematogenous cells (lymphocytes, plasma cells, macrophages) are formed.

## ***Chronic hepatitis***

*General pathomorphological features*:

1. Dystrophy and necrosis of hepatocytes.
2. Regeneration.
3. Cellular inflammatory infiltrates.
4. Sclerosis of the stroma.
5. Cholestasis in the bile ducts.

*Macroscopically:* the liver is enlarged, dense, the capsule is thickened, the tissue in section has a colorful appearance.
*Microscopically:*

*Morphological types of chronic hepatitis*

| **Active chronic hepatitis (destructive)** | **Persistent chronic hepatitis** | **Cholestatic chronic hepatitis** |
|---|---|---|
| Severe dystrophy (Malloy's hyaline), necrosis of hepatocytes on the periphery of the lobe on the border with the portal tracts (border bridge-like necrosis) | Preservation of normal architecture of the body<br><br>Lack of hepatocyte necrosis (or rare) | Dystrophy, necrosis of hepatocytes |
| Lymphocytic infiltration of the portal tracts | Diffuse infiltration (lymphocytes, monocytes) of portal tracts | Severe cholestasis, cholangitis, cholangiolitis; stroma infiltration |
| *Consequences:* the development of liver cirrhosis | *Consequences:* favorable, except for viral hepatitis C (progression to chronic active hepatitis and cirrhosis) | *Consequences:* sclerosis of the stroma |

## Viral hepatitis

Etioepidemiological characteristics of hepatitis

| Characteristic | **HEPATITIS A (Botkin's disease)** | **HEPATITIS B** |
|---|---|---|
| *Etiology* | Hepatitis A RNA virus | Hepatitis B DNA virus |
| *Epidemiology* | - fecal-oral transmission<br>- incubation period | - parenteral transmission (blood transfusion, injections, tattoos, etc.) |

| | | |
|---|---|---|
| | 15-45 days,<br>- epidemic outbreaks (epidemic hepatitis)<br>- cirrhosis of the liver does not develop. | - incubation period up to 180 days<br><br>-characteristic development of liver cirrhosis. |
| *Course* | acute | acute, chronic. |

*Pathogenesis of viral hepatitis B:*

- primary reproduction of the virus in regional intestinal lymph nodes;
- viremia (lymphadenopathy, splenic hyperplasia);
- virus replication in hepatocytes;
- immune cytolysis;
- hepatocyte damage – parenchymal jaundice;
- production of antiviral IgM (anti HAV-IgM) and stop virus replication;
- formation of humoral immunity (antiHAV-IgM antibodies).

*Clinical and morphological forms of viral hepatitis B:*

- Acute cyclic (jaundice);
- Jaundiceless;
- Necrotic (malignant, lightning);
- Cholestatic (most common in the elderly);
- Chronic.

***Acute cyclic (jaundice) form***

Heat stage (1-2 weeks).

*Macroscopically*: the liver is enlarged, dense, red, the capsule is tense ("big red liver").

*Microscopically*

Parenchyma:

- hydropic and balloon dystrophy of hepatocytes,
- focal necrosis of hepatocytes,
- Councilmen's bodies in the form of spherical eosinophilic formations (mummified hepatocytes).

Stroma:

- diffuse infiltration by lymphocytes, macrophages, plasma cells, leukocytes;
- increased number of stellate reticuloendotheliocytes;
- many bile-filled capillaries;
- vascular hyperemia;
- destruction of hepatocyte membranes, which leads to an enzymatic "explosion".

Recovery stage (4-5 weeks).

*Macroscopically:* the liver gradually acquires normal size, the capsule is thickened, dull, redness decreases.

*Microscopically:*

- restoration of the beam structure of the lobules;
- reduction of hepatocyte dystrophy and necrosis;
- enhanced hepatocyte regeneration;
- many binuclear cells;
- cellular inflammatory infiltrates gradually disappear;
- sclerosis develops.

### ***Jaundiceless form***

*Macroscopically:* the changes are similar to the first stage of the cyclic form.
*Microscopically:*

- hydropic and balloon dystrophy of hepatocytes, Counsilmen's bodies are rare;
- significant diffuse infiltration by lymphocytes, macrophages, plasma cells and leukocytes;
- sharply increased number of stellate reticuloendotheliocytes;
- no cholestasis.

### ***Necrotic (lightning, malignant) form***

It is characterized by the predominance of necrotic processes in the liver parenchyma.
*Macroscopically:* the liver decreases in size, the tissue is gray-brown or yellow, the capsule is wrinkled.
*Microscopically:*

- massive necrosis of hepatocytes;
- Councilman's bodies;
- pronounced bile stasis in the capillaries;
- lumens of sinusoids expand sharply, plethora at resorption of necrotic masses;
- numerous hemorrhages.

Consequences:

- death in the acute period from hepatic coma;
- large nodular liver cirrhosis.

### ***Cholestatic form***

*Macroscopically:* the liver is slightly enlarged, yellow-green.
*Microscopically:*

- cholestasis in the intraorganic bile ducts;
- inflammation of the bile ducts (cholangitis, cholangiolitis);
- many bile-filled capillaries;
- diffuse infiltration by lymphocytes, macrophages, plasma cells and leukocytes.

### ***Chronic forms*** *(types):*

1. Active hepatitis
2. Persistent hepatitis

#### Active chronic viral hepatitis B

*Macroscopically:* the liver is slightly enlarged, yellow-brown.
*Microscopically:*

- dystrophy and necrosis of a significant number of hepatocytes;
- sclerosis of the portal tract;
- cellular infiltrates of portal fields;
- ground-glass (matte-glass) hepatocytes, sandy nuclei.

*Consequence:* large-node cirrhosis of the liver.

#### Chronic persistent viral hepatitis B

*Macroscopically*: the liver is enlarged, dense.
*Microscopically*:

- infiltration of lymphocytes, histiocytes and plasma cells of sclerosed portal tracts,
- dystrophic changes of hepatocytes are minimally expressed, necrosis is not expressed.

*Extrahepatic morphological changes:*

- hepatic jaundice,
- hemorrhage into the skin, mucous membranes,
- enlargement of lymph nodes and spleen,
- vasculitis, glomerulonephritis.

*Consequences:*

- death from acute or chronic liver failure,
- nodular cirrhosis of the liver,
- hepatorenal syndrome.

*Hepatitis C* is characterized by minor inflammatory changes, activation of Kupffer cells, accumulation of lymphoid cells and fatty degeneration of hepatocytes. Sometimes there is a proliferation of the epithelium of the bile ducts without violating the integrity of the basal membrane.

*Hepatitis D* is characterized by small-drip fatty liver dystrophy.

*Hepatitis E* is characterized by severe cholestasis.

**Alcoholic hepatitis**

*Etiology:* ethanol – a hepatotropic poison, at a certain concentration causes necrosis of hepatocytes and inhibition of liver regenerative capacity.

*Classification:*

1. Acute
2. Chronic

Acute alcoholic hepatitis

*Macroscopically:* the liver is pale, with reddish areas and scarring.

*Microscopically:*

- necrosis of hepatocytes,
- diffuse cellular infiltration,
- a significant amount of alcoholic hyaline in the cytoplasm of hepatocytes and out of them – abnormal protein (Mallory's body).

*Consequences:*

- abstinence from alcohol leads to recovery,
- with continued ethanol use – cirrhosis of the liver and liver failure.

Chronic alcoholic hepatitis

*Macroscopically:* the liver is dense, pale, often with scarring.

*Microscopically:*

- hydropic and balloon fatty degeneration of hepatocytes,
- step necrosis of hepatocytes,
- diffuse lymphohistiocytic infiltration of the stroma,
- multiple sclerosis.

*Consequences:*

- death from acute or chronic liver failure,
- •cirrhosis.

***Training macropreparations***

**Fatty hepatosis**. The body has a doughy consistency, increased in size, in section - yellow-brown ("goose", "clay" liver).

**Toxic liver dystrophy in the stage of red dystrophy**. The shape of the organ is preserved, the weight and size are reduced, the capsule is slightly wrinkled; on a

section of a parenchyma motley, on a yellow background red and gray spots are visible.

### *Training micropreparations*

**Hepatic steatosis** (hematoxylin and eosin staining): Hepatocytes are found on the periphery (mostly) and in the centers of the lobules, the cytoplasm of which contains colorless vacuoles of various sizes, which push the nucleus to the periphery and the hepatocyte becomes like a fat cell.

**Hepatic steatosis** (Sudan staining III): in the cytoplasm of hepatocytes fat droplets of different sizes, which turn yellow-orange

**Cholestatic hepatitis** (staining with hematoxylin and eosin): bile ducts and capillaries are sharply dilated, overflowing with bile, bile capillary walls are thickened with lymphohistiocytic infiltration, hepatocytes in a state of protein dystrophy.

### *Questions for self-control*

1. Define the concept of "hepatosis", "hepatitis".
2. Etiology, pathogenesis and classification of hepatosis.
3. Pathomorphology of acute hepatosis in different stages.
4. Pathomorphology and consequences of chronic hepatosis.
5. Definition, etiology and epidemiology of hepatitis.
6. Features of the pathomorphology of viral hepatitis B.
7. Features of the pathomorphology of alcoholic hepatitis.
8. Forms and features of pathomorphology of chronic hepatitis.
9. Complications and causes of death in hepatitis.

### *Examples of tests*

1. In a 45-year-old woman who died of chronic alcohol intoxication, at autopsy the liver was sharply enlarged, of a doughy consistency, yellowish in color. Microscopically, optically empty vacuoles of different sizes are detected in the cytoplasm of hepatocytes during staining with hematoxylin and eosin. What type of dystrophy occurs?

A. * Parenchymal fatty
B. Carbohydrate parenchymal
C. Hyaline-drop
D. Mesenchymal fat
E. Hydropic

2. The study of liver biopsy revealed: hepatocyte dystrophy, hepatocyte stasis necrosis, massive sclerosis of periportal fields and cellular infiltrates, lymphocytic infiltration of the lobules. Identify the form of hepatitis.

A. * Chronic active hepatitis
B. Viral hepatitis B
C. Acute alcoholic hepatitis
D. Chronic persistent hepatitis
E. Toxic liver dystrophy

3. A 60-year-old man was hospitalized with a diagnosis of mushroom poisoning, where he died on the 12th day with signs of acute liver failure. On the section - macroscopically: the liver is flabby, yellow-gray, clay-like both on the surface and in section. Microscopically: areas of necrosis with autolytic decay and formation of fat-

protein detritus in the center and a narrow strip of hepatocytes in the state of fatty dystrophy on the periphery of the liver lobes. What is the most likely diagnosis?
A. * Toxic liver dystrophy in the stage of yellow dystrophy
B. Toxic liver dystrophy in the stage of red dystrophy
C. Chronic toxic liver dystrophy
D. Wilson-Konovalov disease
E. Hereditary pigmented hepatosis
4. Puncture biopsy of the liver of a patient with hepatocellular insufficiency revealed vacuolar, balloon hepatocyte dystrophy, necrosis of individual cells, Councilman's body, infiltration of the portal and lobular stroma, mainly lymphocytes, macrophages with a small number of polymorphic nuclei. Your diagnosis.
A. * Acute viral hepatitis
B. Alcoholic hepatitis
C. Chronic active hepatitis
D. Autoimmune hepatitis
E. Chronic persistent hepatitis.
5. In which hepatitis in the biopsy are detected Mallory bodies?
A. * Alcoholic
B. Viral
C. Cholestatic
D. In all types of hepatitis
E. Not at one.

## DISEASES OF THE HEPATOBILIARY SYSTEM AND PANCREAS: liver cirrhosis, gallstone disease, pancreatitis. Liver tumors. Pancreatic cancer.

### Cirrhosis

*Cirrhosis of the liver* is a chronic disease characterized by scarring and structural remodeling of the liver with the development of liver failure.
*Etiology:*

- Infectious cirrhosis (viral hepatitis, parasitic and infectious diseases of the biliary tract);
- Toxic and toxic-allergic cirrhosis (alcohol, industrial and food poisons, drugs, allergens);
- Biliary cirrhosis (cholangitis, cholestasis of various origins);
- Metabolic cirrhosis (protein deficiency, vitamins, lipotropic factors, cirrhosis accumulation in hereditary metabolic disorders);
- Circulatory cirrhosis (chronic venous stasis in the great circle of blood circulation);
- Cryptogenic cirrhosis (of unknown etiology).

*Classification*.
According to macroscopic changes:

- incomplete septal cirrhosis;
- small-node (nodes up to 1 cm in diameter);
- large-node (nodes up to 5 cm in diameter);
- mixed (small-large).

By morphogenesis:

- postnecrotic,
- portal,
- biliary,
- mixed.

By functional state:

- compensated,
- decompensated.

## ***Postnecrotic cirrhosis***

*Etiology:*

- after progressive massive liver necrosis,
- after hepatitis B.

*Macroscopically:* deformed liver, hilly, always reduced, dense. The appearance of the liver resembles a bunch of grapes (nodular cirrhosis).

*Microscopically:*

- large regeneration nodes, separated by wide connective tissue areas;
- due to the collapse of the stroma there is a convergence of portal fields and central zones (three or more portal triads in one field);
- false lobes (may consist of newly formed liver tissue);
- fat in the liver cells is absent;
- protein hepatocyte dystrophy predominates;
- active regeneration often with the formation of multinucleated liver cells.

*Consequences:*

- develops rapidly,
- early hepatocellular insufficiency,
- late portal hypertension.

## ***Portal cirrhosis***

*Etiology:*

- after alcoholic hepatitis,
- after chronic viral hepatitis,
- chronic pulmonary or right ventricular heart failure,
- food imbalance.

*Macroscopically:* the liver is reduced, its surface is small-nodular (small-nodular cirrhosis).

*Microscopically:*

- connective tissue is wedged into the liver parenchyma from the enlarged periportal spaces;
- central veins and portal vessels converge;
- cellular infiltration along the course of connective tissue strands is determined;
- the walls of the arteries are thickened;
- lobular structure is lost;
- small "false lobules";
- in hepatocytes the phenomenon of fatty degeneration.

*Consequences*:

- develops slowly,
- late hepatocellular insufficiency,

- early portal hypertension.

## ***Biliary cirrhosis***

*Etiology:*

- cholangitis, cholangiolitis,
- use of certain drugs (aminazine, methyltestosterone, etc.).

*Types:*

- primary,
- secondary.

*Primary biliary cirrhosis* occurs in necrotic cholangitis and cholangiolitis.

*Macroscopically*: the liver is enlarged, dense, in section – gray-green, the surface is smooth or fine-grained.

*Microscopically*:

- stasis in the bile vessels of various calibers;
- septal bile ducts are swollen, their epithelium is necrotized;
- development of inflammatory infiltrates consisting of lymphocytes and plasma cells, sometimes the inflammatory reaction takes the form of granulomas resembling those of sarcoidosis;
- dense connective tissue strands appear around the portal tracts;
- small "false lobules" are formed;
- the architecture of the particle is not disturbed.

*Secondary biliary cirrhosis* occurs against the background of obstruction of the extrahepatic bile ducts.

*Etiology:*

- formation of stones in the gallbladder,
- cancer of the Fater's nipple of the duodenum.

*Macroscopically*: the liver is enlarged, dense, green, in section with bile ducts.

*Microscopically:*

- dilated and bile-filled ducts and capillaries – severe cholestasis;
- cholangitis, cholangiolitis;
- "bile lakes";
- development of fibrosis in periportal spaces;
- regeneration nodes ("false lobules").

*Consequences of cirrhosis*:

- hepatic coma;
- splenomegaly;
- bleeding from varicose veins of the esophagus, stomach, hemorrhoidal veins;
- ascites;
- peritonitis;
- thrombosis of the portal vein;
- development of liver cancer.

## Liver cancer

Relatively rare tumor. Often occurs on the background of liver cirrhosis.

*Classification.*

By macroscopic manifestations:

- nodal,
- diffuse,

- massive.

Depending on the histogenesis:

- hepatocellular (hepatocellular);
- from the epithelium of the bile ducts (cholangiocellular).

*Macroscopically*: the liver is sharply enlarged, dense or stony density, hilly.
*Microscopically*: cellular and tissue atypism.
Histological types:

1. Trabecular,
2. Tubular,
3. Acinous,
4. Solid,
5. Light cell.

Metastases:

- lymphogenic,
- hematogenous (lungs, bones).

*Consequences*:

- hepatargia,
- hemorrhages into the peritoneal cavity from disintegrating cancerous nodules,
- cachexia.

## Cholecystitis

***Cholecystitis*** – inflammation of the gallbladder of various etiologies.
*Etiology*:

- infection (viruses, Escherichia coli, cocci, etc.);
- helminthiasis (roundworms);
- damage to the mucous membrane of the gallbladder when throwing pancreatic juice into it;
- stagnation of bile in the gallbladder;
- gallbladder dyskinesia;
- long breaks in eating;
- sedentary lifestyle.

*Classification*.
By duration:

- acute (catarrhal, purulent, phlegmonous, gangrenous);
- chronic.

By the presence of concretions:

- calculous,
- non-calculous.

### *Acute cholecystitis*

*Acute catarrhal cholecystitis*

*Macroscopically:* the gallbladder is slightly enlarged; edema and redness of the mucous membrane, bile with impurities of muco-serous or mucopurulent exudate.
*Microscopically:*

- the wall of the gallbladder is full-blooded, swollen;
- infiltration of leukocytes, lymphoid cells, macrophages in the mucous membrane and submucosa;
- desquamation of epithelial cells.

*Acute purulent cholecystitis*

*Macroscopically:* the gallbladder is enlarged, tense, serous integuments are dull, covered with fibrinous layers, the wall of the gallbladder is sharply thickened (up to 0.5-1 cm), the mucous membrane is swollen, full-blooded, with erosions, ulcers, in the lumen of the gallbladder accumulates purulent stained with bile.

*Microscopically*:

- significant diffuse infiltration of the gallbladder wall by segmental leukocytes (phlegmonous cholecystitis);
- hemorrhage into the wall and lumen of the bladder (purulent-hemorrhagic cholecystitis);
- necrotized tissues of the mucous membrane are abundantly impregnated with fibrinous exudate and take the form of dirty green pellicles;
- necrosis of the mucous membrane with the formation of ulcers of various sizes (phlegmonous-ulcerative cholecystitis).

*Acute gangrenous cholecystitis*

*Macroscopically:* the necrotic process extends to the entire thickness of the gallbladder wall, which thus becomes black and brown.

*Microscopically:*

- fibrinoid vascular necrosis;
- purulent vasculitis, thrombovasculitis;
- diffuse infiltration of all layers of the gallbladder wall by segmental leukocytes.

*Consequences of acute cholecystitis*:

- perforation of the bladder wall;
- peritonitis;
- acute pancreatitis;
- gallbladder empyema;
- purulent cholangitis and cholangiolitis;
- pericholecystitis with the formation of fibrotic fusions;
- sepsis.

***Chronic cholecystitis***

*Macroscopically:* the gallbladder is deformed, reduced in size, splised with neighboring organs by coarse fusions, the outer surface of the gallbladder "glazed", the wall is thickened, compacted, sclerosed, the mucosa is atrophied with fibrous bands, there are mucous membrane ulcers.

*Microscopically:* atrophy of the mucous membrane, sclerosis, infiltrates of lymphoid and plasma cells, under the epithelium there is a large number of macrophages containing cholesterol (xanthoma cells), petrification of the bladder wall.

*Consequences*:

- exacerbation of cholecystitis;
- peritonitis;
- acute and chronic pancreatitis;
- mechanical jaundice and cholangitis;
- gallbladder cancer.

**Gallstone disease**

Stones of bile ducts and gallbladder are the cause of gallstone disease, calculous cholecystitis.

*Etiology:*

- infection (viruses, Escherichia coli, cocci, etc.);
- metabolic disorders;
- bile stasis.

*Complication*:

- perforation of the bladder wall;
- peritonitis;
- cholangitis;
- obstruction of the common bile duct with the development of subhepatic jaundice.

## Gallbladder cancer

*Gallbladder cancer* accounts for 2-8% of all malignancies and is 5-6 in frequency among digestive tumors. The ratio of men to women is 1:14; 90% of patients are older than 60 years.

*Localization*: in the neck or bottom of the gallbladder, mostly occurs on the background of calculous cholecystitis.

*Histologically* – adenocarcinoma.

*Metastasis*:

- lymphogenous – pancreatoduodenal, paracaval lymph nodes;
- hematogenous – both lobes of the liver, large omentum, peritoneum, ovaries.

## Pancreatitis

*Pancreatitis* – inflammation of the pancreas.

*Classification:* acute, chronic

*Acute pancreatitis* is a severe inflammatory process that is accompanied by necrosis of acinar structures and adipose tissue (fat necrosis), edema, hemorrhage, areas of suppuration, cysts, sequesters.

*Etiology:*

- dyskinesia of the pancreatic ducts;
- biliopancreatic reflux;
- nutritional disorders;
- alcohol poisoning;
- thrombosis, thromboembolism of the branches of the abdominal trunk and superior mesenteric artery;
- medications (antibiotics, estrogens and diuretics);
- helminth invasion into the pancreatic duct (roundworms, etc.).

*Classification:*

- purulent (apostematous (abscessing) and phlegmonous) pancreatitis;
- hemorrhagic pancreatitis;
- pancreatic necrosis.

*Macroscopically:*

- with purulent pancreatitis, the gland is enlarged, flabby, yellowish, full-blooded, turbid fluid flows from the surface of the incision;
- white and white-yellow areas of fatty necrosis (steatonecrosis) appear in the adipose tissue surrounding the pancreas and in the omental tissue;
- there are foci of necrosis in combination with hemorrhagic infiltration on the surface of the incision of the pancreas. Sometimes such foci merge to form

large, dense, and black necrotic masses that replace large areas of organ tissue and surrounding tissue (apostematous pancreatitis).

*Microscopically:*

- swelling of the epithelium and interstitial tissue with lymphocytic infiltration;
- in the parenchyma there are areas of necrosis, which include blood vessels;
- hemorrhage with hemorrhagic infiltration of necrotized tissue;
- neutrophilic infiltration is expressed on the periphery.

*Consequences:*

- acute necrosis of the pancreas, peritonitis;
- toxic shock (caused by intoxication);
- gastrointestinal bleeding;
- acute renal failure.

*Chronic pancreatitis* is a progressive chronic inflammatory disease of the pancreas, characterized by a chronic inflammatory-degenerative process of glandular tissue, which results in the development of sclerosis of the organ with loss of its exo- and endocrine function.

*Etiology:*

- unsystematic irregular diet, frequent consumption of spicy and fatty foods, infectious diseases (acute hepatitis, tuberculosis, syphilis);
- chronic alcoholism, systemic deficiency of proteins and vitamins;
- diseases of the gallbladder and bile ducts;
- hemochromatosis, vascular lesions;
- allergies, hereditary predisposition.

*Macroscopically:* the pancreas shrinks, becomes dense. In section – the tissue is grayish and moderately dense as a result of diffuse fibrosis. Large ducts are often dilated, there are cysts, full of thick secretions, stones.

*Microscopically:*

- strictures of the ducts with the presence of protein precipitates and inflammatory exudate;
- hyperplasia of small ducts in the areas of fibrosis develops;
- the presence of stones that clog the branches of large ducts;
- atrophy of the parenchyma of the gland and the growth of adipose and connective tissue.

*Consequences*:

- pancreatic cancer,
- malabsorption syndrome.

**Pancreatic cancer**

*Localization*: head – 60%, body – 15-20%, tail – 5%.

*Histogenesis:*

- from the exocrine part of the gland (organ-nonspecific) – adenocarcinoma (from the ductal epithelium) and acinar cancer (from the acinuses);
- from pancreatic islets (organ-specific).

*Macroscopically*: tumors of the head of the pancreas may be small foci of compaction, invisible on external examination, or have a large nodular form of growth, reaching 8-10 cm in diameter. When spread beyond the pancreas, the tumor can grow into the duodenum and common bile duct.

*Microscopically*: in 95% of cases of pancreatic cancer – adenocarcinoma (papillary, skirrhous, mucinous), solid cancer of the ductal epithelium.
*Metastasis*:

- lymphogenous in 40-50% of cases are affected first regional and then distant lymph nodes: mesenteric, of gate of the liver, of stomach, omental, of mesentery of the transverse colon;
- hematogenously into the liver.

*Consequences*:

- mechanical jaundice;
- liver failure;
- cachexia;
- pneumonia.

### *Training macropreparations*

**Portal cirrhosis of the liver**. The liver is reduced in size, dense, small-humped (small-node cirrhosis).
**Mixed cirrhosis of the liver**. The surface of the liver is uneven, tuberous; in section it is built of many small knots of 1-3 mm and large knots of gray-yellowish color 5-7 cm in size, separated by layers of gray tissue.

### *Training micropreparations*

**Portal cirrhosis of the liver** (van Gizon staining): violation of the lobular structure of the liver, the formation of false lobules, which are separated by narrow bundles of connective tissue infiltrated by lymphocytes and macrophages.
**Postnecrotic cirrhosis of the liver** (hematoxylin and eosin staining): the presence of false lobes, which are separated by wide bundles of connective tissue with the convergence of triads.

### *Questions for self-control*

1. Cirrhosis: definition, etiology, classification.
2. Macro-microscopic changes of the liver in cirrhosis.
3. Macro- and microscopic characteristics of liver cancer.
4. Definition, etiopathogenesis, classification, pathomorphology of cholecystitis.
5. Pathomorphology of gallbladder cancer.
6. Gallstone disease, morphological characteristics.
7. Definition, etiopathogenesis, classification, pathomorphology of pancreatitis.

### *Examples of tests*

1. During the autopsy of a 52-year-old woman suffering from gallstones for a long time, the following was found: macroscopically - the liver is moderately enlarged, deformed, the surface of the organ is tuberous, the tissue is dense, the incision is brownish-green with green consists of multiple nodules with a diameter of 8-10 mm. Microscopically, hepatocellular nodules are surrounded by layers of connective tissue, which contains an increased number of small bile ducts with cholestasis. Diagnose liver disease.
A. * Biliary cirrhosis of the liver
B. Cholelithiasis
C. Toxic liver dystrophy
D. Portal cirrhosis of the liver
E. Postnecrotic cirrhosis of the liver

2. Histological examination of the liver reveals a sharp violation of the lobular structure with intense fibrosis and the formation of regeneration nodes. Microscopically: hepatocyte proliferation, appearance of false lobules, dystrophy and necrosis of hepatocytes. Your diagnosis.
A. * Cirrhosis of the liver
B. Alcoholic hepatitis
C. Fatty hepatosis
D. Viral hepatitis
E. Progressive massive liver necrosis
3. A 59-year-old patient had been suffering from chronic alcoholism for a long time. Repeated attacks of alcoholic hepatitis were diagnosed by repeated examination of liver biopsy material. At macroscopic research the liver of yellow color of a dense consistence, its edge is pointed, the surface of a liver is tuberous, on a section a liver with set of small knots. Your diagnosis.
A. * Cirrhosis of the liver.
B. Liver cancer.
C. Liver dystrophy.
D. Chronic hepatitis.
E. Acute hepatitis.
4. The gallbladder, sent to the pathoanatomical department after cholecystectomy, is thickened and enlarged in size, the outer shell is dull, the vessels are full-blooded, a yellow-green liquid is secreted from the lumen in the incision. In what form of cholecystitis do such changes occur?
A. Phlegmonous
B. Simple catarrhal
C. Superficial catarrhal
D. Gangrenous
E. Apostematous
5. Histological examination of the liver biopsy of a woman suffering from hepatitis B for a long time, the pathologist found diffuse liver tissue fibrosis with the formation of fibrous porto-portal and porto-central septa and disorders of the lobular structure of the liver (appearance of false lobules). Which process is characterized by such morphological changes?
A. * Cirrhosis of the liver
B. Chronic hepatitis
C. Hepatocellular cancer
D. Acute hepatitis
E. Cholestasis

## INTESTINAL INFECTIONS:
## typhoid fever, salmonellosis, dysentery, cholera.
## APPENDICITIS. TUMORS OF THE SMALL INTESTINE AND COLON

### Typhoid fever

***Typhoid fever*** is an acute infectious disease with a cyclic course, which is characterized by local changes in the lymphatic system of the small intestine (rarely

colon) and general changes in the human body due to bacteremia (fever, roseola-papular rash, etc.).

*Epidemiology:*

- The source of infection is a sick person.
- The pathogen with the patient's feces enters the environment.
- Transmission mechanism: fecal-oral.
- Noticeable seasonality of this disease - summer and autumn months.
- There are sporadic cases in Ukraine. Mortality 0.1 - 3.5%.

*Etiology:* Salmonella typhi abdominalis of the genus Salmonella.

*Pathogenesis:*

- the pathogen multiplies in the terminal part of the ileum;
- penetrates between enterocytes and deepens into the lymphoid apparatus (group and single lymphatic follicles) with the development of local changes - the primary infectious complex;
- at the end of the first week bacteremia develops, which lasts from several days to several weeks (positive blood culture);
- antibodies appear (Vidal's positive reaction);
- the pathogen begins to be excreted with sweat and urine, bacteriocholia develops (bile is the best breeding ground for salmonella) and excretion of the pathogen with fecal masses (coproculture is positive from 2-3 weeks);
- repeated mass penetration of the pathogen into the lymphoid apparatus during sensitization is accompanied by a hyperergic reaction of the immediate type and leads to the development of intestinal necrosis.

*Localization:* **small intestine**, lower part (ileotype) with a tendency to further lower the process into the large intestine (ileocolotype).

*Pathological anatomy*. There are general and local changes.

*General changes* in the patient's body are associated with *bacteremia*.

1) Typhoid exanthema - roseola-papular rash on the skin of the abdomen and torso (7-11 days).
2) *Microscopically:* hyperemia, edema and lymphoid-macrophage infiltration of the papillary layer of the skin, containing salmonella.
3) Granulomas in the spleen, lymph nodes, bone marrow, lungs, gallbladder. With the predominance of the above granulomas develops pneumotyphoid, laryngotyphoid, cholangiotyphoid.
4) Hyperplasia of the spleen, liver, lymph nodes, dystrophy of parenchymal organs.

*Local changes occur in the lymphoid apparatus* of the small intestine.

There are 5 stages (each lasts an average of 1 week).

1) Medullar swelling – acute productive inflammation in the lymphoid apparatus.

*Macroscopically:* group follicles (Peyer's patches) are enlarged, explode into the lumen of the intestine, their surface with furrows and convolutions, resembles the brain.

*Microscopically:* in lymphatic follicles – proliferation of histiocytes, reticular cells, monocytes with their transformation into macrophages (typhoid cells), which displace lymphocytes - the formation of **typhoid granulomas.**

2) Stage of necrosis of typhoid granulomas.

*Macroscopically*: necrotic changes in Peyer's patches, which are imbibed by bile pigments and acquire a green color.
*Microscopically*: in the center of the granuloma – tissue detritus, limited by the demarcation band of inflammation.
3) Stage of ulcer formation.
*Macroscopically:* the rejection of necrotic masses leads to deep defects of the intestinal mucosa. The edges of the ulcers are uneven, covered with necrotic masses - "dirty ulcers".
*Microscopically:* sequestration of tissue detritus and the appearance of deep defects and ulcers at the site of granulomas.
4) Stage of "pure ulcers"
*Macroscopically*: ulcers of the correct shape, elongated along the length of the intestine.
*Microscopically*: the growth of granulation tissue along the edges of the defect.
5) Stage of healing.
*Macroscopically:* pigmented, barely visible scars covered with epithelium are formed. In the lymph nodes – petrification of necrosis.
*The course* is acute.
*Complication.*
Intestinal:
- bleeding (3rd week);
- ulcer rupture (4th week): perforations in many lesions;
- peritonitis.

Extraintestinal:
- bronchopneumonia (more often associated with a secondary infection);
- purulent perichondritis of the larynx;
- Cenker's (waxy) necrosis of the rectus abdominis;
- purulent osteomyelitis and intramuscular abscesses;
- sepsis;
- pyelonephritis.

*Consequences and prognosis:*
- favorable – recovery
- unfavorable – bacteriocarriers, complications and death.

**Salmonellosis**

*Salmonellosis* is a group of acute intestinal infectious diseases.
*Etiology:* Salmonella typhimurium, S. enteritidis, S. cholerae suis.
The source of the disease – anthropozoonosis (sick person or bacteriocarrier, animals).
Mechanism of infection:
- alimentary (eating eggs, dairy products, infected animal meat, birds, etc.);
- contact:
  - direct (contact with a sick person);
  - indirect (through infected objects).

The incubation period is 12-36 hours. Seasonality: June-September.
*Pathogenesis.*
- ingestion of salmonella in the gastrointestinal tract;

- reproduction, death, release of endotoxin;
- local and general intoxication:
  - dystrophy,
  - edema,
  - bleeding into the gastrointestinal tract;
- hyperplasia and inflammation of regional (mesenteric) lymph nodes;
- parenchymal dystrophy;
- decreased immunity and septicemia.

*Forms of salmonellosis*

1) Typical
2) Typhoid
3) Septic
4) Influenza-like
5) Local

*Forms of course*

A. Gastrointestinal (toxic).
B. Generalized.

A. Gastrointestinal (toxic) form

The most acute gastroenteritis:

- vomiting,
- diarrhea,
- rapid development of dehydration - "home cholera".

In severe cases, the inflammation becomes hemorrhagic.

B. Generalized form

- septicemia variant: salmonellosis sepsis with the development of abscesses in the internal organs;
- typhoid variant.

*Complication:*

- infectious-toxic shock,
- purulent complications,
- acute renal failure,
- dysbacteriosis.

*Features in young children:*

- high susceptibility;
- contact form of infection;
- more often dyspeptic, colitis forms;
- less cholera-like and septic forms;
- frequent complications: otitis, bronchopneumonia, pyelonephritis;
- long, wavy course;
- the possibility of death.

## Dysentery

*Dysentery* is an infectious disease of bacterial etiology, which is characterized by general intoxication and a predominant lesion of the distal part of the colon.

*Epidemiology:*

- The source of infection is a sick person who releases the pathogen into the environment.

- Transmission mechanism: fecal-oral.
- The disease mainly affects preschool children.
- Prevalence is wide; pronounced seasonality of the disease is not observed.

*Etiology:* Often associated with 4 species of Shigella: Sh.Dysenteriae, Sh.Flexneri, Sh.Sonnei, Sh. Boydi.

*Pathogenesis:*

- the development of the disease is associated with the cytopathic action of Shigella and their exotoxins and endotoxins;
- exotoxin causes cytotoxic (damages the cell), enterotoxic (increases the secretion of enterocytes) and neurotoxic (damages the intramural ganglia of the intestine) effect;
- in the colon Shigella penetrate the epithelium (colonocytes) and multiply, with the destruction of the epithelial cell Shigella penetrate into neighboring colonocytes, which leads to erosions;
- vasoparalytic action of toxins increases vascular permeability and exudation, which leads to the development of fibrinous inflammation;
- bacteremia in dysentery is not observed.

*Localization:***distal part of the colon** (rectum and sigmoid).

*Pathological anatomy*. There are local and general changes.

*Local changes.*

*Stages:*

1) Catarrhal colitis.

*Macroscopically:* edema, hyperemia of the intestinal mucosa with small hemorrhages. There are foci of necrosis on the surface of the mucous membrane.

*Microscopically:* plethora, sladging of forming elements in the lumen of blood vessels (thrombosis). Leukocyte infiltration of the intestinal mucosa.

2) Fibrinous colitis.

*Macroscopically:* dirty-gray dense deposits on the mucous membrane (croupous, often diphtheria).

*Microscopically:* the pellicle that covers the mucous membrane consists of necrotized mass, leukocytes and fibrin. Necrosis at a considerable distance approaches the submucosal base, which is sharply thickened. Duration 5-10 days.

3) Ulcerative colitis.

*Macroscopically:* melting and rejection of necrotic masses impregnated with fibrin and the formation of ulcers of different depths with dense edges (10-12 days of illness).

*Microscopically:* sequestration of necrotized masses with the formation of defects of varying depth, delimited by leukocyte infiltration.

4) Stage of healing: with shallow ulcers complete regeneration is possible; at deep – formation of scars with deformation of a gut and narrowing of its lumen.

*General changes:* moderate hyperplasia of the spleen, fatty degeneration of the liver and myocardium.

*Course:*

- acute,
- chronic (due to incomplete phagocytosis). More often in children with underdeveloped lymphoid tissue.

*Complication:*
Intestinal:
- perforation of the intestinal ulcer with the development of peritonitis or paraproctitis;
- intestinal phlegmon;
- intra-intestinal bleeding (rare);
- cicatricial stenosis of the intestine.

Extraintestinal:
- bronchopneumonia (due to the accession of a secondary infection);
- pyelonephritis;
- serous (toxic) arthritis;
- liver abscesses;
- in chronic course – amyloidosis of the organs and depletion.

*Consequences and prognosis:*
- favorable – recovery.
- unfavorable – bacteriocarriers, chronic course, complications and death.

## Cholera

*Cholera* is the most acute infectious disease in the quarantine group, characterized by a predominant lesion of the stomach and small intestine.
*Etiology and epidemiology.*
The source of the disease is a sick person or a vibrio carrier. Typical anthroponosis.
Pathogens: Vibrio Asian cholera – Vibrio Koch, Vibrio El Tor.
Reservoir – water. The route of infection is fecal-oral.
The incubation period is 1-6 days.
*Pathogenesis:*
- vibrio entering the intestines, alkaline reproduction and destruction, release and accumulation of toxins (cholerogen);
- increased secretion of isotonic fluid;
- dehydration;
- blood clotting, slow blood flow, hypoxemia, hypoxia;
- metabolic acidosis with accumulation of toxic products;
- extrarenal urinary incontinence (hypohydremia) up to anuria, in severe cases – extrarenal coma.

Stages of cholera.

1. Cholera enteritis is manifested by serous or serous-hemorrhagic nature. The mucous membrane is swollen, full-blooded, with punctate hemorrhages. Sometimes, with timely treatment ends in recovery, but more often goes to the next stage.
2. Cholera gastroenteritis – vacuolation of epitheliocytes, some of cells die and desquamate. Enteritis is accompanied by serous or serous-hemorrhagic gastritis.
3. Algic period (algor – cold) – in the mucous membrane of the small intestine: plethora, edema, necrosis and desquamation of epithelial cells. The serous membrane of the intestine is dry, dull, with a yellowish tinge, covered with punctate hemorrhages. There is a large amount of translucent liquid in the lumen, resembling "rice broth". Sharply expressed manifestations of exsiccosis.

*Specific complications of cholera.*
Cholera typhoid:

- diphtheria colitis;
- extracapillary productive glomerulonephritis or necrosis of the epithelium of the renal tubules;
- hyperplasia of the spleen with areas of infarction.

Chlorhydropenic uremia – necrotic nephrosis with cortical necrosis.

*Nonspecific complications of cholera:*

- joining a secondary infection,
- focal pneumonia,
- abscesses, phlegmon, sepsis.

*Death* from: dehydration (exsiccosis), uremia.

## Appendicitis

*Appendicitis* – inflammation of the appendix.

*Epidemiology*. The most common surgical disease. Every year, 1 in 200 people suffers from acute appendicitis. Women - 2-3 times more often than men.

*Etiology and pathogenesis*:

1. Stagnation in the lumen of the appendix of intestinal contents due to impaired peristalsis, atony, formation of fecal stones, getting into the appendix of animal parasites and foreign bodies (L. Ashchof's theory).
2. Autoinfection due to disorders of the vascular wall of nervous origin (angioneurotic theory).

*Classification and pathological anatomy.*

I. Acute appendicitis:

1) Simple appendicitis.

*Macroscopically*: the mucous membrane is swollen, hyperemic.

*Microscopically*: vascular plethora, erythrocyte stasis in capillaries and venules, diapedetic hemorrhage.

2) Superficial appendicitis.

*Macroscopically*: the appendix is thickened, the serous membrane is dull, hyperemic.

*Microscopically*: in the mucous membrane of the area of purulent inflammation with foci of necrosis - the primary affect.

3) Phlegmonous appendicitis.

*Macroscopically*: the appendix is enlarged, the serous membrane is dull, covered with a fibrinous pellicles, diapedetic hemorrhages are possible. The wall is thickened, impregnated with pus.

*Microscopically*: leukocyte infiltration extends beyond the mucosa and extends to the entire wall thickness of the appendix, vascular plethora, hemorrhage. If on the background of these changes are ulcerative defects, it is a phlegmonous-ulcerative variant of the disease.

4) Gangrenous – occurs in the case of the accession of putrefactive microflora and the spread of inflammation to the mesentery of the appendix and its vessels.

*Macroscopically*: the appendix is dirty green, sharply thickened. There is a large amount of pus and necrotized masses in the lumen.

*Microscopically*: massive neutrophilic infiltration of the process wall, significant hemorrhage, total necrosis of the mucous membrane. In necrotic detritus – colonies of microorganisms.

II. Chronic appendicitis: develops after a previous acute appendicitis. It is characterized by sclerotic and atrophic processes.

*Complication:*

Intestinal:

- perforation of the appendix,
- peritonitis,
- paratyphoid fever,
- empyema of the appendix.

Extraintestinal:

- pyelonephric abscesses of the liver,
- sepsis.

*Prognosis:*

- favorable – recovery,
- unfavorable – complications.

## Intestinal tumors

Tumors are observed in both the small and large intestines.

Small intestine cancer is rare, mainly in the area of the papilla of the duodenum.

Colon cancer tends to increase and is more often localized in the rectum, less often in the cecum, sigmoid, transverse colon and other parts of the colon.

## Rectal cancer

*Epidemiology*. More often than other forms of cancer, it is associated with the level of economic development of the country: the highest incidence – in industrialized countries, the lowest – in rural areas. In Ukraine – 8.0 per 100 thousand inhabitants.

*Risk factors:*

- carcinogenic substances in food when smoking meat, fish;
- low fiber content in food;
- work with occupational hazardous substances;
- genetic predisposition.

*Background diseases:*

- chronic proctitis, chronic ulcerative colitis, chronic sigmoiditis;
- polyps of the rectum; cracks and fistulas of the anus;
- prolapse of the mucous membrane of the rectum from the anus;
- chronic sigmoiditis.

*Precancerous processes:*

- polyps,
- neoplastic proliferation of the glandular epithelium of the intestine.

*Types of tumor growth*:

- exophytic,
- endophytic,
- transitional forms.

*Tumor growth forms*:

- polyposis,
- large nodes,
- plaque-like,
- diffuse-infiltrative,
- saucer-shaped,

- ulcerative.

*Histological classification*:

- adenocarcinoma,
- squamous cell carcinoma with or without keratinization,
- undifferentiated cancer.

*Metastases:* lymphogenic to regional lymph nodes and liver.

*Prognosis:* extremely unfavorable.

### *Training macropreparations*

**Medullar swelling of Peyer's patches in typhoid fever**. The shape of the organ is preserved, the weight and size are normal The ileum is whitish in color, pronounced folding of the mucous membrane, which determines the formations of 4x2.5 cm and 1x1.5 cm, protruding above the surface of the mucous membrane. Furrows and convolutions are visible on them, the surface is uneven, fluffy. There is a formation with a diameter of 0.5 cm, with a loss of characteristic folds, whitish color, slightly deepened and compacted.

**Stage of necrosis and ulceration of Peyer's patches**. There is a violation of the surface structure of Peyer's patches, necrosis deepened to the muscular layer of the intestine. Dead tissues of greenish color due to their impregnation with bile.

**Diphtherityc colitis in dysentery**. Fragment of the colon measuring 15x10x2 cm. The mucous membrane is changed. The anatomical pattern is erased, the folds are poorly visible, the color is dirty gray, the mucosa is rough. On the surface of the mucosa there is an overlay of brown-green color. The wall is thickened, the lumen is narrowed.

**Acute simple appendicitis**. The appendix is enlarged, the walls are swollen, the vessels are dilated, full-blooded.

**Phlegmonous appendicitis**. The appendix is enlarged, the walls are thickened, diffusely impregnated with pus, the surface is dull, reddish-bluish, with full-blooded vessels.

**Gangrenous appendicitis**. Appendix is enlarged, black and gray, dull.

### *Training micropreparations*

**Diphtherityc colitis in dysentery** (hematoxylin and eosin staining): inflammatory changes in different layers of the intestinal wall are determined: necrosis in the mucous membrane, fibrinous plaque, in the submucosal membrane - plethora, leukocyte infiltration.

**Phlegmonous appendicitis** (staining with hematoxylin and eosin): all layers of the appendix wall are impregnated with purulent infiltrate, edema, inflammatory hyperemia.

**Chronic appendicitis** (staining with hematoxylin and eosin): the wall of the appendix is thickened, it is determined by sclerosis, atrophy of the glands.

### *Questions for self-control*

1. Dysentery: definition, etiology, pathogenesis, morphological characteristics, complications, consequences, causes of death.
2. Typhoid fever: definition, etiology, pathogenesis, morphological characteristics, complications, consequences, causes of death.
3. Salmonellosis: definition, classification, etiology, pathogenesis, morphological characteristics, complications, consequences, causes of death.

4. Cholera: definition, classification, etiology, pathogenesis, morphological characteristics, complications, consequences, causes of death.
5. Appendicitis: definition, etiology and pathogenesis. Pathomorphological classification of appendicitis and their consequences.
6. Tumors of the intestine, clinical and morphological characteristics.

***Examples of tests***

1. At the autopsy of an elderly man, who during the last 2 weeks suffered from acute intestinal disorders, changes were found in the rectum and sigmoid colon: a brownish-green pellicls is observed on the surface of the mucous membrane. The intestinal wall is thickened, the cavity is sharply narrowed. Microscopically, necrosis of the mucous membrane penetrating to different depths is detected, necrotic masses are permeated with fibrin threads, with leukocyte infiltration. Your diagnosis.
A. * Fibrinous colitis
B. Catarrhal colitis
C. Ulcerative colitis
D. Follicular colitis
E. Phlegmonous colitis
2. A removed worm-like appendix was sent for histological examination. Its dimensions are enlarged, the serous membrane is dull, full-blooded, covered with fibrin pellicls, the walls are thickened, and pus is excreted from the lumen in the section. Microscopic examination reveals plethora of blood vessels, edema of all layers and diffuse infiltration of their leukocytes. Name the form of acute appendicitis:
A. * Phlegmonous
B. Apostematous
C. Simple
D. Superficial
E. Gangrenous
3. At the autopsy of the body of the deceased in the infectious department were found: fibrinous-purulent peritonitis; in the mucous membrane of the ileum there are numerous oval defects up to 3-5 cm, which are located along the intestine and repeat the shape of the Peyer's patches, the edges of the ulcers are smooth, rounded, the bottom is clean, represented by muscular or serous membrane. Holes up to 0.3 cm in diameter were found in the bottom of two ulcers. For which disease are these changes most characteristic?
A. * Typhoid fever
B. Dysentery
C. Nonspecific ulcerative colitis
D. Crohn's disease
E. Paratyphoid
4. A 71-year-old man had diarrhea with mucus and blood in his stool for 10 days. The patient was hospitalized in serious condition, died 2 days later. When the body of the deceased was dissected, diphtheria colitis with multiple ulcers of irregular shape of different depth was found in the sigmoid and rectum. Shigella were sown during bacteriological research. Your diagnosis.
A. * Dysentery

B. Typhoid fever
C. Salmonellosis
D. Nonspecific ulcerative colitis
E. Yersinia
5. A 36-year-old man was in an infectious disease hospital with profuse diarrhea, signs of exsiccosis, and a drop in body temperature. He died of uremia. During the autopsy found: in the lumen of the small intestine colorless liquid in the form of rice broth; the mucous membrane is swollen. Microscopy of the small intestine - full blood vessels, focal hemorrhages, desquamation of enterocytes, hypersecretion of goblet cells and lympho- and leukocyte infiltration of the stroma of the mucous membrane. Your diagnosis.
A. * Cholera
B. Salmonellosis
C. Dysentery
D. Typhoid fever
E. Crohn's disease.

## ACUTE BRONCHITIS. PNEUMONIA

### Acute bronchitis

*Acute bronchitis* is an acute inflammation of the bronchial mucosa.
Acute bronchitis can be:

- independent disease;
- manifestation of a number of diseases: pneumonia, chronic glomerulonephritis with renal failure (uremic acute bronchitis).

*Etiology.*

- viruses, especially respiratory syncytial virus (RS virus);
- bacteria, most commonly Haemophilus influenzae and Streptococcus pneumonia;
- effect of chemical agents in the air (tobacco smoke, sulfur dioxide and chlorine vapor, nitrogen oxides);
- effect of physical agents: dry or cold air, radiation;
- effect of dust: domestic and industrial in high concentrations.

*Macroscopically*: the mucous membrane of the bronchi is full-blooded, swollen, possible minor hemorrhages, ulcers.
*Microscopically*: in the mucous membrane of the bronchi develop almost all forms of catarrhal inflammation, purulent, fibrinous, fibrinous-hemorrhagic inflammation. Sometimes the destruction of the mucous membrane with the development of ulcers is possible. In such cases, talk about destructive ulcerative bronchitis. In the proximal bronchi, only the mucous membrane (endobronchitis) or the mucous and muscular membranes (endomesobronchitis) are affected. In distal partitions all covers of a wall of bronchial tubes (panbronchitis or panbronchiolitis) are involved in inflammatory process. At the same time transition of an inflammation to peribronchial tissue (peribronchitis) is possible.
*Complication:*

- bronchopneumonia (mostly the result of aspiration of infected mucus into the respiratory tract);
- peribronchial interstitial pneumonia (occurs as a result of the transition of inflammation not only to the peribronchial but also to the interstitial tissue).

*The consequences* depend on the depth of the lesion of the bronchial wall. Serous and mucous catarrh quickly end in recovery. Purulent, fibrinous and fibrinous-hemorrhagic catarrh, ulcerative-destructive bronchitis have a prolonged course and often turn into a chronic form or pneumonia.

## Pneumonia

***Pneumonia*** – a group of different etiology, pathogenesis and morphological characteristics of acute infectious inflammatory diseases of the lungs with a predominant lesion of the respiratory tract and the presence of intraalveolar exudate.

*Classification of pneumonia*:

1. By nosological characteristics and pathogenesis.

Primary – pneumonia as an independent disease and as a manifestation of another disease that has nosological specifics: influenza, plague pneumonia.

Secondary – pneumonia as a complication of the underlying disease:

- immunodeficient,
- septic,
- postoperative,
- hypostatic,
- aspiration,
- exacerbation of chronic bronchitis.

2. By etiology (infectious agents):
   - bacteria,
   - viruses,
   - fungi,
   - rickettsiae,
   - chlamydia,
   - legionella,
   - mycoplasmas, etc.
3. By the size of the foci:
   - miliary or alveolitis – inflammation of individual alveoli;
   - acinous – inflammation in some acinuses;
   - lobular – inflammation in the pulmonary lobule;
   - lobular merged – inflammation in several adjacent lobules;
   - segmental – inflammation in the lung segment;
   - polysegmental – inflammation in several segments of the lung;
   - partial (lobar) – inflammation of the entire pulmonary lobe.
4. By the nature of the inflammatory process:
   - serous,
   - serous-desquamative,
   - serous-hemorrhagic,
   - hemorrhagic,
   - purulent,
   - fibrinous.

5. Clinical and morphological forms of pneumonia:

- lobar pneumonia – inflammation of the lung parenchyma;
- bronchopneumonia (focal) – inflammation of the bronchial wall and adjacent lung parenchyma;
- interstitial – inflammation in the interstitium of the lungs.

**Lobar pneumonia** (synonyms: fibrinous, pleuropneumonia) – an acute infectious-allergic disease with lesions of the lung and adjacent pleura in the form of fibrinous inflammation.

The disease mainly affects adults, rarely children.

*Etiology:*

- autoinfection,
- pneumococci of I-IV types, sometimes gram-negative Friedlander's diplobacillus.

*Pathogenesis of pneumonia*:

- autoinfection – an acute onset in full health and in the absence of contact with patients;
- sensitization of the body by pneumococci;
- influence of starting factors – cooling, injuries, etc.;
- hyperergic reaction in the lungs in the form of immediate hypersensitivity.

Stages of lobar pneumonia:

Stage I – the inflow – 1 day;
Stage II – red hepatization – 2-3 days;
Stage III – gray hepatization – 4-8 days;
Stage IV – completion (solution of inflammation) – 9-11 days.

*Pathological anatomy.*

| **Stages** | **Macroscopic manifestations** | **Microscopic manifestations** |
|---|---|---|
| *Inflow stage* | The lungs are somewhat compacted, red | Hyperemia of lung tissue, blood stasis in the capillaries, microbial edema |
| *Stage of red hepatization* | Lung of liver density, dark red, airless | Hyperemia, erythrodiapedesis in the alveoli, exudation with fibrin |
| *Stage of gray hepatization* | The lobe of the lung is enlarged, heavy, gray, on the pleura villous gray overlays, in section - lung tissue gray, granular, turbid fluid, enlarged lymph nodes of the lung root | Moderate hyperemia, in the alveoli, on the pleura fibrin threads, neutrophils, alveoli strongly stretched by exudate, the melting of fibrin;<br>in the lymph nodes of the root of the lung leukocyte infiltration |
| *Stage of completion or development of complications* | The lung acquires the previous sizes, moderate density, grayish color or a share of a lung with a cavity and pus. | Melting and resorption of fibrinous-hemorrhagic exudate under the action of proteolytic enzymes, purification of alveoli from exudate, gradually restoring the airiness of the respiratory zone of the lungs. |

*Complications:* pulmonary and extrapulmonary.
*Pulmonary complications* occur due to impaired fibrinolytic function of neutrophils:

- with excessive neutrophil activity:
  - lung abscess,
  - gangrene (moisture) of the lungs,
  - pleural empyema (accession of pus to fibrinous pleurisy),
- with insufficient neutrophil function – carnification (Latin carno – meat) – fibrin masses in the alveoli are subject to organization, ie germinate granulation tissue, which, maturing, turns into mature fibrous connective tissue. The lung turns into an airless dense fleshy tissue.

*Extrapulmonary complications* are observed in the generalization of infection:

- with lymphogenic generalization:
  - purulent mediastinitis?
  - pericarditis;
- with hematogenous generalization:
  - peritonitis,
  - metastatic abscesses in the brain, purulent meningitis,
  - acute ulcerative or polyposis-ulcerative endocarditis,
  - purulent arthritis.

*Causes of death*:

- acute heart and lung failure,
- brain abscess, purulent meningitis,
- lung gangrene, lung abscess, purulent pleurisy.

**Bronchopneumonia (focal)** – inflammation of limited areas of the lungs, which occurs in connection with bronchitis or bronchiolitis (bronchoalveolitis).
*General characteristics*:

- has a focal nature,
- focal pneumonia is based on acute bronchitis or bronchiolitis,
- can be a morphological manifestation of:
  - primary pneumonia (with respiratory viral infections),
  - secondary pneumonia (as a complication of many diseases).

The disease mainly affects children, the elderly and patients with weakened resistance.
*Etiology:*

- bacteria: staphylococci, streptococci, enterobacteria, pneumococci, Haemophilus influenza;
- viruses: influenza, RS-virus, adenovirus, measles, chickenpox, cytomegalovirus;
- intracellular parasites: mycoplasma, rickettsiae, chlamydia, legionella;
- pathogenic fungi: Candida, S. Aspergillus, actinomycetes;
- dust, radiation.

*Pathogenesis:* bronchopneumonia is a continuation of acute bronchitis or bronchiolitis.

A prerequisite for its development is a violation of the drainage function of the bronchi.

Inflammation spreads to the lung tissue:

- intrabronchial (descending, most often in catarrhal bronchitis or bronchiolitis);
- peribronchial (with destructive bronchitis or bronchiolitis);
- hematogenous (septic pneumonia);
- autoinfection;
- aspiration pneumonia;
- hypostatic pneumonia (venous plethora in the lungs);
- postoperative (neuroreflex disorders);
- immunodeficiency pneumonia.

*Pathological anatomy* is largely determined by the type of pathogen.

*Stereotyped changes characteristic of all types of bronchopneumonia*:

- formation of a focus of inflammation around the small bronchus and bronchioles with the phenomena of bronchitis and/or bronchiolitis, which is represented by various forms of catarrh (serous, mucous, purulent, mixed);
- violation of the drainage function of the bronchi promotes the penetration of pathogens into the respiratory tract of the lungs, so the inflammation spreads to the respiratory bronchioles and alveoli;
- the walls of the bronchioles are infiltrated by inflammatory infiltrate cells;
- exudate accumulates in the lumens of the alveoli and bronchioles, as well as the bronchi;
- exudate may be serous, purulent, hemorrhagic, mixed in nature, which is largely determined by the etiology of the disease and the severity of the process;
- on the periphery of the foci – preserved lung tissue with the phenomena of perifocal emphysema.

*Macroscopically*: dense airless foci of various sizes are detected, usually formed around the bronchi, the lumen of which is filled with liquid turbid gray-red content, and localized, as a rule, in the posterior and posterior-lower segments of the lungs (II, VI, VIII, IX, X ).

Types of bronchopneumonia *depending on the size* of the foci:

- miliary (alveolitis),
- acinous,
- lobular,
- segmental,
- polysegmental.

*Features of bronchopneumonia at different ages*

In newborns: on the surface of the alveoli are often formed, the so-called hyaline membranes, consisting of compacted fibrin.

In debilitated children up to 1-2 years: foci of inflammation are localized mainly in the posterior, adjacent to the spine regions (II, VI, X segments) – paravertebral pneumonia.

In people older than 50 years: due to age-related reduction of the lymphatic system – resorption of inflammatory foci is slow, foci of pneumonia undergo carnification and end in pneumosclerosis.

*Complications* of focal pneumonia:

- carnification,
- formation of abscesses,
- pleurisy with possible development of pleural empyema.

*Causes of death*: abscesses, purulent pleurisy.

**Interstitial (intermediate) pneumonia** (synonym: pneumonitis) – a disease of infectious nature, characterized by the primary development of acute inflammation in the alveolar wall and pulmonary interstitium with the possible secondary formation of exudate in the lumen of the alveoli and bronchioles.

*Etiology:*

- viruses,
- mycoplasma,
- chlamydia,
- legionella,
- pathogenic fungi,
- rickettsiae (Ku fever – pneumoriketsioz),
- pneumocysts.

*Forms of intermediate pneumonia* depending on the localization of the inflammatory process in the intermediate lung tissue:

1. Peribronchial,
2. Interlobular,
3. Interalveolar.

Peribronchial pneumonia: an inflammatory process that began in the bronchial wall (panbronchitis), spreads to the peribronchial tissue and spreads through the lymphatic vessels to the adjacent interalveolar septa.

*Microscopically*: the thickening of the interalveolar septa is determined; exudate with a large number of alveolar macrophages, single neutrophils, and sometimes fibrin threads accumulates in the alveoli.

Interlobular pneumonia:

- occurs during the spread of inflammation caused mainly by streptococcus or staphylococcus to the interlobular septa – from the lung tissue, visceral pleura (with purulent pleurisy) or mediastinal pleura (with purulent mediastinitis);
- sometimes the inflammation takes the form of phlegmonous and is accompanied by melting of the interlobular septa, there is a "stratification" of the lungs into lobes – stratifying, or sequestering, intermediate pneumonia.

Interalveolar (interstitial) pneumonia: may joins any of the acute pneumonias and have, in such cases, an acute course.

*Macroscopically:*

- numerous foci of gray-red color in the form of honeycombs, strands with light gray gaps of lung tissue;

- in the section of lung tissue – spotted plethora or different sizes of the focus of gray-red color, strengthening of the pulmonary pattern.

*Microscopically:*

- young mesenchymal cells, histiocytes, monocytes, lymphocytes, plasma cells, labrocytes, single neutrophils, eosinophils in alveoli, alveolar macrophages are determined in the pulmonary stroma in the inflammatory focus;
- sequestration of lung tissue.

*Complications:* in the chronic course, interalveolar pneumonia can be the morphological basis of a group of diseases called interstitial lung diseases.

**Lung abscesses**

Abscesses are characterized by the presence in the lungs of a focus of limited purulent inflammation with melting of tissues and the formation of a cavity filled with pus.

*Classification:*

- pneumogenic – occur as a complication of pneumonia;
- bronchogenic – develop during the destruction of the wall of bronchiectasis and the transition of inflammation to the adjacent lung tissue;
- solitary (single);
- multiple;
- acute – the boundaries of the abscess - lung tissue or granulation tissue;
- chronic – the walls of the cavity contain a pyogenic shell and an outer fibrous capsule.

***Training macropreparations***

**Lobar pneumonia (stage of gray hepatization).** Affected lobe of the lung, increased in size, dense, airless, fine-grained in section (fibrin), gray; pleura in the affected area is dull, covered with gray-yellow fibrin plaque.

**Lung carnification**. The tissue of the lung lobe is airless, dense, fleshy.

**Bronchopneumonia**. In section, the lung is variegated with yellow-gray foci of dense consistency, protruding above its surface. The walls of the bronchi are thickened, in the lumen - mucopurulent contents.

***Training micropreparations***

**Bronchopneumonia** (staining with hematoxylin and eosin): all membranes of the bronchial wall are infiltrated with polymorphonuclear leukocytes (panbronchitis), in the lumen of the bronchus serous leukocyte exudate with admixtures of exfoliated epithelial cells. There are areas of destruction of the bronchial wall. In the adjacent alveoli also serous-leukocyte exudate.

**Lobar pneumonia (gray hepatization stage)** (hematoxylin and eosin staining): dilated alveolar lumens are filled with exudate consisting of fibrin threads, neutrophilic leukocytes, individual alveolar macrophages; the capillaries of the alveolar septa become empty, invisible. At coloring on fibrin - threads of fibrin of violet color are defined.

***Questions for self-control***

1. Definition of acute bronchitis, etiology, pathogenesis, classification.
2. Macro-microscopic characteristics of acute bronchitis, age features.
3. Definition of pneumonia. Etiology, pathogenesis, classification of pneumonia.

4. Macro-microscopic characteristics of lobar pneumonia, complications.
5. Macro-microscopic characteristics of bronchopneumonia, complications.
6. Macro-microscopic characteristics of intermediate pneumonia, complications.

***Examples of tests***

1. The autopsy of the carcass of a 5-month-old child revealed the following changes: the upper lobes of the lungs are pink, of normal consistency, the lower lobes are bright red, dense, full-blooded in section. Microscopic examination of the lungs reveals foci of inflammation of various sizes with a predominance in the exudate of erythrocytes with admixtures of single neutrophilic leukocytes. Your diagnosis.
A. * Bronchopneumonia
B. Lobar pneumonia
C. Interstitial pneumonia
D. Bronchiectasis
E. Tuberculosis
2. At the autopsy of the body of the deceased from cardiopulmonary insufficiency revealed: in the pleural cavities turbid fluid with gray threads, lungs increased in volume, airless with gray films and threads on the pleura. In section, the lungs are dense with a grainy surface. Microscopically: the alveoli contain fibrinous-leukocyte exudate. Name the stage of lobar pneumonia.
A. * Stage of gray hepatization
B. Stage of red hepatization
C. Inflow stage
D. Stage of resolution
3. At autopsy of the deceased, who suffered from right-sided pneumonia, in the right lung found a cavity connected to the bronchus and filled with purulent masses; the inner surface of the cavity is uneven. Microscopically, the cavity wall is formed by granulation tissue, diffusely infiltrated with leukocytes. Your diagnosis.
A. * Acute pneumogenic abscess
B. Acute bronchogenic abscess
C. Chronic bronchogenic abscess
D. Chronic pneumogenic abscess
E. Echinococcus lung
4. A 67-year-old patient suffered a severe form of influenza with a fatal outcome. In the section, the changes in the lungs were similar to the changes in the "large variegated lung". Microscopically revealed: sharp plethora of blood vessels, hemorrhage, edema of lung tissue, bronchial and alveolar lumen exudate, which contains mainly erythrocytes. Your diagnosis.
A. * Hemorrhagic bronchopneumonia
B. Catarrhal bronchopneumonia
C. Purulent bronchopneumonia
D. Desquamative bronchopneumonia
E. Fibrinous pneumonia
5. A patient suffering from chronic glomerulonephritis, on the background of chronic renal failure, had a cough with discharge of mucous sputum. At bronchoscopy: the bronchial mucosa is full-blooded, swollen, with small hemorrhages. There is a lot of mucus in the bronchial lumen. Establish the process in the bronchi.

A. * Secondary acute catarrhal bronchitis
B. Primary acute catarrhal bronchitis
C. Chronic catarrhal bronchitis
D. Destructive ulcerative bronchitis
E. Catarrhal-purulent bronchitis

## CHRONIC OBSTRUCTIVE PULMONARY DISEASES: chronic bronchitis, bronchiectasis, emphysema. LUNG CANCER.

**Chronic obstructive pulmonary diseases (COPD)** – groups of lung diseases of various etiologies, pathogenesis and morphology, which are characterized by the development of chronic cough with sputum and paroxysmal or persistent breathing difficulty, not associated with specific infectious diseases (pulmonary tuberculosis).
COPD includes:

- chronic bronchitis,
- emphysema of the lungs,
- bronchial asthma,
- bronchiectasis,
- interstitial lung diseases,
- pneumofibrosis (pneumocirrhosis).

These diseases develop as a consequence of chronic bronchitis, complications of acute pneumonia by abscessing or carnification.
*Development mechanisms:*

- bronchitogenic,
- pneumogenic,
- pneumonitogenic.

*Bronchitogenic mechanism* – violation of bronchial drainage function and bronchial conduction.
These are *chronic obstructive pulmonary diseases*:

- chronic bronchitis,
- bronchiectasis,
- bronchial asthma,
- emphysema of the lungs.

*Characteristics of chronic (diffuse) obstructive diseases*

Reversible or non-reversible disorders of the structure of the bronchi or bronchioles, which lead to impaired lung ventilation.
At considerable lesion of bronchial tubes there is a decrease in functional indicators of lungs, namely:

- decrease in vital capacity of lungs (VC);
- reduction of the ratio of the maximum volume of inhalation and exhalation to the VC;
- reduction of the maximum speed of forced exhalation.

*Pneumogenic mechanism* – associated with acute pneumonia and its complications. Leads to the development of chronic non-obstructive pulmonary disease: chronic lung abscess.
*Pneumonitogenic mechanism* – determines the development of chronic interstitial lung disease: various forms of fibrosing alveolitis, or pneumonitis.
In the end, all three mechanisms of COPD lead to development:

- pneumosclerosis (pneumocirrhosis),
- secondary pulmonary hypertension,
- right ventricular hypertrophy,
- heart and lung failure.

## Chronic bronchitis

*Chronic bronchitis* – inflammation of the bronchial walls, which occurs due to prolonged acute bronchitis or prolonged exposure to the bronchial mucosa of biological, physical and chemical factors.
The diagnosis of chronic bronchitis is made when a persistent cough with sputum lasts at least 3 months a year for 2 years or more.
*Etiology.* Chronic bronchitis occurs as a result of:

- acute bronchitis, which lasts a long time;
- prolonged exposure to the bronchial mucosa:
  - bacteria (eg Haemophilus influenzae, Streptococcus pneumoniae),
  - viruses (eg RS virus, adenoviruses),
  - physical and chemical factors (smoking, cooling of the respiratory tract, pollination, air pollution by industrial waste).

Smokers have the disease 4-10 times more often than non-smokers.
*Classification* of chronic bronchitis by prevalence:

- local (more often in the bronchi II, IV, VIII, IX, X segments of the lungs);
- diffuse – the inflammatory process covers the entire bronchial tree.

Forms of chronic bronchitis:
1) Chronic mucous or purulent catarrh

- with atrophy of the mucous membrane,
- cystic degeneration of the glands,
- metaplasia of the prismatic epithelium into a multilayered squamous,
- increase in the number of goblet cells.

2) Polyposis chronic bronchitis – in the wall of the bronchus and especially in the mucous membrane sharply expressed cellular inflammatory infiltration and growth of granulation tissue, which protrudes into the lumen of the bronchus in the form of a polyp.
3) Deforming chronic bronchitis – with the maturation of granulation and connective tissue growth in the muscle membrane, there is sclerosis and atrophy of the mucous membrane, the bronchus is deformed.
*Macroscopically:*

- bronchial walls are thickened and dense due to multiple sclerosis,
- in the lumen of the bronchi mucopurulent exudates,
- bronchiectasis may develop during prolonged bronchitis.

*Consequences and complications* of chronic bronchitis:

- atelectasis (active collapse of the respiratory part of the lungs due to obstruction or compression of the bronchi);
- bronchiectasis;
- obstructive emphysema;
- pneumosclerosis, pulmonary heart;
- chronic pulmonary vascular insufficiency.

## Bronchiectasis

*Bronchiectasis* – persistent pathological enlargement (protrusion) of the bronchi with structural changes in the walls and the development of a chronic inflammatory infectious process.

*Types:* congenital and acquired.

*Congenital bronchiectasis*: are relatively rare (2-3% of the total number of COPD) and develop due to disorders of the bronchial tree. Histological sign: disorderly arrangement of structural elements of the bronchus in their wall.

*Acquired bronchiectasis*: intrabronchial pressure, which increases during coughing, affecting the altered bronchial wall in chronic inflammation, leads to its protrusion towards the least resistance, the bronchial lumen expands.

*Macroscopically*:

- bronchiectasis occurs in the form of a cylinder or bag;
- expansion of bronchioles – bronchioloectasis;
- incised lung in multiple bronchiectasis and bronchioloectasis resembles bee hives (honeycomb lung).

*Microscopically*:

- the mucous membrane is represented by a multilayered squamous epithelium (at a metaplasia);
- in the wall – chronic inflammation and multiple sclerosis;
- in the cavity – purulent exudates,
- in the surrounding tissue – pneumosclerosis, foci of inflammation;
- in the vessels – sclerosis.

*Bronchiectatic disease* – the whole complex of pulmonary and extrapulmonary changes in the presence of bronchiectasis.

Mechanism of occurrence:

- lung tissue adjacent to bronchiectasis changes sharply, there are foci of inflammation (abscesses, areas of exudate), fields of fibrosis;
- there is obstructive emphysema, which leads to hypertension in the pulmonary circulation and hypertrophy of the right ventricle (pulmonary heart);
- in this regard develop hypoxia, followed by impaired tissue trophism;
- characteristic thickening of the tissues of the nail phalanges of the fingers and toes: the fingers take the form of drumsticks.

*Complications and consequences:*

- lung abscesses,
- pneumosclerosis,
- emphysema of the lungs,

- chronic pulmonary heart disease,
- pulmonary hemorrhage,
- secondary amyloidosis, which leads to chronic renal failure.

## Emphysema of the lungs

*Emphysema of the lungs* – a disease characterized by excessive air content in the lungs and an increase in their size.

Types of emphysema:

- chronic diffuse obstructive – most often;
- chronic focal (perifocal, scar);
- vicar (compensatory);
- primary panacinar (idiopathic);
- senile (emphysema in the elderly);
- intermediate (interstitial).

### *Chronic diffuse obstructive emphysema*

*Etiology and pathogenesis:*

- development is associated with previous chronic bronchitis and bronchiolitis and their consequences - multiple bronchiectasis, pneumosclerosis;
- in emphysema, the elastic and collagen skeleton of the lung is affected due to the activation of leukocyte proteases - elastase and collagenase;
- in the conditions of failure of a stroma of a lung (especially elastic) the so-called valve mechanism joins. Namely, the mucous plug which is formed in a gleam of small bronchial tubes and bronchioles at chronic diffuse bronchitis, at inhalation passes air in alveoluses, but does not allow it to leave at an exhalation;
- air accumulates in the acinuses, expands their cavities, which leads to diffuse obstructive emphysema.

*Macroscopically*, the lungs are enlarged, cover the edges of the anterior mediastinum, swollen, pale, soft, do not sag, cut with a crunch.

*Microscopically*:

- stretching of the walls of the acinus leads to stretching and thinning of elastic fibers, dilation of alveolar passages, changes in alveolar septa;
- the walls of the alveoli become thinner and straightened, the interalveolar pores expand, the capillaries run down;
- respiratory bronchioles expand, alveolar sacs shorten;
- collagen fibers grow in the interalveolar capillaries, intracapillary sclerosis develops;
- at the same time formation of new, not absolutely typically constructed, capillaries which has adaptive value is observed.

*Consequence* – in the lungs there is hypertension of the pulmonary circulation, which leads to hypertrophy of the right heart (pulmonary heart).

### *Chronic focal emphysema*

*Etiology:*

- develops around old tuberculous foci, postinfarction scars, more often in I-II segments (perifocal, or cicatricial);

- chronic focal emphysema is mostly panacinar: in dilated acinuses the walls become smooth, smooth cavities are formed;
- possible development of bullous emphysema – in the presence of several cavities.

*Vicar (compensatory) emphysema*

Excessive swelling and stretching of alveolar tissue in response to the loss of a significant volume of the lung parenchyma (eg, pulmonectomy or even unilateral lobectomy).

*Microscopically*: no destructive processes in the alveolar walls.

*Primary (idiopathic) emphysema*

It is very rare, the etiology is unknown.

*Microscopically:*

- atrophy of the alveolar wall;
- reduction of the capillary wall;
- severe hypertension of the pulmonary circulation.

*Senile emphysema:*

- develops due to age-related lung involution;
- no destruction of the alveolar wall;
- with aging there is a progressive decrease in the surface of the alveoli, which leads to increased airiness of the lungs;
- this process is a normal senile involution of the lungs.

*Intermediate (interstitial) emphysema:*

- occurs when air enters the interstitium as a result of traumatic rupture of the alveoli (with increased coughing movements) or spontaneous rupture of the bulla (cavity);
- may spread to the mediastinum and subcutaneously (subcutaneous emphysema);
- when you press on the swollen area of skin you hear a crunch (crepitation).

## Interstitial lung diseases

Interstitial lung diseases – a heterogeneous group of diseases characterized by a predominance of diffuse and usually chronic lesions of the pulmonary interstitium of the respiratory lungs, especially the alveoli and bronchioles.

### *Idiopathic fibrosing alveolitis*

Idiopathic fibrosing alveolitis (IFA) is a group of diseases that includes the following units:

- classic interstitial pneumonia,
- "nonspecific" interstitial pneumonia,
- desquamative pneumonia,
- obliterating bronchiolitis with pneumonia,
- giant cell interstitial pneumonia.

Early stage of IFA – in patients with a disease duration of up to 1 year.

*Macroscopically:* the lungs may be slightly changed, unevenly airy, full-blooded, with increased density.

*Microscopically*: the manifestations of the initial changes in IFA fit into the picture of exudative and exudative-productive inflammation. In the alveolar septa – the

phenomena of edema, inflammatory infiltration and the initial manifestations of sclerosis. Impaired vascular permeability leads to accumulation of exudate in the lumens of the alveoli, desquamation of the epithelium, loss of fibrin until the formation of hyaline membranes.

Late stage IFA.

*Macroscopically*: compaction of lung tissue, which thus acquires rubber density, reduced lightness and elasticity with the formation of porous structures resembling bee hives – "honeycomb lung".

*Microscopically:* severe sclerosis of the interstitium of the respiratory lungs and cystic remodeling of lung tissue with squamous cell metaplasia, epithelial dysplasia and the formation, in some cases, foci of adenomatosis.

*Consequence:*

- progressive respiratory failure;
- lung cancer (develops in approximately 12.5% of IFA patients).

## Occupational lung diseases

*Occupational lung diseases* are referred to as *pneumoconiosis*. Pneumoconiosis – professional diseases caused by inhalation of dusty air.

*Classification of pneumoconioses:*

1. Dust fibrosis of the lungs from the effects of fibrogenic dust.
2. Interstitial lung diseases caused by organic dust.
3. Chronic dust bronchitis.
4. Chronic obstructive pulmonary disease.

*Dust fibrosis of the lungs* from the effects of fibrogenic dust was the basis for the selection of a group of pneumoconioses, which includes:

- silicosis (from silica dust),
- asbestosis (from asbestos dust),
- anthracosis (from coal dust),
- berylliosis (from dust of beryllium compounds), etc.

*Morphological changes* in the lungs in pneumoconiosis can be of two types:

1) diffuse interstitial fibrosis – when exposed to dust particles with a pronounced catalytic ability (asbestos, zinc oxide) is the formation of a hydroxyl radical and the pathological process becomes similar to fibrosing alveolitis with the development of "cellular lung"

2) granulomatous process – under the influence of silicon dioxide, macrophages generate reactive oxygen species and mediators of lipoxygenase and cyclooxygenase pathways with the development of delayed-type hypersensitivity and the formation of granulomas.

### *Anthracosis*

*Anthracosis* (black lung) is a pneumoconiosis that develops with prolonged inhalation of coal dust. Coal pigment causes the development of multiple sclerosis, the degree of which depends on the nature of the coal and the composition of the rock in which the coal seams lie.

Anthracosis is characterized by the deposition of coal dust (pigment), which gives a gray-black color.

*Forms of anthracosis:*

1) benign anthracnose pulmonary fibrosis, or "spotted anthracosis";
2) progressive massive fibrosis.

In the lightest benign form of anthracnose fibrosis, or "spotted anthracosis", the lung contains only local foci of black pigmentation, separated by wide areas of healthy tissue – "anthracite spot". It consists of clusters of carbon-filled macrophages around the respiratory bronchioles, pulmonary arterioles and veins. Similar cells are found in the lymph vessels and lymph nodes of the lung roots. Fibrosis is mild, but often there is local dilatation of respiratory bronchioles, which is a manifestation of local centrolobular emphysema. As spotted anthracnose progresses, nodules up to 10 mm in diameter appear – a "nodular form of spotted anthracnose".

Progressive massive fibrosis is a further development of the disease and is mainly considered secondary, resulting from intercurrent complications. At the same time pigmentation becomes much more intense. Anthracite spots are large and numerous ("black lung disease"), gradually surrounded by fibrous tissue. Progressive massive fibrosis is characterized by the formation of large nodules of fibrosis of irregular shape (diameter greater than 10 mm). Progression of the disease leads to fibrosis and destruction of lung tissue.

In the final disease of the lungs have the form of honeycombs, there is the formation of the pulmonary heart. Patients die either from pulmonary heart failure or the accession of intercurrent diseases.

*Silicosis*

*Silicosis* or halicosis – a disease that develops as a result of prolonged inhalation of dust containing free silicon dioxide. Silicon dust is found in gold, tin and copper mines, in the grinding of stones, in the manufacture of glass, metal smelters, in the manufacture of pottery and porcelain.

*Forms of silicosis*: nodular and diffuse sclerotic (or interstitial).

In nodular form, a significant number of silicotic nodes and nodules are found in the lungs, which are miliary and more significant sclerotic areas of round, oval or irregular shape, gray or gray-black (in coal miners). In severe silicosis, the nodules merge into large silicotic nodes, which occupy most of the lobe or even the entire lobe. In such cases, talk about a tumor-like form of pulmonary silicosis.

In the diffuse-sclerotic form, typical silicotic nodules in the lungs are absent or very few, they are often found in bifurcated lymph nodes. In this form, the connective tissue in the lungs grows in the alveolar septa, peribronchially and perivascularly. Diffuse emphysema, bronchial deformity, various forms of bronchiolitis, bronchitis (often catarrhal-desquamative, less often – purulent) develop.

Patients die from progressive pulmonary heart failure.

*Asbestosis*

*Asbestosis* – pneumoconiosis that develops with prolonged contact with asbestos dust. Asbestos fibers, despite their large length (5-100 μm), have a small thickness (0.25-0.5 μm), so they penetrate deep into the alveoli of the basal parts of lungs. Fibers are found not only in the lungs but also in the peritoneum and other organs. The fibers damage the walls of the alveoli and bronchioles, which is accompanied by small hemorrhages and is the basis for the formation of hemosiderin inside the macrophages. Complexes, which consist of asbestos fibers, most often coated with

glycosaminoglycans, on which iron-containing grains of hemosiderin are deposited, are called "asbestos cells".
*Microscopically*: "asbestos bodies" – reddish or yellowish oblong structures that have the shape of rings or stringed pearls, resembling the appearance of "elegant dumbbells". Interstitial fibrosis is observed in the lungs.
*Macroscopically*, the lungs in the late stages have the appearance of honeycombs. Fibrosis and emphysema of the lungs are found mainly in the basal regions of lungs.
Patients die from pulmonary and cardio-pulmonary insufficiency.

*Berylliosis*

Pulmonary berylliosis is a pneumoconiosis caused by dust or vapors of beryllium metal (Be) and its compounds – oxide (BeO), beryllium fluoride, etc., which have high toxicity. Beryllium dust and vapors are very dangerous by lung damage and the development of systemic complications.
Types of berylliosis: acute and chronic (most common).
Acute berylliosis mostly occurs when soluble acid salts of beryllium enter the body. Acute bronchopneumopathy develops.
*Microscopically*, it has the character of "acute chemical pneumonia". The edema is sharply expressed, the wall of alveoluses is infiltrated with polynuclear neutrophils, as a part of exudate – impurity of erythrocytes and fibrin. After a few days, macrophages and lymphocytes appear in the exudate. Then there is an intraalveolar organization of exudate (carnification), and interalveolar fibrosis develops.
Within a few weeks, patients may die of pulmonary insufficiency. In acute berylliosis there is no granuloma.
Chronic berylliosis ("granulomatous berylliosis") is characterized by the development of small granulomas resembling tuberculosis or sarcoidosis.
*Microscopically*: granulomas are numerous, localized subpleurally in the interstitial tissue around small vessels and bronchi. Granulomas consist of epithelioid, lymphoid, plasma cells, as well as cells such as Langhans or giant cells of foreign bodies. Progressive diffuse interstitial chronic fibrous pneumonia develops.
In chronic berylliosis, granulomatous changes are also observed in the liver, kidneys, spleen, lymph nodes and skin. When beryllium particles penetrate the damaged skin, granulomatous inflammation develops with the formation of wounds that do not heal for a long time.
Unlike asbestosis, berylliosis does not cause predisposition to lung cancer.

## Lung cancer

*Lung cancer* is a malignant tumor that develops from the epithelium of the bronchi (bronchogenic, central cancer), rarely (up to 1% of cases) – from the epithelium of the bronchioles and alveolar epithelium (pneumonogenic, peripheral cancer).
*Risk factors:*

- smog,
- smoking,
- work with occupational hazards,
- genetic predisposition.

*Background diseases:*

- tuberculosis,

- pulmonary infarction,
- chronic smoker's bronchitis,
- pneumocirrhosis,
- focal pneumosclerosis.

*Precancerous changes:*

- hyperplasia,
- dysplasia,
- squamous cell metaplasia.

*Clinical and anatomical classification of lung cancer*

By localization:

- basal (central) – arises from the epithelium of the large bronchi;
- peripheral (alveolar) – arises from the epithelium of the bronchioles;
- mixed (massive).

By the nature of growth:

- exophytic (endobronchial, grows in the lumen of the bronchus);
- endophytic (exo- and peribronchial, grows into the bronchial wall).

In macroscopic form:

- plaque-like,
- polypoid,
- endobronchial (diffuse),
- nodular,
- branched,
- nodular-branched.

By microscopic structure:

- squamous (epidermoid);
- adenocarcinoma;
- undifferentiated (small cell, large cell);
- glandular-squamous (dimorphic);
- carcinoma of the bronchial glands:
  - adenoid-cystic,
  - mucoepidermoid.

***Central cancer*** (45-50% of all lung cancers).

*Macroscopically*:

- develops in the mucous membrane of the trunk, partial and initial section of the segmental bronchus;
- initially in the form of a small nodule (plaque) or polyp;
- further – depending on the nature of growth (exo- or endophytic), takes the form of endobronchial diffuse, nodular, branched or nodular-branched.

*Microscopically*: the structure of squamous cell and small cell cancer.

*Complications* – often and early, not reaching large sizes:

- atelectasis (segmental or partial) – a constant companion of basal cancer;
- pneumonia, abscess, bronchiectasis.

These changes mask the small size of the cancer.

From a large bronchus the tumor at endophytic growth extends to tissue of a mediastinum, a pericardium and a pleura. Serous-hemorrhagic or hemorrhagic pleurisy occurs.

***Peripheral cancer*** (50-55% of lung cancers).

*Macroscopically*:

- occurs in the mucous membrane of the peripheral segment of the segmental bronchus, its smaller branches and bronchioles, rarely – from the alveolar epithelium;
- grows expansively for a long time in the form of a node, sometimes reaching 5-7 cm;
- often develops in the area of the scar (capsule of healed tuberculosis foci, scar after pulmonary infarction) near the pleura in any area of the lung;
- may spread to the pleura, as a result of which it thickens and accumulates in the pleural cavity serous-hemorrhagic or hemorrhagic exudate that compresses the lung.

*Microscopically*:

- squamous cell carcinoma,
- adenocarcinoma,
- undifferentiated cancer.

*Squamous cell (epidermoid) cancer*, types: high-, moderate- and low-differentiated.

Highly differentiated: squamous cell carcinoma with keratinization - the formation of keratin by cells and the formation of **"cancer pearls".**

Moderately differentiated: mitosis and cell polymorphism, some of which contain keratin.

Low-differentiated – significant polymorphism of cells and nuclei (presence of polygonal and spindle-shaped cells), many mitoses, keratin only in individual cells.

*Adenocarcinoma*, types: highly-, moderate- and low-differentiated.

Highly differentiated: consists of acinar, tubular or papillary structures, the cells of which produce mucus.

Moderately differentiated: has a glandular-solid structure, many mitoses, mucus is observed only in some cells.

Lowly differentiated: consists of solid structures, polygonal cells are able to produce mucus.

A type of adenocarcinoma is *bronchiolar-alveolar cancer*.

*Undifferentiated anaplastic cancer*.

Types: small-celled, large-celled.

Small cell carcenoma:

- consists of small lymphocyte-like cells with hyperchromic nuclei;
- cells grow in layers or strands;
- may have hormonal activity – produce ACTH, serotonin, calcitonin and other hormones.

Large cell carcinoma: represented by large polymorphic, often multinucleated cells that cannot produce mucus.

*Glandular squamous cell carcinoma* (mixed). Combination of adenocarcinoma and squamous cell carcinoma.

*Carcinoma of the bronchial glands*. It has an adenoid-cystic or mucoepidermoid structure. Rare.

*Complications of lung cancer*: metastases (70%):

- lymphogenic – first in the peribronchial and bifurcated lymph nodes, then – cervical and other;
- hematogenous – in the liver, brain, bones (often in the spine), adrenal glands;
- contact – on the pleura.

Secondary pulmonary changes are associated with the development of atelectasis, cavity formation, bleeding, and suppuration.

*Causes of death:*

- metastases,
- pulmonary complications,
- cancerous cachexia.

### *Training macropreparations*

**Chronic bronchitis with bronchiectasis and pneumosclerosis**. The surface of the incision of the lung is small-pore due to the protrusion of the wall of the bronchioles - "honeycomb lung ".

**Pulmonary emphysema**. The lungs are significantly increased in size, light gray, contain large amounts of air. At the top of the lungs – a lot of air-filled blisters (bullous emphysema).

**Central (basal) lung cancer**. Exo-endophytic growth of the tumor, which is represented by a node of yellow-gray color, destroying the central bronchus.

**Peripheral lung cancer**. Infiltrative growth of the tumor, which is located in the peripheral part of the segmental bronchus, is quite large.

**Anthracosis of the lungs**. The lungs are dense, black, slightly reduced in size.

### *Training micropreparations*

**Bronchiectasis and pneumosclerosis** (staining with hematoxylin and eosin): bronchial lumen is enlarged, contains squamous epithelium, leukocytes. Bronchial epithelium in places with signs of squamous cell metaplasia, its basal membrane thickened, hyalinized, sclerosis and diffuse inflammatory infiltration (leukocytes, lymphocytes, macrophages) of the submucosal layer, mucous glands and muscle membrane hypertrophied or atrophic.

**Chronic obstructive pulmonary emphysema** (hematoxylin and eosin staining): dilated lumens of respiratory bronchioles and alveoli, interalveolar septa are significantly thinned, torn in many areas, resulting in cavities of different sizes and shapes, walls and walls of the vessel.

### *Questions for self-control*

1. Classification of diseases belonging to COPD.
2. Chronic bronchitis, definition, morphological characteristics, complications.
3. Bronchiectasis, definition, morphological changes in the lungs in bronchiectasis and its complications.
4. Emphysema: definition, classification, morphological changes in the lungs, complications.
5. Idiopathic fibrosing alveolitis, definition, morphological characteristics.

6. Pneumoconiosis, definition, types, general morphological characteristics of asbestosis, silicosis, beryllium.
7. Lung cancer, classification, morphological characteristics.

***Examples of tests***

1. In the biopsy of the tumor of the bronchial mucosa found cells of atypical epithelium of various shapes and sizes with hyperchromic nuclei. Tumor cells form glandular structures of various shapes and sizes that penetrate the basal membrane into the submucosal layer. Specify the histological form of the cancer.
A. * Adenocarcinoma.
B. Solid cancer.
S. Skin.
D. Squamous cell carcinoma.
E. Cancer "in situ".
2. The patient for 20 years complained of cough with purulent sputum and shortness of breath. Death occurred from pulmonary insufficiency. At autopsy: in the bronchi - purulent sputum, their walls are thickened; in the heart - hypertrophy of the right departments. Microscopically: the bronchial mucosa is atrophic, the bronchial wall is diffusely infiltrated with leukocytes with the growth of connective tissue around the bronchi and blood vessels. Your diagnosis.
A. * Chronic bronchitis.
B. Deforming bronchitis.
C. Chronic polyposis bronchitis.
D. Bronchiectasis.
E. Pneumosclerosis.
3. In the section of the deceased, who for a long time suffered from chronic bronchitis, repeatedly suffered from pneumonia, it was found that the lungs are dense, low air, in the context of "cellular" appearance. The walls of the bronchi are dense with saccular protrusions that contain purulent masses. Heart weighing 520 g, right ventricular wall - 2 cm, left - 1.2 cm, right ventricular cavity dilated. Your diagnosis.
A. * Bronchiectasis.
B. Pneumosclerosis.
C. Chronic obstructive emphysema
D. Chronic bronchitis.
E. Chronic lung abscesses.
4. In the section of the deceased, who worked in the chemical industry and suffered from attacks of expiratory dyspnea, accompanied by cough with thick sputum, it was found that the lungs are enlarged, cover the mediastinum, swollen, pale, do not fall, cut with crunch. Purulent mucus is squeezed out of the bronchial lumens. Your diagnosis.
A. * Chronic diffuse obstructive emphysema.
B. Bronchiectasis.
C. Chronic pneumonia.
D. Atypical bronchial asthma.
E. Chronic bronchitis.
5. At the deceased, who worked at the coal mine for more than 20 years, the autopsy revealed compacted gray-black lungs with significant areas of newly formed

connective tissue and the presence of a large number of macrophages with black pigment in the cytoplasm. Your diagnosis.
A. * Anthracosis
B. Anthracosilicosis
C. Silicoanthracosis
D. Talcose
E. Siderosis

## TUBERCULOSIS

**Tuberculosis** is a common chronic infectious disease caused by Mycobacterium tuberculosis, which affects all human organs, but most often the lungs.
*Etiology of tuberculosis*: Mycobacterium tuberculosis (Koch's bacillus).

*The main types of mycobacteria (MBT)*

1) Human (typus humanus or mycobacterium tuberculosis) the main causative agent of tuberculosis in humans.
2) Bovine (typus bovinus or mycobacterium bovis). Pathogenic to humans, cattle.
3) The African species isolated in West Africa, it has the characteristics of the two previous species.

*Ways of infection and gates of infection*

Primary infection

a. Air-drop (aerogenic) path. 90-95% of cases: during coughing, talking, spitting a patient with an active ("open") form of tuberculosis.
b. Alimentary way (less often) – through milk, meat: lesions of the intestines, tonsils.
c. Contact route (very rare) – through damaged skin and mucous membranes.

Secondary infection

The development of secondary tuberculosis is associated with:
a. reactivation of tuberculosis in old post-primary foci;
b. superinfection – re-infection.

Immunity in tuberculosis is non-sterile, ie it exists in the presence of tuberculosis in the body.

*Clinical and morphological manifestations of tuberculosis:*

1. Primary,
2. Hematogenous (hematogenously disseminated),
3. Secondary.

### Primary tuberculosis

*Characteristics of primary tuberculosis:*

- development of the disease during infections, ie during the first meeting of the body with the infection;
- sensitization and allergy, immediate hypersensitivity reactions;
- dominance of exudative-necrotic changes;
- predisposition to hematogenic and lymphogenic (lymph node) generalization;
- paraspecific reactions in the form of vasculitis, arthritis, serositis.

As a rule, the way of infection is aerogenic, possible and alimentary.
Children and adolescents sick.

***Primary tuberculosis complex is a morphological manifestation of primary tuberculosis.***

- ***primary focus or affect*** – the focus of the lesion in the organ in which the tubercle bacillus;
- ***lymphangitis*** – tuberculous inflammation of the outgoing lymphatic vessels;
- ***lymphadenitis*** – tuberculous inflammation of regional lymph nodes.

At aerogenic infection

***Primary affect***

- primary tuberculous focus (affect) occurs subpleurally in the most actively aerated segments (III, VIII, IX, X), often the right lung;
- affect is represented by a focus of exudative inflammation, which is rapidly susceptible to caseous necrosis;
- a focus of caseous pneumonia is formed, which is surrounded by a zone of perifocal inflammation.

***Lymphangitis*** is an inflammation of the lymphatic vessels that go from the affect. Lymphostasis. Formation of tuberculous granulomas.

***Lymphadenitis*** – tuberculous inflammation of regional lymph nodes (bronchial or broncho-pulmonary). They are subject to caseous necrosis. As a result, the nodes increase. Tuberculous granulomas are formed.

At alimentary infection

The primary tuberculosis complex develops in the intestine.

***Primary affect*** – in the lymphoid tissue of the lower part of the jejunum or cecum, tuberculous tubercles are formed with necrosis and subsequent formation of ulcers in the mucous membrane.

***Lymphangitis*** is an inflammation of the lymphatic vessels that come from affect.

***Lymphadenitis*** is a tuberculous inflammation of the regional lymph nodes in relation to the primary affect. They are subject to caseous necrosis.

*Variants of the course of primary tuberculosis*

1) healing of foci of the primary complex with the formation of *foci of Gon*;
2) progression of primary tuberculosis with generalization of the process:
   - lymphogenic (lymph nodes),
   - hematogenic,
   - growth of primary affect,
   - mixed;
3) chronic course.

*Ways of progression of primary tuberculosis*

Lymphogenic – involvement in the process of specific inflammation of various lymph nodes, most often lymph nodes of the lung root - bronchoadenitis, paratracheal nodes. Lymph nodes of the neck are enlarged, subject to caseous necrosis, tuberculous granulomas are formed.

*Consequences:*

- atelectasis (due to bronchial compression);
- breakthrough of caseous masses; at their aspiration - caseous pneumonia;
- possible formation of fistulas on the neck during the breakthrough of caseous masses;
- paraspecific reactions – rashes and conjunctivitis.

Hematogenic, types:

- miliary tuberculosis,
- large-focal tuberculosis,
- hematogenous screening.

The primary affect does not heal, in the area of caseous necrosis there is a vessel with the affected wall, through which the tubercle bacillus enters the blood.

*Miliary (millet) tuberculosis* – the formation of tuberculous granulomas in many organs. Possible tuberculous lesion of the meninges: tuberculous meningitis, in which tuberculous granulomas appear at the base of the brain, in the cerebrospinal fluid – lymphocytosis.

*Large-focal tuberculosis* – groups of tubercles together.

*Hematogenous screening* – tubercle bacillus is entered into any organ, with tubercle bacillus is in a weakened state, clinically not detected, but when weakening of immunity develops tuberculous lesions.

Growth of primary affect – the area of caseous necrosis is surrounded by a zone of perifocal inflammation, which can turn into caseous necrosis, thus may develop caseous pneumonia – primary pulmonary tuberculosis.

Chronic course is observed in cases when the primary affect heals, and in the lymph gland complex healing processes alternate with exacerbation, which causes sensitization of the body.

In response to this, paraspecific manifestations occur in the internal organs:

- nodular or diffuse proliferation of lymphocytes and macrophages;
- hyperplasia of hematopoietic organs;
- fibrinoid changes of connective tissue, arterioles;
- dysproteinosis;
- amyloidosis (sometimes).

*Consequences of primary tuberculosis*

*Favorable*:

- organization,
- encapsulation,
- petrification (especially lymphadenitis),
- ossification (formation of bone tissue, and it is believed that the tubercle bacillus dies).

*Unfavorable* – death from:

- intoxication (with generalization of the process),
- tuberculous meningitis, peritonitis.

## Hematogenous tuberculosis (post-primary)

It develops on the basis of foci of elimination of the period of primary infection. It occurs in people who have clinically recovered from primary tuberculosis, but they retain the infection in incompletely healed foci and retain hypersensitivity to tuberculin against the background of developed immunity to mycobacteria. Under adverse conditions (trauma, inflammation, beriberi, stress, etc.) infection from the site of inflammation at the site of elimination, or latent lymphadenitis penetrates the bloodstream.

*Types of hematogenous tuberculosis:*

1. Generalized hematogenous tuberculosis:

- the most acute tuberculous sepsis – the most severe form of the disease with an even rash of tuberculous tubercles and foci in the organs;
- acute general miliary – the appearance of small miliary bumps in the organs;
- acute general large-focal – formation in the organs of large (up to 1 cm) tuberculous foci.

2. Hematogenous tuberculosis with a predominant lung lesion:
   - acute miliary tuberculosis,
   - chronic miliary tuberculosis,
   - chronic focal or hematogenously disseminated tuberculosis.
3. Hematogenous tuberculosis with predominant extrapulmonary lesions
   - bones and joints, genitourinary system, skin, other organs.

## Secondary tuberculosis

Secondary tuberculosis appears in people, mostly sensitized, carriers of tuberculosis bacilli of exogenous or endogenous origin. It often develops in the body of an adult who has previously suffered a primary infection, which provided him with relative immunity, but did not protect against the possibility of recurrence.

*Characteristics of secondary tuberculosis:*

- selective pulmonary localization of the process;
- contact and intracanalicular (bronchial tree, digestive tract) spread;
- change of clinical and morphological forms, which are phases of the tuberculous process.

*Clinical and morphological forms of secondary tuberculosis:*

1. Acute focal,
2. Fibrofocal,
3. Infiltrative,
4. Tuberculoma,
5. Caseous pneumonia,
6. Acute cavernous,
7. Fibrous-cavernous,
8. Cirrhotic.

***1. Acute focal tuberculosis.***

*Macroscopically:* the presence in the I and II segments more often than the right lung of one or two inflammatory foci.

*Microscopically*: productive inflammatory reaction with the formation of typical tuberculous tubercles. With progression, a specific process of bronchioles passes to the lung parenchyma – develops acinous or lobular cheesy bronchopneumonia, around which a shaft of epithelioid cells with admixtures of lymphoid and giant Langhans cells quickly forms.

***2. Fibrofocal tuberculosis*** – a phase of acute focal tuberculosis, when after a period of remission the process is reactivated. At healing – there is a petrification of the centers (the Ashoff-Poole center). With exacerbation – there are acinous, lobular foci of caseous pneumonia, which are again encapsulated. The process does not go beyond segments I and II, and among the encapsulated and petrified foci of tuberculosis there are not only foci of reinfection, but also those that are the result of hematogenous screening during the primary infection (foci of Simon).

***3. Infiltrative tuberculosis*** – with the progression of acute focal or exacerbation of fibro-focal tuberculosis, and exudative changes around the caseous foci go beyond the lobe and even the segment. Perifocal inflammation predominates over caseous changes, which may be minor (Asman-Redecker foci).
***4. Tuberculoma*** – a form of secondary tuberculosis that occurs as a kind of phase of evolution of infiltrative tuberculosis, when perifocal inflammation is resorbed and remains the focus of cheesy necrosis, surrounded by a capsule. Tuberculoma reaches 2-5 cm in diameter, located in the I or II segment, more often on the right. Radiologically resembles a tumor.
***5. Caseous pneumonia*** – with the progression of infiltrative tuberculosis, as a result of which caseous changes begin to prevail over perifocal. The lung in caseous pneumonia is enlarged, dense, in section yellow-gray. Often combined with fibrinous pleurisy.
***6. Acute cavernous tuberculosis*** – the rapid formation of the decay cavity, and then the cavity at the site of the infiltrate or tuberculoma. The decay cavity occurs as a result of purulent melting and thinning of caseous masses, which contain mycobacteria and are excreted with sputum through the drainage bronchus. This creates a great danger of bronchogenic contamination of the lungs, as well as the release of mycobacteria into the environment. The resulting cavity is usually localized in the I or II segment (at the site of the foci from which it developed), has an oval or round shape, 2-5 cm in diameter, connects with the lumen of the segmental bronchus.
***7. Fibro-cavernous tuberculosis*** arises from acute cavernous tuberculosis, when the process becomes chronic. The cavity may occupy one or both segments. Three layers are defined in a wall of a cavity: internal – necrotic; middle – shaft of tuberculous granulation tissue; outer – fibrous connective tissue.
***8. Cirrhotic tuberculosis*** – there is a deformation of lung tissue and the development of bronchiectasis together with massive, diffuse growth of connective tissue. Cavities are absent or in the form of slit-like cavities.
*Complications of secondary tuberculosis.*

- bleeding,
- breakthrough of the contents of the cavity into the pleural cavity,
- pneumothorax,
- purulent pleurisy (pleural empyema).
- Amyloidosis.

*Causes of death of patients with pulmonary tuberculosis:*

- pulmonary heart failure;
- pulmonary hemorrhage;
- secondary amyloidosis (uremia).

***Training macropreparations***

**Primary pulmonary tuberculosis complex**. In the third segment of the right lung, a subpleural lesion of white-yellow color 1.5 cm (primary affect), from it to the basal lymph nodes extends whitish path (lymphangitis) and enlarged yellow-white lymph nodes (lymphadenitis).

**Tuberculosis of the kidneys**. The kidney is significantly increased in size, in section – large cavities filled with yellow-gray brittle masses (tuberculous cavities).
**Tuberculosis of the spine (spondylitis)**. Vertebral bodies are destroyed, areas of yellow-white damage (caseous necrosis).
**Miliary pulmonary tuberculosis**. Lungs fluffy, swollen, there are small areas of 1-2 mm yellow-white color (tuberculous granulomas).
**Fibrous-cavernous pulmonary tuberculosis**. The organ is gray, the parenchyma of the lung is porous, the stroma is represented by connective tissue layers of whitish color. In the parenchyma, black spotting is the vessels of the lung. Against the background of this picture you can see multiple rounded formations with a diameter of 0.5 cm whitish color. The configuration of the lung section is broken by three caverns. The first has dimensions of 8x7x4 cm, the second – 4x3x1.5 cm, the third – 6x5x3 cm.
**Caseous pneumonia**. Part of the lung yellow-gray, dense.
**Tuberculoma**. In the second segment of the right lung there is a round shape, 5 cm in diameter, surrounded by a capsule, filled with dense gray masses.
**Cirrhotic tuberculosis**. The lungs are reduced, deformed, white, airless.

### *Training micropreparations*

**Miliary pulmonary tuberculosis** (hematoxylin and eosin staining): tuberculous granuloma is present in the lung. It has the following structure: in the center a small area of caseous necrosis, around – epithelioid cells with 1-3 giant multinucleated Pirogov-Langhans cells; the outer layer of the infiltrate is represented by lymphocytes.

### *Questions for self-control*

1. Definition of tuberculosis, etiology, pathogenesis, ways of infection.
2. Components of the primary complex in tuberculosis. Options for the progression of primary tuberculosis.
3. Clinical and anatomical forms of hematogenous tuberculosis, morphological characteristics.
4. Clinical and anatomical forms of secondary tuberculosis, morphological characteristics.
5. Complications and causes of death from tuberculosis.

### *Examples of tests*

1. A 48-year-old man died of progressive pulmonary insufficiency. The autopsy revealed: pulmonary emphysema, reticular pneumosclerosis, cortico-pleural nodules of white-gray color, in the middle fields of the lungs symmetrically located cavities up to 3.5 cm in diameter with dense walls, right ventricular hypertrophy. Your diagnosis.
A. * Hematogenously disseminated pulmonary tuberculosis
B. Fibrous-cavernous pulmonary tuberculosis
C. Acute pulmonary tuberculosis
D. Chronic lung abscesses
E. Bronchiectasis
2. At the autopsy of the deceased 25 years old in the III segment of the right lung is the primary tuberculous focus that has healed. Multiple millet-like bumps were found in the kidneys, liver, spleen, and soft membrane of the brain. Microscopically: the

nodules are foci of caseous necrosis, surrounded by epithelioid, lymphoid and single giant multinucleated Pirogov-Langhans cells. What is the form of tuberculosis?
A. * Small-focal generalized tuberculosis.
B. The most acute (necrotic) tuberculous sepsis.
C. Focal generalized hematogenous tuberculosis.
D. Primary tuberculosis.
E. Secondary tuberculosis.
3. An autopsy of the deceased, who suffered from a progressive form of secondary tuberculosis, revealed an enlarged, dense right lung, yellow in section with fibrinous overlays on the pleura. The predominance of necrotic changes was revealed microscopically. Your diagnosis.
A. * Caseous pneumonia.
B. Infiltrative tuberculosis.
C. Acute focal tuberculosis.
D. Fibro-focal tuberculosis.
E. Fibrous-cavernous tuberculosis.
4. In a patient who died of tuberculosis, in the I segment of the right lung was found a gray focus with a diameter of 3 cm, surrounded by a capsule. Microscopically: the center of necrosis with a connective tissue capsule, perifocal inflammation is absent. Name the form of tuberculosis.
A. * Tuberculoma
B. Acute cavernous tuberculosis
S. Fibrous-cavernous tuberculosis
D. Cirrhotic tuberculosis
E. Caseous pneumonia
5. An autopsy of a 16-year-old teenager who died of intoxication revealed: moderate exhaustion, in the second segment of the right lung the foci of Gon, peribronchial and bifurcated lymph nodes enlarged, dense, gray-yellow in section, crumbling. Microscopically: in the lungs the primary affect that has healed, in the lymph nodes - caseous necrosis. Specify the form of tuberculosis.
A. * Lymphogenic progression of tuberculosis.
B. Chronic course of primary tuberculosis.
C. Hematogenously disseminated tuberculosis.
D. Acute focal tuberculosis.
E. Caseous pneumonia.

## INFECTIOUS DISEASES. CHARACTERISTICS OF THE INFECTIOUS PROCESS. BACTERIAL AIR DROP INFECTIONS: diphtheria, scarlet fever, meningococcal infection. VIRAL AIR DROP INFECTIONS: flu, parainfluenza, measles. HIV infection

**Infection** is a broad general biological concept that characterizes the penetration of a pathogen into another, more highly organized plant or animal organism and their subsequent antagonistic coexistence.

**Infectious process** – time-limited complex interaction of biological systems of micro- (pathogen) and macroorganism, which occurs in certain environmental conditions, manifests itself at the submolecular, subcellular, cellular, tissue, organ and organismal levels and naturally ends in either the death of the macroorganism or its complete dismissal.

As a result of the infectious process, an infectious disease often develops.

**Infectious disease** – a specific form of manifestation of the infectious process, which reflects the degree of its development and has characteristic nosological features.

**Pathogenicity** is a genetically fixed trait of a microorganism that characterizes the ability to cause disease. On this basis, organisms are divided into pathogenic, opportunistic, non-pathogenic (saprophytes).

The main factors determining pathogenicity: virulence, toxicogenicity, invasiveness.

**Virulence** – the degree of pathogenicity, individually inherent in a particular strain of the pathogen.

**Toxicogenicity** – the ability to produce and release various toxins (exotoxin and/or endotoxin).

**Invasiveness** – the ability to penetrate into the tissues and organs of a macroorganism and spread in them.

## Air-drop infections

Air-drop infections are a group of acute inflammatory diseases with a predominant localization of changes in the upper respiratory tract.

*Features of air-drop infections.*

1) Air-drop transfer.
2) A variety of pathogens: viruses, bacteria, protozoa, fungi.
3) Entrance gate – the mucous membrane of the upper respiratory tract.
4) The spread is facilitated by overcrowding.
5) People with chronic tonsillitis, laryngitis are prone to air-drop infections; children get sick more often.
6) Epidemics occur every few years.

Among air-drop infections the most important are:

- acute respiratory viral infections (influenza, parainfluenza, adenoviral and respiratory syncytial infection, measles);
- bacterial infections (diphtheria, scarlet fever, meningococcal infection).

## Bacterial air-drop infections

## Diphtheria

***Diphtheria*** is an acute infectious disease characterized by fibrinous inflammation in the area of the entrance gate and general intoxication.

*Etiology and pathogenesis.*

The causative agent is toxigenic strains of corynobacteriae (Lefler's bacillus).

Sick people who do not have antitoxic immunity (not vaccinated children and adults who have expired postvaccination immunity).

The source of infection – sick people and carriers.

Transmission route – air-drop; a contact path is also possible (the pathogen is stored for a long time in the environment during drying).

Entrance gate – the mucous membrane of the upper respiratory tract, rarely – damaged skin.

The incubation period is 2-10 days.
Diphtheria bacteria multiply in the area of the entrance gate, releasing an exotoxin, which is associated with both local and general changes.
*The mechanism of action of the toxin*. The toxin specifically binds to cellular receptors, interacting with the protein – translocase, blocks the synthesis of all proteins in the cell, including respiratory enzymes, resulting in cell death.
*Cells with receptors (sensitive) to exotoxin:*

1) the epithelium of the oral cavity, upper respiratory tract;
2) cardiomyocytes;
3) peripheral nervous system (nerve trunks, ganglia);
4) adrenal glands;
5) the epithelium of the proximal tubules of the kidneys;
6) erythrocytes and leukocytes.

*Pathological anatomy.*

*Local changes*. Fibrinous inflammation in the entrance gate: in the pharynx and tonsils, larynx, trachea and bronchi; extremely rare in the nasal membranes, on the skin (in wounds), external genitalia. Lymphadenitis of regional lymph nodes (mainly cervical).
*General changes*:

a. fatty dystrophy of cardiomyocytes and intermediate myocarditis with foci of myolysis, which is often complicated by arrhythmias and acute heart failure in the 1-2nd week of the disease ("**early heart failure**"). In case of a favorable consequence, diffuse cardiosclerosis develops;
b. parenchymal neuritis (demyelination), often lingual-pharyngeal, diaphragmatic, vagus, sympathetic nerves with the development of "**late paralysis**" of the soft palate, diaphragm, heart (after 1.5-2 months);
c. dystrophic and necrotic changes, hemorrhages in the adrenal glands with the development of acute adrenal insufficiency;
d. necrotic nephrosis – acute renal failure.

*Clinical and morphological classification of diphtheria:*

- diphtheria of the throat;
- diphtheria of the respiratory tract;
- rare forms: diphtheria of the nose, of the wounds.

***Pharyngeal diphtheria:***
It develops in 80-95% of patients.
It is characterized by diphtheritic inflammation of the tonsils (diphtheritic angina), which can spread to the palate, tongue and pharyngeal wall; the pellicles are tightly bound to the underlying tissues, have a pearly appearance.
The expressed cervical lymphadenitis with a hyperplasia and frequent necrotic changes of follicles, is followed by the expressed hypostasis of adipose tissue.
Intoxication and related general changes.
Guided by this, there are subtoxic, toxic and hypertoxic forms.
***Respiratory diphtheria:***
Occurs in less than 20% of patients; usually joins diphtheria of a throat, the isolated forms are seldom observed.

Local changes develop in the larynx, trachea and bronchi, represented by croupous inflammation – a real croup.
Fibrinous pellicles are not tightly bound to the underlying tissues, are easily rejected and can obturate the lumen of the trachea, leading to asphyxia.
Intoxication is much less pronounced than in diphtheria of the throat.
Rarely croupous inflammation descends into the small bronchi and bronchioles with the development of bronchopneumonia – descending croup.
*Mortality from diphtheria:*

- in the past reached up to 60% and was associated mainly with infectious-toxic shock, acute heart failure or asphyxia:
- with the beginning of serotherapy decreased to 3.5-22%;
- currently, complications of diphtheria are associated mainly with intubation and tracheotomy and are due to the accession of secondary infection.

## Scarlet fever

*Scarlet fever* is an acute infectious disease of streptococcal nature, manifested by local inflammatory changes in the throat and rash.
The disease mainly affects children aged 3-12 years.
Air-drop infection
*Etiology*.
Toxigenic strains of β-hemolytic streptococcus group A.
The disease occurs in the absence of antitoxic immunity (streptococcal sore throat or bacteriocarriers).
The incubation period is 3-7 (up to 11) days.
Entrance gate – the mucous membranes of the throat and pharynx, very rarely – the wound surface, genital tract (extrabuccal scarlet fever).
*The pathogenesis* is determined by three factors:

- action of erythrogenic toxin;
- microbial invasion;
- allergic reactions.

1) *General changes*: the appearance of a rash and fever.
2) *Local changes*: necrosis and the development of purulent-necrotic complications.
3) *Allergic* (immunopathological) reactions occur in the 3-5th week of the disease and are determined by the similarity of antigens of β-hemolytic streptococcus and some antigens of body tissues (cardiomyocyte sarcolemma protein, heart valve glycoprotein, glomerular filter proteins).

*Pathological anatomy.*

Two periods.
***A. The first period***: 1-2nd week.
*Local changes* – the primary scarlet fever complex:

- primary affect,
- lymphangitis and cervical lymphadenitis,
- rash.

1) Primary affect – catarrhal or necrotic angina.
*a) Catarrhal angina:*

- severe hyperemia of the throat ("burning faucet"), which extends to the oral cavity

- "raspberry tongue" - hypertrophy of the papillae of the tongue,
- tonsils enlarged, juicy, bright red.

*b) Necrotic angina* occurs on the 2nd day in severe cases; currently rare:

- on the surface and in the depth of the tonsils appear dull grayish foci of coagulation necrosis, ulcers;
- microscopically: in the tissue of the tonsils – foci of necrosis, surrounded by infiltrates of polymorphonuclear leukocytes, which penetrate into the underlying tissue. Streptococcal colonies are often found on the periphery of necrosis.

2) Lymphadenitis: cervical lymph nodes are enlarged, juicy, full-blooded, there may be foci of necrosis.

3) Rash (appears on the 2nd day)

- bright red erythema with small papules;
- covers the entire surface of the body, except for the nasolabial triangle.

*Microscopically*: vacuolation of the epithelium and parakeratosis with subsequent necrosis, which determines the characteristic lamellar peeling that occurs later.

*General changes:*

- in the liver, kidneys, myocardium – dystrophic changes and intermediate inflammation;
- hyperplasia of lymphoid tissue.

*Complications* of the first period: in severe forms of scarlet fever due to the spread of purulent-necrotic inflammation of the pharynx to the surrounding tissues:

- pharyngeal abscess;
- phlegmon of the neck;
- purulent otitis;
- purulent sinusitis;
- purulent osteomyelitis of the temporal bone;
- the transition of the purulent process from the temporal bone to the brain tissue can lead to the development of purulent leptomeningitis or brain abscess.

***B. The second period (allergic)*** – 3-5th week:

- observed rarely, and therefore there is a tendency to consider the changes that occur in some patients at 3-5 weeks, not as a period of scarlet fever, but as allergic complications;
- the probability of development of the second period does not depend on the severity of the first period.

*Typical manifestations:*

- acute poststreptococcal immunocomplex glomerulonephritis;
- rheumatism: warty endocarditis, arthritis, vasculitis.

*Complications*: glomerulonephritis, arthritis, etc.

## Meningococcal infection

***Meningococcal infection*** is an acute infectious disease that manifests itself in three main forms: nasopharyngitis, purulent meningitis and meningococcemia.

*Source*: sick person or bacteriocarrier (carrier in healthy people exceeds 20%). Susceptibility 1%.

*Etiology* – Neisseria meningitides. Features of the pathogen:

- secretes endotoxin;

- has lashes with which it is fixed to the shells;
- produces hyaluronidase and neuraminidase – permeability factors;
- there is a capsule that protects against digestion, the action of antibiotics and antibodies;
- in smears of cerebrospinal fluid are found in the cytoplasm of leukocytes.

*Pathogenesis*.

Penetration of meningococcus into the mucous membrane in 10-30% leads to the development of acute nasopharyngitis.

Less often, mainly in young children, the pathogen enters the bloodstream and, having overcome the blood-brain barrier, enters the soft meninges with the development of serous (1st day), and then purulent leptomeningitis.

In 0.1-1% of cases there is meningococcemia – meningococcal septicemia.

In some cases, meningococcemia occurs as a complication of purulent leptomeningitis.

*Pathological anatomy.*

*Acute nasopharyngitis.* Catarrhal inflammation of the mucous membranes of the nose and pharynx with redness and swelling of the posterior wall of the pharynx, serous or mucous exudate. Bacteriological examination of throat swabs is required for diagnosis.

*Purulent leptomeningitis:*

- purulent inflammation begins on the basal surface, spreads to the spherical surface of the brain; affected membranes of the frontal, temporal and parietal areas have the appearance of "green cap";
- fibrinous exudate appears in the subarachnoid space;
- often the purulent process spreads to the meninges of the spinal cord.

*Complication*:

- purulent ependidimitis and pyocephaly;
- meningoencephalitis – the spread of purulent inflammation from the meninges to the brain tissue;
- cerebral edema with dislocation;
- hydrocephalus, which occurs during the organization of exudate in the subarachnoid space and impaired outflow of cerebrospinal fluid; further leads to the development of cerebral cachexia.

*Meningococcemia.* Duration 24-48 hours.

Development is associated with bacteremia and endotoxemia, which leads to endotoxic shock, which is usually accompanied by disseminated intravascular coagulation syndrome (DIC).

*Changes in organs:*

- hemorrhagic stellate rash on the skin, mainly on the buttocks, lower extremities, sclera;
- generalized vascular lesions of the microcirculatory tract;
- hemorrhage into the mucous membranes and serous membranes;
- serous arthritis (with possible suppuration);
- in the adrenal glands necrosis, massive hemorrhage with the development of acute adrenal insufficiency (Waterhouse-Friedrichsen syndrome);
- necrotic nephrosis (acute renal failure);

- in the soft meninges – serous meningitis, possible hemorrhage.

*Causes of death:*

- 90% of fatalities are associated with meningococcemia – bacterial-toxic shock: acute adrenal insufficiency, acute renal failure, hemorrhage, etc.
- death can also occur from complications of purulent leptomeningitis.

## Viral air-drop infections

### Influenza

***Influenza*** is an acute viral infectious disease with a predominant lesion of the mucous membrane of the respiratory tract and the phenomena of general intoxication.

*Etiology* – pneumotropic RNA virus from the family Orthomyxoviridae. There are three types of virus: A, B (causes outbreaks between major epidemics) and C (low virulence). The virus has tropism (the ability to specifically bind and reproduce in certain cells) to the epithelium of the upper respiratory tract, bronchi and alveoli, as well as vascular endothelium.

*Pathogenesis*:

- source – a sick person;
- mechanism of infection – air-drop;
- incubation period – from 12 hours to 1-3 days, often 1-2 days;
- the virus is adsorbed on the epithelium of the upper respiratory tract, bronchi and alveoli (as well as endothelium), in which its primary reproduction occurs;
- there is a primary viremia, accompanied by prodromal phenomena;
- the virus again penetrates the epithelium of the respiratory tract, its secondary reproduction occurs with subsequent viremia and the development of manifestations of the disease – local and general (the height of the disease).

*Pathological anatomy.*

*Local changes:*

- develop in the upper respiratory tract and lungs;
- associated with the cytopathic and vasopathic action of the virus;
- characteristic presence in the cytoplasm of epithelial cells of small basophilic inclusions (virus colonies) and fuchsinophilic inclusions (destruction of intracellular organelles under the influence of the virus).

*General changes* are associated with viremia and intoxication. Presented by dystrophic, inflammatory changes of internal organs, combined with circulatory disorders.

*Clinical and morphological forms* of influenza (depending on the severity of local changes and the ratio of local and general changes):

- mild (ambulatory flu),
- moderate,
- severe.

*Mild form of influenza:*

- acute catarrhal (serous, mucous, desquamative) laryngotracheobronchitis. Mucous membrane full-blooded, swollen, with serous-mucous exudate;
- duration of 5-6 days, ends with complete recovery of the mucous membrane.

With influenza *of moderate severity*:

- in the upper respiratory tract – serous-hemorrhagic inflammation with severe lymphomacrophage infiltration and areas of necrosis;

- interstitial pneumonia in the lungs with:
  - lymphomacrophage infiltration of the interalveolar septa,
  - hyaline membranes,
  - serous-hemorrhagic effusion in the lumen of the alveoli,
  - atelectases (in pneumocytes due to the cytopathic action of the virus reduces the production of surfactant).

*Severe form of influenza*.

*A. With a predominance of toxicosis:*

- local changes correspond to the flu of moderate severity, but more pronounced hemorrhagic and necrotic components; possible hemorrhagic pulmonary edema;
- numerous hemorrhages occur in the internal organs, sometimes fatal;
- possible development of serous (serous-hemorrhagic) meningitis, meningoencephalitis, cerebral edema.

*B. With pulmonary complications:*

- develops at accession of a secondary infection (staphylococcus, streptococcus, pneumococcus, Pseudomonas aeruginosa);
- in the upper respiratory tract and bronchi – fibrinous-hemorrhagic (or purulent-necrotic) inflammation – tracheobronchitis;
- in the lungs – bronchopneumonia with a tendency to abscess, necrosis, hemorrhage, the development of atelectasis, alternating with emphysema, a pronounced interstitial component (virus action);
- these changes give the lungs a variegated appearance – "large variegated (trout) influenza lung."

*Mortality* from influenza is currently low, associated with complications of severe influenza, often with pneumonia.

## Parainfluenza

*Parainfluenza* is a flu-like illness:

- caused by RNA virus (similar to influenza virus);
- children get sick more often;
- the disease resembles the flu, but occurs in milder, erased forms;
- catarrhal inflammation develops in the upper respiratory tract with the appearance of multinucleated cells in the epithelium;
- catarrhal laryngitis, which is often accompanied by false croup in children (swelling of the larynx, ligaments with the development of asphyxia).

## Adenovirus infection

It is caused by a DNA virus that has tropism to many cells: respiratory tract epithelium, alveoli, enterocytes, hepatocytes, nephrocytes, lymphocytes, which determines the susceptibility of adenoviral infection to generalization.

*The pathogenesis* of the disease is similar to that of influenza.

*Local changes:*

- catarrhal inflammation, the appearance of cells with intranuclear inclusions and ugly nuclei are determined in the upper respiratory tract.
- characteristic involvement in the process of the lymphoid apparatus with the development of angina and pharyngitis
- conjunctivitis often develops

- at accession of a secondary infection there is a purulent-necrotic bronchitis, bronchiolitis and bronchopneumonia (more often purulent-hemorrhagic)

## Measles

*Measles* is an acute highly contagious disease characterized by general intoxication, fever, catarrhal inflammation of the mucous membranes of the upper respiratory tract, conjunctivitis and maculopapular rash.

*Etiology and epidemiology*.

The disease mainly affects children, there are outbreaks of the disease among adolescents and young people.

It is caused by an RNA virus from the group of paramyxoviruses.

It is transmitted by air-drop route. The incubation period is 9-11 days.

*Local changes:*

- catarrhal inflammation of the mucous membranes of the throat, trachea, bronchi and conjunctiva;
- the presence of giant multinucleated cells in the epithelium;
- characteristic squamous cell metaplasia of bronchiolar and alveolar epithelium in areas of damage and desquamation;
- photophobia, lacrimation, conjunctivitis;
- possible development of interstitial (giant cell) pneumonia: among the cellular infiltrate of lymphoid, plasma cells, macrophages in the interalveolar septa appear giant multinucleated cells.

*General changes* are associated with viremia.

- enanthema – whitish spots on the mucous membrane of the cheeks, on the level of premolares – appear on day 2-3 of the disease;
- exanthema – a large-spotted papular rash on the skin of the face, neck, torso, on the extensor surfaces of the extremities. As a result, there is a bran-like (small-plate) peeling;
- hyperplasia of lymphoid tissue (lymph nodes, spleen, etc.) with the appearance of giant multinucleated macrophages;
- occasionally, cortical encephalitis may occur.

*Complications* are associated with the accession of a secondary infection:

- destructive (necrotic or purulent-necrotic) panbronchitis,
- pneumonia,
- cortical encephalitis,
- false croup – swelling of the larynx, ligament with the development of asphyxia),
- noma – moist gangrene of the soft tissues of the face in very weak children.

## HIV-related AIDS

*HIV infection* is a disease that develops as a result of long-term persistence of HIV in lymphocytes, macrophages and nerve tissue cells and is characterized by slow progression of immune system dysfunction.

AIDS is the final stage of HIV infection, affects the immune and nervous systems and is manifested by the development of severe viral, bacterial, parasitic lesions and/or malignant neoplasms that lead to the death of the patient.

*Etiology*. The causative agent is the T-lymphocytic (lymphotropic) human immunodeficiency virus – HIV (HTLV-III or HIV).

*Epidemiology*. The spread of HIV-associated AIDS is a pandemic. According to the WHO, about 8,500 people are infected with HIV every day.

*The source* of infection is a sick person and a virus carrier. The highest concentration of the virus is found in blood, semen, cerebrospinal fluid, to a lesser extent – in tears, saliva, cervical and vaginal secretions of patients.

To date, 3 ways of infection have been proven:

- sexual (with homo- and heterosexual contacts);
- parenteral administration of the virus with blood products or when using infected instruments;
- perinatal – from mother to child during pregnancy and childbirth (vertical) and during breastfeeding (horizontal).

*Pathogenesis.* The main target of HIV in peripheral blood are T lymphocytes that carry CD4+receptors on their surface.

In adults, HIV enters the bloodstream either parenterally by injection or sexual contact through damaged genital mucosa. Possessing tropism to CD4+receptors, the virus attaches to epitopes of the cell membrane, most often helper T lymphocytes. After that, it penetrates inside, where it is integrated into the genetic apparatus of the cell. By reverse transcriptase, using the chromosomal DNA of the target cell, the virus encodes the production of similar particles until the cell dies. After cell death, the virus populates new cells that have CD4+receptors. In CD4+helper lymphocytes, HIV can remain dormant indefinitely. The disease of HIV infection develops over a long period of time.

*Periods of HIV infection:*

1) incubation (asymptomatic carrier);
2) lymphadenopathy syndrome (LAS) or persistent generalized lymphadenopathy;
3) AIDS-associated syndrome (pre-AIDS) or AIDS-associated complex (AAC);
4) acquired immunodeficiency syndrome (AIDS).

*The incubation period* can last from 6 weeks to 12 years or more. In most cases, the incubation period does not show symptoms. During this period, you can establish the actual fact of infection in the determination of antigen or anti-HIV antibodies in the blood. Serological changes can be registered only on day 17-43 after the appearance of the first clinical and morphological signs.

*The period of persistent generalized lymphadenopathy* is a stable, for several months, increase in various groups of lymph nodes. It is based on nonspecific hyperreactivity of B cells, which is manifested by follicular hyperplasia of lymph nodes (enlargement of lymphoid follicles and their light centers). Duration 3-5 years.

*AIDS-associated complex*, or pre-AIDS, develops against a background of moderate immunodeficiency and is characterized by a decrease in body weight of up to 20%, development of fever, diarrhea, progressive polylymphoadenopathy, recurrent acute viral respiratory infections such as shingles. It lasts for several years.

*The period of acquired immunodeficiency syndrome* (AIDS) is accompanied by a sharp loss of body weight, up to cachexia, the development of dementia. In the end, there is a sharp suppression of cellular and humoral parts of the immune system, which is manifested in the clinic by the development of opportunistic infections (viral, bacterial, fungal) and malignant tumors (malignant B-cell lymphoma and Kaposi's sarcoma).

Injuries observed in human immunodeficiency virus (HIV) infection can be classified as follows:

- lymph node involvement;
- injuries caused by opportunistic infections;
- development of malignant tumors.

Changes in the lymph nodes are manifested by multiple, often symmetrical adenopathies, which are most often localized in the cervical, inguinal and submandibular areas.

Histological changes of lymph nodes schematically develop in three stages:

*A. The stage of follicular hyperplasia* is characterized by an increase in the size of follicles with large light centers. Around the follicles – a narrow peripheral lymphocytic corolla (or it is absent), medullary strands are difficult to identify.

*B. The stage of diffuse hyperplasia* of the angioimmunoblastic lymphadenopathy type is characterized by the loss of the normal structure of the lymph node. Lymph node contains either very few follicles, or completely devoid of them, and is represented by many vessels. Its cellular composition is polymorphic: the presence of small round or irregularly shaped lymphocytes, plasma cells, immunoblasts, interdigitating cells, eosinophils and tissue basophils. Follicles are small, atrophic. It is often hyalinosis of follicle centers.

*C. Stage of lymphoid depletion* – in the late stages of development. The lymph node consists of one stroma; there is a sharp expansion of the sinuses, full of large mononuclear cells, often with phagocytosed erythrocytes. Lymph nodes become small, sclerosed, with a significant decrease in the number of lymphoid elements and the preservation of only some plasma cells and immunoblasts, contain many macrophages with phagocytosis. Similar changes are found in the spleen and thymus, as well as in the lymphoid apparatus of the intestine. There is a gradual atrophy of the lymphoid tissue of these organs, which is clearly determined macroscopically.

Injuries caused by opportunistic infections have a variety of localization and nature: bacterial, fungal, parasitic or viral. Opportunistic are infections that are caused by opportunistic pathogens (low virulence), infection of which in a healthy person is not accompanied by pathological changes.

Such pathogens are:

- the simplest (pneumocysts, toxoplasmas, cryptosporidia);
- fungi (genus Candida, cryptococcus);
- viruses (cytomegalovirus, herpes virus, some viruses of slow infections);
- bacteria (Musobacterium avium intracellulare, legionella, salmonella).

Lungs in HIV-associated AIDS are affected most often (up to 80% of patients). Hyperplasia of alveolocytes can be detected, followed by their exfoliation, which resembles moderate desquamative pneumonia in other RNA viral infections. Most often, pneumonia caused by Pneumocystis carinii and cytomegalovirus is accompanied by damage to both lungs by the type of interstitial pneumonia.

The central nervous system in HIV infection ranks 2nd in the frequency of lesions:

- encephalopathies, often caused by cytomegalovirus, less often by herpes virus or mycobacteria;
- HIV-associated subacute encephalomyelitis. Changes, mostly in white matter and subcortical structures, including basal ganglia and semiotic centers.

*Microscopically*, microglial nodules are found, multinucleated symplasts, in which HIV particles can be detected. It is considered pathognomonic formation of multinucleated cells such as symplasts, which can be located in isolation or in combination with microglial nodules. Damage to the meninges in the form of sluggish non-purulent leptomeningitis, most commonly caused by Cryptococcus neoformans, is common. Characteristic vacuolation of white matter (spongiosis). Particularly common but nonspecific vacuolar myelopathy with damage to the lateral and posterior stems of the spinal cord. White matter looks "perforated". CNS changes may be the first symptom of HIV infection, which progresses rapidly and ends in death.

Gastrointestinal damage is the third localization of opportunistic infections. Candidal esophagitis is the most common. At the level of the small and large intestines, other opportunistic infections can be observed, which are manifested mainly by diarrhea.

Skin and mucosal lesions are associated with generalized septicemia, such as histoplasmosis and cryptococcosis.

In the kidneys, the deposition of immune complexes in the glomeruli, dystrophic changes of the nephrothelium and hyperplasia of its individual cells, microcystic tubuloectasia and enlargement of the capsules of the renal corpuscles, as well as focal glomerulosclerosis.

In the adrenal glands – focal necrosis and widespread hemorrhage.

The main types of tumors in AIDS.

***Kaposi's sarcoma***, which is the initial manifestation of AIDS, especially in homosexuals.

*Macroscopically*: bright red skin nodules of different localization. Kaposi's sarcoma is combined with damage to the mucous membrane, palate, lymph nodes, in some cases – multiple visceral lesions, develops slowly.

*Microscopically*: many newly formed, chaotically located thin-walled vessels with well-defined endothelium and bundles of spindle-shaped cells. In a loose stroma hemorrhages and accumulations of hemosiderin are frequent. Kaposi's sarcoma is malignant, a generalization of the process involving the lymph nodes, gastrointestinal tract, lungs and other internal organs.

***Malignant non-Hodgkin's lymphomas***, which are observed in AIDS – type B lymphomas, which are often located outside the lymph nodes and affect the central nervous system, gastrointestinal tract, upper respiratory tract, bone marrow.

***AIDS always ends in death***.

### *Training macropreparations*

**Meningococcal purulent meningitis**. Soft meninges are thickened, dull, impregnated with purulent exudate of greenish-yellow color. These changes are particularly clear on the basal surface of the brain and on the convex surface of the anterior hemispheres in the form of a "cap".

**Influenza bronchopneumonia**. In the section of the lung "motley" appearance with yellow-gray foci of dense consistency, protruding above its surface. The walls of the bronchi are thickened, in the lumen - mucopurulent contents.

### *Training micropreparations*

**Hemorrhage in the adrenal glands** (staining with hematoxylin and eosin): redness, edema, hemorrhage, vacuolation of cortical cells, focal necrosis - karyopyknosis and

lack of nuclei in cells. The cerebral layer is sharply hyperemic, with areas of hemorrhage.

**Influenza bronchopneumonia** (staining with hematoxylin and eosin): desquamation of the epithelium, hyperemia of the bronchial wall and infiltration of its polymorphonuclear leukocytes, lymphoid cells; there are foci of necrosis, ulceration of the mucous membrane (destructive panbronchitis). Peribronchial alveoli are filled with purulent-hemorrhagic exudate, there are areas of necrosis of the lung parenchyma. Around the foci of pneumonia, the alveoli are dilated.

### *Questions for self-control*

1. Diphtheria, definition, macro-microscopic characteristics, consequences.
2. Scarlet fever, definition, macro-microscopic characteristics, consequences.
3. Meningococcal infection, definition, forms, macro-microscopic characteristics, consequences.
4. Definitions: measles, influenza, parainfluenza, adenoviral infection, HIV.
5. Etiology, pathogenesis of measles, influenza, parainfluenza, adenoviral infection, HIV infection.
6. Macro-microscopic characteristics of measles, influenza, parainfluenza, adenoviral infection.
7. Macro-microscopic characteristics of HIV infection depending on the severity of the course. Stages of HIV infection.
8. Consequences of measles, influenza, parainfluenza, adenoviral infection, HIV infection.

### *Examples of tests*

1. At the autopsy of the deceased addict, crimson-red spots, plaques and nodules (Kaposi's sarcoma) were found on the skin of the distal parts of the lower extremities. Acute pneumonia caused by pneumocysts was detected. Your diagnosis.

A. * AIDS
B. Influenza
C. Cyrus
D. Diphtheria
E. Anthrax

2. A 7-year-old child had a fever of 39 ° C, rhinitis, conjunctivitis, and cough. There was a large spotty rash on the skin. On examination of the oral cavity - whitish rash on the mucous membrane of the cheeks. Suddenly there was heavy breathing and death with asphyxia. Your diagnosis.

A. * Cyrus
B. Scarlet fever
C. Diphtheria
D. Meningococcal nasopharyngitis
E. Influenza

3. A 42-year-old man died of severe intoxication and respiratory failure. In section, the lung tissue in all parts is variegated, with multiple small-focal hemorrhages and foci of emphysema. Histologically in the lungs: hemorrhagic bronchopneumonia with abscessing, in the cytoplasm of bronchial epithelial cells eosinophilic and basophilic inclusions. Your diagnosis.

A. * Influenza

B. Parainfluenza
C. Adenovirus infection
D. Respiratory syncytial infection
E. Staphylococcal bronchopneumonia
4. A 6-year-old child became acutely ill. The clinical picture was dominated by nausea, vomiting, headache. Two days later the child died. At autopsy, the soft meninges are sharply full-blooded, impregnated with thick, turbid yellow-green exudate. The brain is swollen. Cerebellar tonsils increased in volume, pronounced strangulation furrow. Your diagnosis.
A. * Meningococcal infection.
B. Diphtheria.
S. Cyrus.
D. Influenza.
E. Scarlet fever.
5. A 15-year-old patient died in an infectious disease hospital on the 3rd day of the disease from intoxication. At autopsy: a small rash on the skin, except for the nasolabial triangle; sharp hyperemia of the pharynx and palatine tonsils ("burning pharynx"), which spreads to the mucous membrane of the mouth, tongue ("crimson" tongue). Microscopically: dystrophic changes and sharp circulatory disorders predominate in the internal organs. Which of the following diagnoses is most likely?
A. * Scarlet fever.
B. Rubella.
C. Diphtheria.
D. Cyrus.
E. Chickenpox

## DISEASES OF THE FEMALE AND MALE GENITAL SYSTEM. DISEASES OF THE CERVICE. DISEASES OF THE UTERUS. DISEASES OF THE MAMMARY GLANDS

Principles of classification of genital diseases:

According to the organ principle:

1. Diseases of the female genitalia:
    - diseases of the uterine body
    - diseases of the cervix
    - ovarian diseases
2. Diseases of the male genitalia:
    - penis diseases
    - prostate gland diseases
    - diseases of the testicles

By the dominance of the pathological process:

- dishormonal
- tumor
- inflammatory
- developmental defects

## Diseases of the uterus

### *Glandular hyperplasia of the endometrium*

*Glandular hyperplasia of the endometrium* is a disease associated with an imbalance of estrogen and /or progesterone.

*Macroscopically:* the endometrium is thickened, juicy, gray-red, with polyp-like growths.

*Microscopically:* increase in the number of both glandular and stromal elements; glands are tortuous, elongated, sawtooth or corkscrew. In glandular-cystic hyperplasia, the number of glands in the scrape is increased, some of them are expanded (cystically altered), the number of cytogenic stroma cells is increased. Atypical hyperplasia shows signs of atypism.

*Current classification (according to WHO 2004):*

- Nonatypical glandular hyperplasia of the endometrium (simple and complex),
- Atypical glandular hyperplasia of the endometrium (simple and complex).

*Consequences*: can be treated with hormones, is a precancerous condition.

### *Endocervicosis*

*Endocervicosis (pseudoerosion of the cervix)* – the appearance in the vaginal part of the cervix areas lined with epithelium of the cervical canal (prismatic). It is more often observed at reproductive age.

Etiology:

- relative or absolute excess of progesterone or androgens,
- ectropion – violation of the healing of true erosions that occur during childbirth, defects of the mucous membrane,
- papillomavirus,
- frequent abortions.

*Macroscopically*: areas around the external orifice are bright red, various sizes, surrounded by a pale pink mucous membrane.

*Microscopically* distinguish endocervicosis:

- proliferating (hyperplasia of reserve cells with the formation of new glands);
- stationary (simple) - new glands are not formed;
- healing endocervicosis – manifested by ingrowth into the glands of the squamous epithelium from the edges of the lesion, as well as the differentiation of reserve cells into multilayered squamous epithelium.

*Consequences and complications*: reversible process, possible malignancy.

## Tumor diseases

There are cervical cancer and uterine cancer.

### *Cervical cancer*

*Etiology*

| *Risk factors* | *Background diseases* | *Precancerous processes* |
|---|---|---|
| • Rupture of the cervix<br>• Cicatricial changes<br>• Hormonal disorders | • Pseudoerosion<br>• Polyps<br>• Papillomas<br>• Leukoplakia (simple form)<br>• Endometriosis<br>• True erosion<br>• Post-traumatic changes | • Dysplasia<br>• Leukoplakia with atypia<br>• Erythroplakia<br>• Adenomatosis |

There are cancer of the vaginal part of the cervix and cancer of the cervical canal.

***Cancer of ectocervix*** grows exophytically, in the vaginal cavity, in the form of "cauliflower".

*Microscopically* – often squamous with varying degrees of differentiation. Metastasizes lymphogenically to regional lymph nodes (pelvic, inguinal, retroperitoneal).

***Cancer of the cervical canal*** grows endophytically, sprouts the cervix, the surrounding tissue and grows into the walls of the bladder and rectum, forming vaginal-bladder or vaginal-rectal fistulas.

*Microscopically*, cervical cancer most often has the structure of adenocarcinoma. Gives metastases both lymphogenic and hematogenous.

Adenosquamous carcinoma, undifferentiated cancers, as well as endometrioid and glassy cell carcinoma are found in the cervix.

### *Uterine body cancer*

*Cancer of the uterine body* (endometrium) is a malignant neoplasm that occurs in women, mostly over 50 years. It ranks second after breast cancer.

*Etiology*

| *Risk factors* | *Background diseases* | *Precancerous processes* |
|---|---|---|
| • Anovulatory uterine bleeding<br>• Infertility<br>• Late menopause<br>• Diabetes, obesity, hypertension (androgens are oxidized to estriol 20 times faster) | • Glandular hyperplasia of the endometrium<br>• Endometrial polyps | • Atypical endometrial hyperplasia |

*Macroscopically*. Endometrial cancer usually grows exophytically in the form of "cauliflower" or a polyp on a broad basis, can ulcerate, undergo necrosis. Endophytic growth is less common.

*Microscopically*, cancer of the uterine body is represented by adenocarcinoma of varying degrees of differentiation (high-, moderate- and low-differentiated). Squamous cell, glandular-squamous, and undifferentiated cancers are less common.

The cancer of the uterine body *metastasizes* lymphogenically to regional lymph nodes. Hematogenous and implantation metastases are relatively rare.

### *Leiomyoma (fibromyoma) of the uterus*

*Uterine leiomyoma* (fibromyoma) is a hormone-induced and hormone-dependent tumor consisting of muscle and connective tissue elements.

*Risk factors:*

- absence of childbirth and lactation up to 30 years;
- abortions;
- prolonged inadequate contraception;
- chronic, subacute and acute inflammation of the uterus and ovaries, fallopian tubes;
- stress;
- ultraviolet radiation;
- formation of cysts and ovarian cysts;
- metabolic disorders (obesity, diabetes).

*Classification:*

1. By the number of nodes:
   - single;
   - multiple – multinodular (80% of cases).
2. By growth rate (progression):
   - with slow growth;
   - rapidly progressing.
3. By location of nodes:
   - the bottom of the uterus
   - body of the uterus } 95%
   - isthmus area
   - cervix } 5%
4. According to the topography of nodes:
   - intramural – in the thickness of the muscular membrane,
   - subserous – under the peritoneum,
   - submucosal.

*Macroscopically:* nodes of gray-pink color, different sizes, clearly separated from the surrounding tissues. Often secondary changes are defined in a tumor: hyalinosis, formation of cysts, etc.

*Microscopically*: bundles of smooth muscle cells are arranged chaotically, the stroma is formed by layers of connective tissue in which blood and lymphatic vessels pass. In the case of severe development of the stromal component, it is called fibromyoma. Secondary changes are possible in the tumor: hyalinosis, calcification.

*Consequences:* in the postmenopausal period, there is usually a reversal of tumor growth.

*Complications:*

- uterine bleeding (mainly in submucosal localization of the node);
- infertility or miscarriage;
- inversion of the uterus (at the birth of the submucosal node);
- transformation into sarcoma (with rapidly progressive fibromyoma).

## Diseases of the mammary glands

### *Non-neoplastic diseases of the mammary glands*

***Fibrocystic disease*** (syn. benign dysplasia of the mammary gland, mastopathy) – a pathology characterized by impaired differentiation of the epithelium, its atypia, but without invasion of the basal membrane of the gland.

The term "mastopathy" is not currently used to refer to fibrocystic disease due to the spread of diseases such as piercing mastopathy and silicone mastopathy.

Forms of fibrocystic disease:

- non-proliferative,
- proliferative.

*Non-proliferative form* is characterized by the presence of focal growth of fibrous tissue in the form of a dense node with areas of hyalinosis, which contains atrophied lobes and cystic-dilated ducts. The risk of cancer is low.

*The proliferative form* is characterized by proliferation of the lobular and ductal epithelium, which leads to the formation of structures of solid, adenomatous and

cribrous type. Simultaneously, the myoepithelium and connective tissue grow. The risk of cancer in the presence of proliferative processes increases significantly.

### *Tumor diseases of the mammary glands*

***Fibroadenoma*** is a benign organ-specific tumor of the breast.

*Macroscopically*: a dense node with clear contours, movable on palpation. It grows slowly.

*Microscopically*: proliferation of ducts with their surrounding stroma, which contains a moderate number of fibroblasts and fibrocytes. The epithelium of the ducts is monomorphic cubic or flattened.

*Morphological classification of fibroadenoma*:

- pericanalicular – the growth of connective tissue around the ducts
- intracanalicular – ingrowth of connective tissue into the ducts with a narrowing of their lumen to the slit.

***Breast cancer*** is the most common malignancy in women.

*Risk factors:*

- genetic predisposition,
- late puberty,
- late first pregnancy,
- menopause after 55 years,
- hypercholesterolemia,
- diabetes,
- increase in triglycerides in the blood,
- insufficiently long breastfeeding,
- ionizing radiation and other physical and chemical factors.

*Background diseases and precancerous processes*:

- fibrocystic disease,
- fibroadenoma,
- gynecomastia in men,
- adenoma,
- duct papilloma.

*Growth type*:

- nodular tumor,
- diffuse form (shell cancer, cancer ulcer).

*Macroscopically*.

Nodular cancer is characterized by the presence of one or more dense, yellowish-gray or soft, juicy, easily disintegrating nodules.

Diffuse cancer occupies a large surface of the gland, the boundaries of the tumor are blurred. If the tumor germinates in the skin and disintegrates, a cancerous ulcer forms on its surface. In some cases, the tumor spreads to the surface of the gland, covering it by dense shell (armor cancer).

*Microscopically* the following forms of breast cancer:

- non-infiltrative (intralobular, intraductal),
- infiltrative (intralobular, intraductal).

Non-infiltrating ductal cancer is characterized by the proliferation of cancer cells that do not germinate the basal membrane ("cancer in situ").

Types:

- Comedocarcinoma – the rapid proliferation of moderately differentiated cancer cells, which, desquamating, fill the lumen of the ducts and come out of them when pressed.
- Cribrous cancer – in the layers of tumor cells form cribrous structures ("perforations") due to secondary changes (cell necrosis or secretion into the epithelial layers)
- Papillary cancer – the formation of papillary structures with pronounced cell polymorphism.

Infiltrating cancer is characterized by varying degrees of tissue and cellular atypism, which allowed to identify many of its variants. The most common of these are infiltrating ductal cancer (50-70%), which usually has a skyr structure. Fragmentary cancer is represented by single-row chains of atypical cells or concentric formations in the form of a shooting target. There are also mucous, medullary and tubular cancers.

Breast cancer *metastasizes* primarily by lymphogenic route to regional lymph nodes – retromammary, axillary, supra- and subclavian, subscapular, cervical, thoracic, along the internal thoracic artery. Hematogenous metastases are found in the bones, lungs, liver, kidneys. Breast cancer is characterized by late recurrences and metastases.

***Nipple and nipple field cancer (Paget's cancer)*** is an organ-specific malignant tumor that occurs in 1-2% of all malignant tumors of the breast. It is characterized by *three features:*

1) eczematous lesion of the nipple and areola;
2) the presence of large, light cells in the epidermis of the nipple and areola;
3) cancer of the duct of the breast.

*Microscopically*, large cells with a pale cytoplasm (Paget's cells) are found in the epidermis of the nipple and the excretory ducts of the breast. They never penetrate the dermis. The tumor develops from the epithelium of large or small ducts and has the structure of the skyr, acne-like or cribrous cancer.

## Pathology of the male reproductive system

***Nodular prostatic hyperplasia*** occurs in 95% of men over 70 years of age due to hormonal changes.

*Macroscopically*: the gland is enlarged, soft and elastic, tuberous. In section, the gland consists of individual nodes separated by layers of connective tissue.

*Microscopically*:

- adenomatous (glandular) hyperplasia – characterized by a large number of glandular elements;
- muscular-fibrous (stromal) hyperplasia – characterized by an increase in the number of muscle fibers, atrophy of the glands, loss of lobular structure;
- mixed hyperplasia – a combination of tissue disorders characteristic of the first two types, the possible formation of retention cysts.

*Complications*: urinary retention; accession of secondary bacterial infection (cystitis, ascending pyelonephritis); malignancy.

***Prostate cancer*** ranks second among cancers in men. Sometimes the development of cancer is preceded by nodular hyperplasia of the prostate.

*Macroscopically*: the gland is enlarged, tuberous, dense, in section consists of white connective tissue strands, between which is a cancerous tissue of gray-yellow color.

*Microscopically*:

- adenocarcinoma (90-95%);
- undifferentiated cancer.

*Metastases:* lymphogenic – lymph nodes of the pelvis (iliac and inguinal); hematogenous – in internal organs, especially in the bones.

***Gynecomastia*** – hyperplasia of the glandular lobes of the breast in men, which leads to an increase in the size of the entire gland.

*Etiology:*

- endocrinopathy (Klinefelter's syndrome, testicular feminization, castration, hypothyroidism, tumors of the testicles, pituitary gland, adrenal glands, choriocarcinoma);
- liver diseases;
- in men who in the past were actively involved in sports, followed by a sharp cessation of training;
- use of certain drugs (digitalis, methyldopa, reserpine, etc.).

*Classification*:

- true – due to the growth of glandular tissue;
- false – associated with massive fat deposits in obesity.

### *Training macropreparations*

**Nodular breast cancer**. In the gland tissue – a tumor in the form of a node, dense, gray, associated with the surrounding tissue septa.

**Diffuse breast cancer**. The tumor without clear boundaries, dense, gray, penetrates into the thickness of breast tissue and reaches the skin.

**Cancer of the uterine body**. In the area of the uterus corner of the tumor with exophytic growth in the form of cauliflower with destruction in the center and hemorrhage.

**Cervical cancer**. In the area of the cervical canal, the tumor is grayish-white, tuberous, loose, with exo-, endophytic growth, partly with decay.

**Nodular hyperplasia of the prostate.** The prostate gland is enlarged, soft, elastic, bumpy. In section, the gland consists of individual nodes separated by layers of connective tissue.

### *Training micropreparations*

**Endometrial hyperplasia** (staining with hematoxylin and eosin): the number of glands in the scrape is increased, some of them are expanded (cystically altered), increased number of cytogenic stroma cells.

**False erosion of the cervix** (staining with hematoxylin and eosin): the area of the vaginal part of the cervix is covered with cylindrical epithelium, under the integumentary epithelium there is an overgrowth of glandular structures.

**Uterine adenocarcinoma** (staining with hematoxylin and eosin): atypical glandular complexes are visible in the scraping of the endometrium among blood clots. The cells that make up these glands are of different sizes and shapes with hyperchromic nuclei. Pathological mitoses are visible in some cancer cells.

**Prostate hyperplasia** (hematoxylin and eosin staining): a large number of glandular elements with the formation of retention cysts; increase in the number of muscle fibers, loss of lobular structure.

## *Questions for self-control*

1. Dyshormonal diseases of the female reproductive system. Glandular hyperplasia of the endometrium, endocervicosis: classification, pathomorphology, consequences.
2. Tumors of the uterus: cancer of the cervix and uterine body. Etiology, pathomorphology, metastasis.
3. Benign tumors of the uterus: leiomyoma (fibromyoma) of the uterus. Causes, classification, pathomorphology, complications.
4. Non-neoplastic diseases of the breast. Fibrocystic disease: morphological picture, consequences.
5. Breast cancer: etiology, classification, pathomorphology, metastasis.
6. Paget's cancer: clinical and morphological picture.
7. Diseases of the male reproductive system. Benign prostatic hyperplasia: pathomorphology, complications.
8. Pathomorphology of prostate cancer, ways of metastasis.
9. Gynecomastia: etiology, classification and manifestations.

## *Examples of tests*

1. An autopsy in a 73-year-old man revealed an enlarged, soft, elastic, slightly bumpy prostate gland, which in section consists of individual nodes separated by layers of connective tissue. Microscopy showed an increase in the number of glandular elements. The size of the lobes and the number of glandular elements in them are different. What is the process in the prostate?

A. * Glandular nodular hyperplasia
B. Muscular-fibrous (stromal) nodular hyperplasia
C. Mixed nodular hyperplasia
D. Adenocarcinoma
E. Undifferentiated cancer

2. The uterus removed during the operation was delivered for histological examination. Numerous rounded nodes are defined under the mucous membrane, which are clearly separated from the surrounding tissue. Microscopically, the tumor is built of smooth muscle bundles with the phenomena of tissue atypism. Your diagnosis?

A. * Leiomyoma.
B. Uterine cancer.
C. Fibromyoma.
D. Chorionepithelioma.
E. Leiomyosarcoma.

3. Histological examination of the node in the removed breast revealed among a large number of stroma of different sizes and shapes complexes of atypical polymorphic epithelial cells with the presence of lumens in the center of the complexes. Cells with large nuclei, increased number of nucleoli, the presence of atypical mitoses. Make a diagnosis.

A. * Adenocarcinoma.
B. Breast fibroadenoma.
C. Solid cancer.
D. Squamous cell carcinoma.
E. Undifferentiated polymorphic cell cancer.

4. Macroscopic examination of the uterine tumor (postoperative material) revealed that it is of soft consistency, with hemorrhages and areas of focal necrosis, in the section resembles "fish flesh". Histological examination revealed signs of severe cellular and tissue atypism, there are cells with pathological figures of mitosis. Make a diagnosis.
A. * Sarcoma.
B. Adenocarcinoma.
C. Angioma.
D. Fibroma.
E. Lipoma.
5. Histological examination of the biopsy of the vaginal part of the cervix in a 47-year-old patient with erosion that does not heal for a long time, revealed signs of cellular atypism, basal membrane - unchanged. Make a diagnosis.
A. * Carcinoma in situ.
B. Erosion.
C. Adenocarcinoma.
D. Papilloma.
E. Endometriosis.

## PATHOLOGY OF PREGNANCY, POSTPARTUM AND PLACENTA. SEPSIS

The pathology of pregnancy includes:

- gestosis,
- ectopic pregnancy,
- miscarriage,
- premature birth,
- trophoblastic disease,
- obstetric infection.

**Gestosis** (gestatio – pregnancy) – a pathological condition that occurs during pregnancy, due to the mismatch of the adaptive capacity of the mother's body to adequately meet the needs of the developing fetus.
*Classification:*

- early preeclampsia (occurring in the first trimester of pregnancy)
  - vomiting of pregnant women,
  - nausea,
  - ptyalism (increased salivation);
- late gestosis (occurring after 25-32 weeks of pregnancy)
  - dropsy of pregnant women,
  - nephropathy,
  - preeclampsia,
  - eclampsia.

*The etiology* of gestosis is not clearly established. Nowadays, great importance is attached to immune, genetic, endocrine and other factors that may be manifested by the peculiarities of placentation. The main risk factor for preeclampsia is extragenital

pathology (70%) – obesity, kidney disease, hypertension. Occupational hazards (33.3%) and adverse social factors also play a role.

*Pathogenesis.* The main component in the pathogenesis of late gestosis is the pathology of the spiral arteries of the uterus in which there are no physiological changes that occur during normal pregnancy: the destruction of the muscular and elastic membranes with the formation of fibrinoid in their place, and increased lumen. The lumen of the spiral arteries remains narrow and the placenta experiences a lack of blood, and the resulting vascular spasm exacerbates placental ischemia. As a result of these changes (generalized vasoconstriction, hypovolemia, violation of the rheological properties of blood, damage to the vascular endothelium [placenta, kidneys, liver, brain, etc.], the development of DIC) there is circulatory and tissue hypoxia, which leads to structural changes in internal organs. Decreased uterine-placental circulation contributes to the development of placental insufficiency, which is one of the most unfavorable complications of gestosis.

*Pathomorphological changes of the placenta*. Involutional-dystrophic and dyscirculatory (hemorrhages, thrombosis, heart attacks) processes dominate in the placenta. Their intensity depends not only on the severity but also on the duration of the disease. The walls of the vessels of the chorionic plate and stem villi are dominated by fibrinoid necrosis with vacuolation and pyknosis of endothelial nuclei, in others - wall thickening due to muscle hypertrophy, sclerosis and hyalinosis; subendothelial membranes are thickened, sclerosed. There is an increase in the number of vessels located subepithelially (angiomatosis). There is hyperplasia of small villi with large syncytial nodules, excessive fibrinoid deposition. In the decidual membrane - lymphoid cell infiltrates, as an expression of immunological reactions. Large decidual cells are absent; small, spindle-shaped cells that do not contain glycogen predominate. Violation of villi maturation (pathological immaturity, dissociated maturation) is noted. Placental infarction is observed in 60% of patients.

*Clinical and morphological manifestations* of late gestosis associated with damage to internal organs:

- edema,
- proteinuria,
- hypertension.

Nephropathy.

*Morphology.* Kidney damage is mainly due to damage to the glomeruli, which increase slightly in size, swell, become anemic, capillaries completely fill the space of the capsule. Capillary lumens are sharply narrowed or not detected at all due to vacuolation and swelling of endothelial cells, which take the form of foam cells. Changes in other structures of the kidneys are not specific and are manifested by dystrophy of the epithelium of the tubules, protein cylinders in their lumen, a slight lymphocytic infiltration of the stroma. Vascular changes in the form of proliferation and swelling of the endothelium, edema of the media, thickening of the walls of the arterioles are also possible.

Preeclampsia: edema, proteinuria, hypertension. Also clinically characterized by severe headache, apathy, insomnia, darkening and flickering in front of the eyes, nausea, vomiting, epigastric pain, and sometimes – loss of vision.

Eclampsia is the most severe form of gestosis, which usually occurs against the background of nephropathy and preeclampsia, when joins the convulsive syndrome, which lasts only 1-2 minutes. The total number of convulsions can be from 1-2 to 10-15. Nonconvulsive forms are possible. Mortality is 5-9%.

*Morphological changes in eclampsia* are associated with changes in the microcirculatory tract: vascular spasm – vascular ischemia – increased permeability – edema – fibrinoid necrosis – microthrombosis, ie the development of DIC syndrome. Most often these changes are found in the vessels of the uterus, sinusoids of the liver, capillaries of the lungs, kidneys, brain, intervillial space of the placenta.

*Liver damage*.

Macroscopically: large subcapsular hemorrhages in the liver, which are often complicated by capsule rupture and bleeding into the abdominal cavity, as well as focal necrosis or subtotal necrosis.

Microscopically: centrolobular necrosis surrounded by leukocyte shaft, foci of periportal necrosis and hemorrhage, fibrin clots in the sinusoids of the lobules and capillaries of the portal tracts, plasma infiltration and vasculitis in the branches of hepatic arteries. The development of fatty hepatosis or acute steatosis is also possible.

In the *kidneys*, vascular changes are observed in the cortical layer in the form of capillary network thrombosis with the development of cortical necrosis and acute renal failure. There may be changes characteristic of mesangial glomerulonephritis with deposition on the basal membrane of immune complexes and proliferation of mesangial cells.

In the *lungs*, vascular thrombosis of the microcirculatory system develops and changes characteristic of the "shock" lung.

Acute gastric and intestinal ulcers with bleeding from them, hemorrhagic pancreatitis, necrosis in the spleen, pituitary gland, suppression of adrenal cortex function are also described.

*Complications of gestosis*: hemorrhage in the brain, severe cerebral edema with dislocation of the cerebellar hemispheres in the occipital foramen, acute renal or hepato-renal failure, heart and lung failure.

## Trophoblastic disease

**Trophoblastic disease** is a group of diseases characterized by impaired proliferation and maturation of trophoblast.

*Classification:*

1. Simple molar pregnancy (hydatidiform mole): complete, incomplete,
2. Destructive molar pregnancy,
3. Chorionepithelioma.

**Molar pregnancy (hydatidiform mole)** is a lesion of the fertilized egg, mainly the chorion, characterized by a complex of morphological changes: cystic and edematous degeneration of the villous stroma, lack of vascularization and hypertrophy of the trophoblastic epithelium.

*Etiology and pathogenesis*. Complete molar pregnancy is characterized by impaired ovogenesis – the formation of an empty egg, which is fertilized by one sperm with subsequent doubling of its genetic material or two sperm (46XX/46XY). The homozygous embryo dies before full placentation. Incomplete molar pregnancy is

characterized by a triploid set of chromosomes (3n): 1n maternal and 2n paternal. The fetus dies within 10 weeks of gestation.
*Macroscopically*, the molar pregnancy resembles a bunch of grapes with bubbles of various sizes, which rarely exceed 25 mm in diameter.
*Microscopically*, the vesicles are abruptly altered villi due to edema and cystic transformation, filled with liquid content.
*Destructive molar pregnancy* morphologically has signs of malignancy, altered villi penetrate through the normally developed decidual membrane deep into the endometrium, destroying muscle fibers and walls of blood vessels (not only arteries but also veins) to the entire wall of the uterus, causing embolism and peritonitis. In exceptional cases, a destructive molar pregnancy can metastasize to the lungs, brain, but most often to the vagina, vulva and urethra.
**Chorionepithelioma** is a malignant tumor of the remnants of manure (after childbirth or abortion) and a destructive bladder.
*Macroscopically*: the tumor has the appearance of a spongy node, dark in color, without clear boundaries.
*Histologically*:

- elements of the cytotrophoblast – *Langhans cells* – light cells with round, chromatin-poor nuclei with numerous mitoses;
- elements of syncytiotrophoblast – dark cells, hyperchromic nuclei, few cells in the division phase;
- no stroma (histoid tumor);
- the role of blood vessels is performed by cavities lined with tumor cells, therefore hemorrhages often occur in the tumor, and tumor cells easily metastasize hematogenously, primarily to the lungs.

The tumor is hormonally active and responds well to hormonal treatment.
**Ectopic pregnancy** – occurs during the implantation of a fertilized egg outside the uterine cavity.
*Causes*: inflammatory diseases of the appendages of the uterus, corpus luteum hypoplasia, endometrioid heterotopia, malformations of the fallopian tubes and uterus, tumors, etc.
*Localization:*

- fallopian tubes (95-99%),
- ovaries,
- abdomen,
- cervix.

*Morphological diagnosis of tubal pregnancy.*
*Macroscopically:* in a removed fallopian tube, which is usually dilated in a certain area, blood clots and / or a fertilized egg are detected in the lumen.
*Microscopically*: chorionic villi, trophoblast cells or embryonic elements, as well as the presence of a decidual reaction in the mucous membrane of the tube, areas of necrosis and hemorrhage in the fallopian tube wall.
*Consequences*:

- tubal abortion (full or incomplete);
- rupture of the tube.

In *complete tubal abortion*, the fertilized egg detaches from the wall of the tube and through the ampullary section enters the abdominal cavity, where it is mummified ("paper fetus") or calcified (lithopedion). In *incomplete tubal abortion,* the fertilized egg, surrounded by a blood clot, remains in the lumen of the tube. Rupture of the tube with the release of a fertilized egg into the abdominal cavity is accompanied by sharp abdominal pain, dizziness, collapse, internal bleeding.

## Postpartum infection

***Postpartum infection*** is an infectious disease in women that is pathogenetically related to pregnancy and childbirth (complications of the postpartum period).

*Etiology*: streptococcus, staphylococcus, Escherichia coli and Pseudomonas aeruginosa.

*Pathomorphology*. Infection of the uterus leads to the development of endometritis, which by the nature of inflammation can be purulent, fibrinous, putrefactive or mixed. The inner surface of the uterus becomes dirty gray, covered with purulent plaque. Possible development: metritis (inflammation of the muscular and mucous layers of the uterus); parametritis (inflammation of the connective tissue (parametrium) around the uterus); panmetritis (inflammation of all layers of the uterus).

*Complications*. The infection spreads along the lymphatic vessels and veins, leading to the development of purulent lymphadenitis, phlebitis, thrombophlebitis and uterine sepsis.

## Sepsis

**Sepsis** (Greek sepsis – rot) – a common generalized infectious disease characterized by certain features:

- polyetiology,
- non-contagiousness,
- acyclic flow,
- specially altered reactivity of the organism – reactivity with simultaneous hyperergic reaction, inability to distinguish infection,
- lack of specific morphological picture,
- does not give immunity.

The *etiology* of sepsis is related to various microorganisms (except viruses).

### *Classification*

*By the entrance gate:*

- wound,
- umbilical,
- uterine,
- surgical,
- otogenic,
- tonsillogenic,
- odontogenic,
- cryptogenic, etc.

*According to the course (depending on the immune response):*

- fulminant,
- acute,
- subacute,

- chronic.

*Clinical and morphological forms:*

- septicemia,
- septicopyemia,
- prolonged septic endocarditis,
- chroniosepsis.

*Pathomorphology*

***Septicemia*** is a clinical and morphological form of sepsis, which is characterized by bacteremia and toxemia without metastatic purulent foci and is accompanied by:

- hemolytic jaundice due to hemolytic action of certain bacterial toxins – anemia occurs,
- allergic vasculitis (petechial rash) – inflammatory processes in blood vessels lead to increased vascular permeability and the development of diapedetic hemorrhages;
- hyperplasia of lymphoid and hematopoietic tissues:
  - replacement of the yellow marrow of the tubular bones with red and an increase in the number of leukocytes in the peripheral blood – leukocytosis,
  - leukemic reaction – the appearance of young forms of leukocytes in peripheral blood,
  - generalized lymphadenopathy – enlargement of all groups of lymph nodes, which become soft, juicy, contain large lymphoid follicles with large light centers of growth,
  - septic spleen, which is significantly enlarged, with a sharply tense capsule; in section the pattern of the structure is blurred, the pulp is light red, with abundant scraping.

***Septicopyemia*** – clinical and morphological form of sepsis, characterized by:

- the presence of a septic focus with lymphangitis, lymphadenitis, in blood vessels (veins) – thrombophlebitis. Microbial colonies (septic thrombus) are often found in thrombotic masses, and the thrombus melts and the possible development of thrombo-bacterial embolism;
- metastatic abscessing of internal organs: first of all – in the lungs, with the development of pulmonary thrombophlebitis; abscesses are formed in the circulatory system – liver, kidneys (purulent nephritis), subcutaneous tissue, bone marrow (purulent osteomyelitis), synovial membranes (purulent arthritis);
- septic spleen.

***Septic endocarditis*** is a special form of sepsis, which is characterized by septic lesions of the heart valves.

*Classification.*

*According to the course*:

- acute (2 weeks),
- subacute (up to 3 months),
- chronic (prolonged) – months and years.

*By the presence or absence of background disease*:

- primary septic endocarditis (Chornogubov's disease) occurs on intact valves (20-30%);

- secondary septic endocarditis develops on altered (rheumatism) valves (70-80%).

*By localization*:

- isolated endocarditis (60-75%) – aortic valve (50%), mitral valve (10-15%);
- combined endocarditis – lesions of the aortic and mitral valves (25-30%);
- other valves (5%).

*Pathological anatomy*. Prolonged septic endocarditis occurs in the form of ulcerative-polyposis endocarditis.

*Macroscopically*: thrombotic layers are formed on the valves in the form of crumbling polyps or may come off (thromboembolism), exposing areas with superficial or deep defects. Sometimes the valve cusps destroy with the formation of perforated defects. Dysfunction of the valves leads to hypertrophy of the left ventricular myocardium.

*Microscopically*: foci of necrosis of valve tissues, surrounded by inflammatory infiltration of lymphoid cells, histiocytes, macrophages. Thrombotic layers appear in the areas of necrosis. The growth and maturation of granulation tissue leads to deformation of the valve with the formation of the acquired defect. In the myocardium - hypertrophy of muscle fibers.

*Peripheral signs of septic endocarditis:*

- petechial hemorrhages in the conjunctiva of the eye near the inner corner of the lower eyelid (Lukin-Liebmann spots);
- nodular thickenings on the palmar surfaces of the hands (Osler's nodes);
- thickening of the nail phalanges ("drumsticks");
- foci of necrosis in the subcutaneous fat;
- hemorrhage into the skin and subcutaneous tissue (Janeway's spots);
- jaundice.

***Chroniosepsis*** is characterized by:

- the presence of a septic focus that does not heal for a long time;
- chronic intoxication;
- brown atrophy of the liver, myocardium, striated muscles;
- development of secondary amyloidosis.

## *Training macropreparations*

**Tubal pregnancy.** The ampullary part of the fallopian tube is dilated, the incision in its lumen determines the fetus, which is attached by the umbilical cord to the placenta, which grows into the wall of the fallopian tube.

**Chorionepithelioma**. There is a tumor-like formation of dark red color in the form of a spongy node without clear boundaries with areas of hemorrhage and necrosis in the myometrium.

**Molar pregnancy**. The formation consists of many cysts resembling bunches of grapes (matte surface) and a diameter of 0.5 to 1.5 cm. These spherical vesicles are located above the uterine tissue. The cavity of the vesicles is filled with a clear mucous fluid.

**Polyposis-ulcerative endocarditis of the aortic valve.** Significant thrombotic overlays in the form of brown warts are visible on sclerosed aortic valves. Defects along the edge of the valves are observed in the places of their removal. Heart with

significantly enlarged left ventricular cavity, left ventricular wall thickness 1.8 cm (myogenic dilatation).

**Embolic purulent nephritis**. The kidney is slightly enlarged, many grayish-yellow foci containing pus can be seen under the capsule and in the incision in the cortical and medullar layer.

### *Training micropreparations*

**Chorionepithelioma** (hematoxylin and eosin staining). Tumor tissue is represented by light cells with round, chromatin-poor nuclei - Langhans cells (cytotrophoblast) and large syncytium cells with hyperchromic nuclei (syncytiotrophoblast). The stroma in the tumor tissue is absent, the role of blood vessels is performed by cavities of different sizes, which are lined with tumor cells. There are numerous foci of hemorrhage in the tumor tissue.

**Tubal pregnancy** (staining with hematoxylin and eosin). Decidual reaction In the mucous membrane of the fallopian tube, the presence of the chorionic membrane with chorionic villi, the remains of the fertilized egg and blood clots in the lumen of the tube. The chorionic villi penetrated the muscular layer and its vessels, destroying the tissue elements of the tube.

**Embolic purulent nephritis** (hematoxylin and eosin staining) Leukocyte infiltrates along the course of hyperemic vessels and microbial colonies.

### *Questions for self-control*

1. Characteristics of gestosis: etiology, pathogenesis, morphology of nephropathy, eclampsia.
2. Etiology of pathogenesis and pathomorphology of ectopic pregnancy.
3. Etiology, classification and pathomorphology of molar pregnancy, chorionepithelioma.
4. The concept and features of sepsis. Local and general changes in sepsis.
5. Classification of sepsis by etiology and entrance gate. Clinical and morphological forms of sepsis, their morphological characteristics.

### *Examples of tests*

1. In a young woman due to acute pain in the iliac region, the fallopian tube was removed with local expansion of its middle third, filled with blood. Histological examination of the fallopian tube reveals chorionic villi, large fields of erythrocytes with an admixture of leukocytes. Your diagnosis:

A. * Tubal pregnancy.
B. Acute purulent salpingitis.
C. Hemorrhage into the fallopian tube.
D. Hemorrhagic salpingitis.
E. Purulent salpingitis.

2. The patient underwent surgery for uterine power. Macrodrug: spongy variegated node in the myometrium. Histologically, there are large light epithelial cells, many of which are dark polymorphic cells. Stroma-free vessels have the appearance of health-lined cells. Multiple hemorrhages are defined. How is the action detected?

A. * Chorionepithelioma.
B. Destructive (malignant) molar pregnancy.
C. Adenocarcinoma.
D. Cavernous hemangioma.

E. Medullary cancer.
3. A young woman suddenly had an abortion at 20 weeks. At the same time from the uterus you can see the whole fertilized egg (fetus and causes), blood clots. Histological examination revealed fetus, chorionic villi and decidual tissue. Name the type of disease.
A. * Spontaneous complete abortion.
B. Premature birth.
C. Molar pregnancy.
D. Destructive molar pregnancy.
E. Artificial abortion.
4. At autopsy of a pregnant woman revealed the development of the brain, hemorrhagic pneumonia, trout with hemorrhages. Microscopically disseminated vascular thrombosis, multiple small necrosis and hemorrhage in internal organs. In the kidneys fibrinoid necrosis of the epithelium of the tubules of the nephron, necrosis of the cortical substance. Your diagnosis?
A. * Eclampsia.
B. Preeclampsia.
C. Septicemia.
D. Septicopyemia.
E. Acute renal failure.
5. In a patient who suffered from lobar pneumonia and died of pulmonary heart failure, the pathologist at autopsy noted some thickening of the crescentic aortic valve, their color is grayish-yellow with defects in the line of closure and the presence of large, up to 2 cm in diameter, three which served as the basis for establishing:
A. * Polyposis-ulcerative endocarditis.
B. Acute warty endocarditis.
C. Rotary-warty endocarditis.
D. Diffuse endocarditis.
E. Fibroplastic endocarditis.
6. After an outpatient abortion, the woman progressed to fatal purulent endomyometritis. At the autopsy of the deceased revealed numerous lung abscesses, subcapsular abscesses in the kidneys, splenic hyperplasia. What form of sepsis did the patient have?
A. * Septicopyemia.
B. Septicemia.
C. Chroniosepsis.
D. Pulmonary sepsis.
E. Urosepsis.

## PRENATAL AND PERINATAL PATHOLOGIES
### Prenatal (antenatal) pathology

**Prenatal (antenatal) pathology** – pathological processes and conditions of the human embryo from the moment of fertilization to the birth of a child.

All human development from the maturation of the gamete to the birth of a mature fetus, is divided into two periods.

- *Period of progenesis* (gametogenesis) – the formation and maturation of germ cells; pathologies that occur during this period are called *gametopathy;*
- The period of *kymatogenesis* (Greek kyema – embryo) – corresponds to the period from fertilization to childbirth (280 days or 40 weeks). There are three periods:
  - blastogenesis – the period from fertilization to 15 days of pregnancy, ending with the formation of embryoblasts and trophoblasts; pathologies that occur during this period are called *blastopathy*;
  - embryogenesis – the period from 16 to 75 days of pregnancy – the main organogenesis occurs and the amnion and chorion are formed; pathology of embryogenesis – *embryopathy*.
  - fetogenesis – the period from 76 to 280 days of pregnancy – is the differentiation and maturation of fetal tissues, the formation of the placenta, and lasts until birth. Pathology of this period – *fetopathy*.
    Fetogenesis is divided into:
    - early fetal period (76-180 days of pregnancy) – immature fetus becomes viable;
    - late fetal period (181-280 days of pregnancy) – ends with fetal maturation.

**Gametopathies** – damage to the male and female gametes (eggs and sperm) that occur during ovo- and spermatogenesis before fertilization.

Etiomorphological factors of gametopathies:

- gene mutations;
- chromosomal aberrations;
- genomic mutations (changes in the number of chromosomes);
- cytoplasmic pathology.

*Down's syndrome* (trisomy on the 21st pair of chromosomes) is a genomic mutation characterized by:

- mental retardation;
- typical appearance: slanted eyes, flattened nose, high palate, open mouth (macroglossia), low location of the auricles, severe muscle hypotension ("frog belly");
- developmental defects (Fallot's tetrad, defects of the main vessels, underdevelopment of the cerebral hemispheres, defects of the digestive and reproductive systems).

**Kimatopathy** – pathology of the period of kimatogenesis.

*Etiology of kimatopathies* – factors that cause malformations, called teratogenic (Greek teratos – ugliness):

- teratogenic viral infections (rubella, HIV, measles, chickenpox, herpes);
- microorganisms (mycoplasma, ureaplasma, toxoplasma, treponema);
- drugs (cytostatics, hormones, vitamins, quinine, antibiotics);
- UV radiation, ionizing radiation;
- maternal disease (diabetes, thyrotoxic goiter);
- bad habits of the mother (alcohol, smoking).

*Classification:*

- blastopathy,
- embryopathy,
- fetopathy.

### *Blastopathies*

The main end results of blastopathy include:

- empty embryo sacs – formed due to aplasia or early death of the embryoblast with its subsequent resorption;
- hypoplasia and aplasia of extraembryonic organs (amnion, amniotic sac, yolk sac);
- ectopic implantation or implantation depth violation (superficial, unusually deep);
- twin malformations – symmetrical and asymmetrical twins, ie twins who are not fully or partially separated:
  - diplopagus – symmetrical fused twins;
  - heteropagus – asymmetric twin, fused (underdeveloped twin is called a parasite);
  - craniopagus – fusion of twins in the head;
  - thoracopagus – fusion of twins in the chest;
  - ischiopagus – the fusion of twins in the pelvis.

### *Embryopathies*

***Embryopathies*** – pathologies of the embryo (from 16 to 75 days of pregnancy), induced by the influence of damaging factors, characterized by disorders of organo- and histogenesis, ending in embryonic death or the formation of congenital malformations.

*Congenital malformation* – a stable morphological change of an organ or tissue, which is formed during the fetal period of development and leads to disorders of their function.

### *Classification of congenital malformations.*

*By morphological changes:*

- aplasia (agenesis) – complete congenital absence of an organ or part of it;
- congenital hypoplasia – underdevelopment of the organ, manifested by a deficit of relative mass or size of the organ;
- congenital hypertrophy (hyperplasia) – an increase in the relative mass (or size) of the organ due to an increase in the number (hyperplasia) or volume (hypertrophy) of cells;
- change in the shape of organs (atresia, stenosis, organ fusion);
- persistence – preservation of embryonic structures, which normally disappear before a certain period of development;
- ectopia – the location of the organ in an unusual place;
- heterotopia – the presence of cells, tissues or whole parts of an organ in another organ or in those areas of the same organ where they should not be.

*By distribution:*

- isolated (localized in one organ);
- systemic (within one system of organs);
- multiple (localized in the organs of two or more systems).

*By localization:*

- central nervous system and sense organs;
- face and neck;
- cardiovascular system;
- respiratory system;
- digestive organs;
- musculoskeletal system;
- urinary organs;
- genitals;
- endocrine organs;
- skin and its appendages, other.

*By etiological basis:*

- hereditary defects (genetic and chromosomal);
- exogenous – malformations caused by teratogenic damage directly to the embryo or fetus;
- multifactorial.

**Congenital heart defects**

*Classification of heart defects.*

*By type of circulatory disorders:*

- blue – a decrease in blood flow in the small circle of blood circulation with the development of hypoxia and redistribution of blood flow from right to left
- white – the direction of blood flow from left to right, no hypoxia.

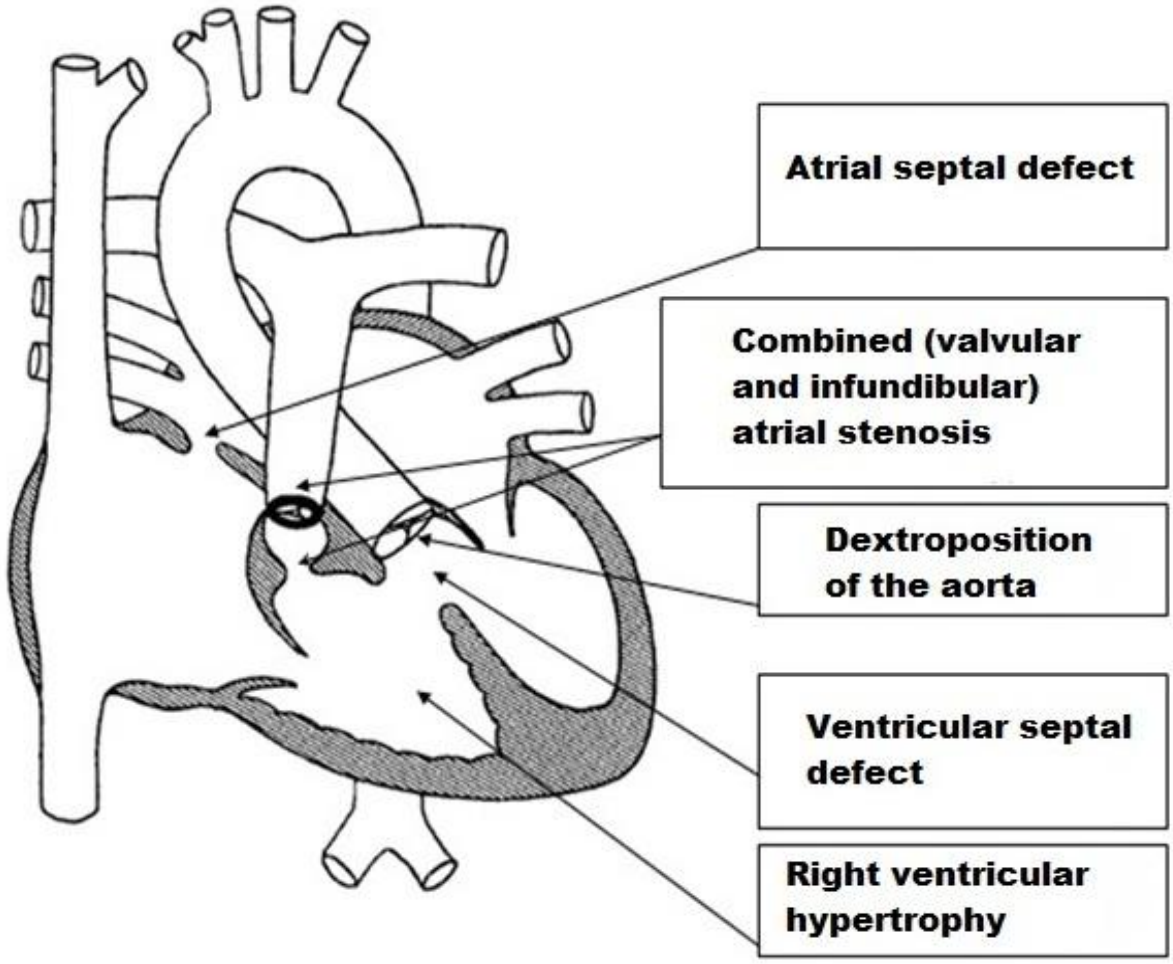


Fig. Fallot's pentalogy

*By morphology:*

a) Congenital heart defects with impaired separation of the heart cavities:
- interventricular septal defect
- atrial septal defect
- complete absence of one septum

b) Congenital heart defects with impaired division of the arterial trunk:
- transposition of the pulmonary artery and aorta
- stenosis and atresia of the pulmonary trunk
- aortic stenosis and atresia
- coarctation of the aorta

c) Combined heart defects:
- *Fallot's triad* – interventricular septal defect, pulmonary artery stenosis, right ventricular hypertrophy;
- *Fallot's tetralogy* – ventricular septal defect, pulmonary artery stenosis, aortic dextroposition and right ventricular hypertrophy;
- *Fallot's pentalogy* – signs of Fallot's tetralogy + atrial septal defect.

All defects of the Fallot's type are blue. Fallot's tetralogy is more common.

**Congenital defects of the central nervous system**

a) Congenital malformations of the cerebrum, which occur as a result of non-closure of the neural tube:
- *anencephalia* – absence of the brain, combined with *acranium* - lack of bones of the skull and soft tissues;
- *craniocerebral hernias* – a sac-like protrusion in the area of the skull bone defect;
- *porencephalia* – characterized by the presence of cysts of different sizes in the brain, lined with ependyma, which are connected with the ventricular system and subarachnoid space.

b) Congenital malformations of the cerebrum, which are the result of impaired migration and differentiation of nerve cells:
- *micro-* and *polygyria* – a large number of small and abnormally located convolutions of the final brain;
- *agiriya* – the absence of furrows, convolutions and layered structure of the cortex in the large hemispheres;
- *microcephalia* – a decrease in the mass, size and histological structures of the brain.

c) Malformations of the spinal cord and spine:
- *spina bifida* – spinal cord hernias associated with dysraphia (non-concrescence) of the dorsal vertebrae;
- *complete rachischis* – a complete defect of the posterior wall of the spinal canal, soft tissues, skin and meninges.

d) Malformations of the ventricular system and subarachnoid space:
- *hydrocephalus* – excessive accumulation in the ventricular system (internal hydrocephalus) or subarachnoid and subdural spaces (external hydrocephalus) of cerebrospinal fluid, accompanied by atrophy of the cerebral substance.

## Fetopathies

***Fetopathy*** – pathology of the fetal period (76th to 280th day of pregnancy).

*Types* of fetopathies:

- infectious,
- non-infectious.

### *Infectious fetopathies*

*Ways of infection:*

- hematogenous;
- infection of amniotic fluid with infection in the placenta, followed by their ingestion by the fetus;
- ascending path;
- descending path.

*Pathomorphology:*

- generalized areactive necrosis develops in viral fetopathies;
- in bacterial infections develops areactive necrosis of septic or granulomatous type;
- severe hemorrhagic syndrome;
- atrophy of the thymus with subsequent immune deficiency;
- in full-term fetuses there are foci of extramedullary hematopoiesis, in premature – hepatosplenomegaly.

### *Non-infectious fetopathies*

*The main non-infectious fetopathies include:*

- diabetic fetopathy;
- hemolytic disease of newborns;
- endocardial fibroelastosis;
- cystic fibrosis, etc.

***Diabetic fetopathy*** is a disease of the fetus caused by prediabetes and maternal diabetes. The child develops hypertrophy of the insular apparatus of the pancreas with subsequent depletion.

*Clinical and morphological signs of diabetic fetopathy:*

- large fetus (weight 4-6 kg) with signs of immaturity;
- short neck, swollen face;
- swollen body;
- hepato- and cardiomegaly;
- microangiopathy (vessels of the eye, kidneys);
- skin petechiae;
- possible development of hyaline membrane disease due to surfactant deficiency.

***Hemolytic disease of the newborn*** is a severe fetopathy that results from the effects of maternal antibodies on the body of the fetus or newborn.

*Etiology* – incompatibility of mother and fetus by Rh factor or AB0 system.

*Forms*:

- edematous form,
- anemic form,
- icteric form.

*Clinical and morphological manifestations:*

| Edematous form | Anemic form | Icteric form |
|---|---|---|
| • pale, translucent, shiny, partially macerated skin with multiple petechiae;<br>• sharp swelling of the brain and meninges;<br>• accumulation of transudate in body cavities;<br>• hepatosplenomegaly;<br>• reduction of lung mass;<br>• hypoxic encephalopathy. | • pale skin and visible mucous membranes;<br>• tissue swelling;<br>• anemia of internal organs;<br>• absence of jaundice<br>• moderate hepatosplenomegaly. | • the appearance of jaundice by the end of the first, beginning of the second day;<br>• bilirubin encephalopathy (nuclear jaundice);<br>• acute hepato-splenomegaly;<br>• severe hemosiderosis of the liver;<br>• bilirubin infarction of the kidneys;<br>• possible development of idiotism. |

***Endocardial fibroelastosis*** is a diffuse thickening of the endocardium of one or more chambers of the heart due to the growth of collagen and elastic fibers.

The *etiology* is not fully established, the main reason is considered to be the factors that cause hypoxia (endo- and myocardium).

*Classification:*

- isolated fibroelastosis - independent nosology;
- combined fibroelastosis (associated with congenital heart defects).

*Macroscopically:* cardiomegaly, diffusely thickened parietal endocardium, grayish-white, left ventricular cavity dilated, flaccid myocardium.

*Microscopically:* the growth of elastic and, to a lesser extent, collagen fibers arranged in parallel rows; muscle fiber hypertrophy, diffuse cardiosclerosis.

***Cystic fibrosis*** is a disease characterized by increased viscosity of mucus, which causes the development of retention cysts and sclerosis in the pancreas, bronchi, digestive and other glands.

*Forms of cystic fibrosis*:

- pulmonary-intestinal,
- pulmonary,
- intestinal,
- military.

*Pathomorphological changes*

*Pancreas*.

Macroscopically: without changes or the formation of small cysts.

Microscopically: thick secretion in the ducts and acinuses of the gland, atrophy of the parenchyma (islet apparatus preserved), diffuse fibrosis and lymphohistiocytic infiltration of the interstitium.

*Lungs*: obstructive atelectasis with secondary infection and development of bronchitis, pneumonia, bronchiectasis, abscesses.

*Intestines*: coprostasis, intestinal obstruction.

*Liver*: thickening of bile, leading to cholestasis and biliary cirrhosis.

## Pathology of the perinatal period

The *perinatal period* begins on the 22nd full week (154 days) of pregnancy (the time

when birth weight is usually 500 g) and ends on the seventh full day (168 hours) after birth. This period is divided into:

- *antenatal* (from 22 weeks before delivery),
- *intranatal* (from the beginning of contractions to birth),
- *postnatal* (from the birth of the baby to the seventh full day of his life).

The *neonatal period* begins at birth and ends at 28 full days after birth.
The most common cause (80%) of stillbirth and perinatal mortality is hypoxia.
***Fetal asphyxia*** is a pathological condition characterized by oxygen starvation.
*Classification:*

- antenatal/prenatal (fetal),
- intranatal (during childbirth).

*Etiology*

| Antenatal hypoxia | Intranatal hypoxia |
|---|---|
| • chronic diseases of the cardiovascular, respiratory, hematopoietic, endocrine (diabetes, thyrotoxicosis) systems of the mother<br>• intoxication during pregnancy (occupational, medical)<br>• gestosis, mainly in the second half of pregnancy<br>• infectious diseases of the fetus<br>• some congenital malformations of the fetus and placenta<br>• • placental insufficiency. | • premature complete or partial detachment of the placenta<br>• placenta previa<br>• excessively long, frequent and strong contractions<br>• loss of umbilical cord loops and pressing them to the anterior part of the fetus<br>• excessive tension of the short umbilical cord<br>• true umbilical cord nodes<br>• • umbilical cord entanglement around the neck of the fetus, etc. |

*Morphological manifestations of intrauterine hypoxia:*

- hemorrhagic diathesis, which is manifested by diapedetic small and focal hemorrhages in the serous, mucous membranes, internal organs (most often in the brain, adrenal glands, lungs, kidneys);
- venous plethora of internal organs and DIC syndrome;
- edema;
- dystrophic and necrotic changes in tissues.

## Pneumopathies

***Pneumopathies*** is a group of diseases of the lungs of newborns of non-inflammatory nature, which are the main cause of the clinical syndrome of respiratory disorders and asphyxia of the newborn. They are more likely to develop in premature babies in the first hours and days after birth.
*The basis of occurrence is*:

- immaturity of lung tissue;
- insufficiency of the surfactant system;
- violation of the respiratory center;
- intrauterine hypoxia.

*Forms of pneumopathies:*

- neonatal aspiration syndrome;
- congenital (primary) pulmonary atelectasis;

- disease of hyaline membranes;
- edematous-hemorrhagic syndrome.

***Neonatal aspiration syndrome*** is characterized by aspiration of amniotic fluid and / or meconium, mucus.

*Macroscopically:* compacted-swollen low-air lungs with alternation of small foci of atelectasis and emphysema without characteristic localization. At aspiration of meconium in a trachea and bronchial tubes greenish mucous masses which at extrusion look like greenish "worms" are visible.

*Microscopically*: plethora of alveolar septa, in the lumens of unevenly straightened alveoli with uneven contours of the septa are found elements of amniotic fluid. Pneumonia develops very quickly during aspiration of infected contents.

*Complications:* pneumonia, pneumothorax, interstitial emphysema.

***Congenital (primary) atelectasis of the lungs*** – incomplete straightening of the lungs or parts thereof, due to immaturity of the lung parenchyma, diaphragm or other respiratory muscles, disorders of central and peripheral regulation of respiration.

*Macroscopically*: airless lungs occupy 1/2-2/3 of the volume of the pleural cavities.

*Microscopically:* much of the lung tissue is airless. The cavities filled with air are small, their contours are uneven, located diffusely, more in the subpleural departments. Vessels of interalveolar septa are full-blooded, dilated.

*Complications:* atelectatic pneumonia, emphysema (alveolar and interstitial), pneumothorax.

***Hyaline membrane disease*** *(hyaline membranopathy, respiratory distress syndrome (RDS))* is an acute respiratory disorder that develops mainly in premature infants in the first hours of life due to lung immaturity, surfactant deficiency.

Morphological substrate of the disease – hyaline membranes – dense eosinophilic masses adjacent to the inner surface of the alveoli in the form of rings or semirings. Chemical composition of membranes: fibrin, plasma proteins, glycosaminoglycans, phospholipids.

*Macroscopically*: the lungs are enlarged, low air, dark red, significantly compacted, sometimes liver density, in the posteroinferior regions with imprints of ribs.

*Microscopically*: atelectasis of the terminal parts of the respiratory parenchyma, dilation of bronchioles and alveolar passages, the presence of hyaline membranes in dilated alveolar passages and bronchioles, stasis, blood clots in the microcirculatory tract (as in DIC syndrome), hemorrhage, edema.

*Stages* in the development of hyaline membranes:

1 day – small loose membranes on the background of edema and atelectasis;
2 days – reduction of edema, dense membranes, atelectasis persists;
4-5 days – the membranes are fragmented, resorbed by alveolar macrophages.

*Complications*: pneumonia, intraventricular hemorrhage (of hypoxic origin), hyaline membranes may be exposed to the organization with the development of focal fibrosis.

***Edema-hemorrhagic syndrome*** – pneumopathy, characterized by pulmonary edema and massive hemorrhages in their stroma.

*Macroscopically*: the lungs do not fill the entire pleural cavity, airless, swollen.

*Microscopically*: underdeveloped lung parenchyma, stroma hypovascularization, airless alveoli filled with edematous fluid, microcirculatory plethora, focal and diffuse hemorrhage in the stroma.
The *prognosis* is unfavorable.

## Birth trauma (injury)

**Birth trauma** – local damage to fetal tissues during childbirth, which occurs due to the impact of mechanical forces directly on the fetus, manifested by tears, fractures, dislocations, tissue rupture and accompanied by circulatory disorders at the site of application.
*Causes of birth injuries*:

- embryo- and fetopathy;
- fast or prolonged childbirth;
- abnormal position and presentation of the fetus;
- prematurity;
- mismatch between the size of the mother's pelvis and the anterior part of the fetus;
- multiple pregnancy.

*Localization:*

- skull,
- ridge,
- nerves,
- skeletal bones,
- internal organs.

*Types of birth injuries of the skull:*

- childbirth tumor,
- cephalohematoma,
- trauma to the skull bones,
- epidural hemorrhage,
- ruptures of duplications of the dura mater.

***Childbirth tumor*** develops on the presentational part of the fetus (head, buttocks, legs), manifested by edema, venous plethora, small hemorrhages in the subcutaneous tissue and aponeurosis. It is resorbed in 1-2 days after a birth, seldom undergoes a necrosis**.**
***Cephalohematoma*** – hemorrhage under the periosteum of the skull. It is located on one or both parietal bones, rarely on the occipital, frontal and even less on the temporal. The edges do not extend beyond the bone. Blood accumulates gradually and therefore the tumor, which appeared during or immediately after birth, continues to grow for 1-2 days.
*Complications:* anemia, jaundice, due to resorption of hemorrhage, suppuration.
***Ruptures of duplicates of the dura mater:***

- unilateral and bilateral,
- complete and incomplete.

Incomplete rupture – only the upper leaf is torn, while the hemorrhage is located supratentorially. At full rupture (two leaves are torn) blood accumulates in a back cranial fossa.

### *Training macropreparations*

**Fetal anencephaly with signs of Down's syndrome**. The fetus lacks the vault of the skull and brain tissue. Face and nape flattened, "Mongoloid" shape of the eyes, flattened wide nose, open mouth, enlarged tongue (macroglossia), increased abdominal size ("frog belly").

**Proboscis**. On the child's face you can see the tubular formation of the skin at the root of the nose, the lack of eyes.

**Siren (sirenomelia).** The fetus has congenital pathology, which is characterized by fusion of the lower extremities by fin type.

**Ventricular septal defect.** The heart is small in size with a defect of the interventricular septum of the heart, right ventricular hypertrophy.

### *Training micropreparations*

**Disease of hyaline membranes.** There are hemorrhage, edema in the lung tissue, presence of the rings and semirings in the lumen of the alveoli and bronchioles.

### *Questions for self-control*

1. Congenital malformations: morphological characteristics
2. Intrauterine infections: morphological manifestations.
3. Morphology of non-infectious fetopathies.
4. Hemolytic and hemorrhagic diseases of the newborn: morphological characteristics.
5. Diseases of the lungs of the perinatal period (pneumopathy): morphological manifestations.
6. Asphyxia (pre- and intrapartum): morphological characteristics.
7. Birth injury: classification, morphological characteristics.

### *Examples of tests*

1. At caesarean section in a 17-year-old woman heteropagus (completely undivided, asymmetric twins) was removed from the uterine cavity. This double flaw of development is a manifestation of:

A * Blastopathy
In Gametopathy
From Embryopathy
D Infectious fetopathy
E Non-infectious fetopathy

2. Microscopic examination of the lung tissue of a premature infant who has died, there is a compaction of protein masses, consisting mainly of fibrin, which are located in the form of rings and semi-rings on the walls of the respiratory lungs. Macroscopically, the lungs are compacted, airless, with isolated small subtle pleural hemorrhages. The content of surfactant in the lung tissue is normal. Diagnosis of "Pneumopathy". What is the form of pneumonia in a child?

A * Disease of hyaline membranes
B Fibrinous pneumonia
C Edematous-hemorrhagic lung syndrome
D Primary pulmonary atelectasis
E Secondary pulmonary atelectasis.

## DISEASES OF THE PITUIARY. DISEASES OF THE THYROID GLAND. DISEASES OF THE ADRENAL GLANDS. DIABETES.

**Endocrine diseases** – disorders of the endocrine glands, the morphological manifestation of which is dystrophy, atrophy, dysplastic and sclerotic processes, manifested:

- *hyperfunction* – increased (compared to normal) activity of the glands
- *hypofunction* – reduced glandular activity
- *dysfunction* – impaired function.

### Pituitary diseases

*Pituitary diseases include:*

- Acromegaly,
- Gigantism,
- Pituitary dwarfism,
- Cerebro-pituitary cachexia,
- Itsenko-Cushing's disease,
- Adiposogenital dystrophy,
- Diabetes insipidus (DI),
- Tumors of the pituitary gland,
- Simmonds disease (cerebral pituitary cachexia).

**Acromegaly** is a disease caused by a hormone-producing tumor of eosinophilic cells of the anterior pituitary gland (eosinophilic adenoma, carcinoma).

*Clinical and morphological signs of acromegaly:*

- growth of tissues derived from the mesenchyme (connective, cartilaginous, bone);
- growth of parenchyma and stroma of internal organs (heart, liver, kidneys);
- increase in the size of the nose, lips, ears, eyebrows, lower jaw, feet;
- changes in other endocrine organs (goiter, atrophy of the insular apparatus, hyperplasia of the thymus, adrenal cortex, atrophy of the gonads).

**Gigantism** – an increase in the amount of somatotropic hormone in children and adolescents.

**Itsenko-Cushing's** disease is a disease caused by a basophilic adenoma of the anterior pituitary gland.

Pathogenesis: ACTH hypersecretion → bilateral hyperplasia of the adrenal cortex with hyperproduction of glucocorticoids.

*Clinical and morphological manifestations*:

- sick more often women, obesity of the upper type (face, torso);
- arterial hypertension (compensatory left ventricular hypertrophy);
- steroid diabetes;
- secondary ovarian dysfunction;
- osteoporosis with spontaneous fractures;
- hypertrichosis – excessive hair growth that is not characteristic of the skin, sex and/or age;
- hirsutism – excessive growth of terminal hair in women of the male type;
- hypergastrinemia, which leads to the formation of gastric ulcers;

- stretch marks – crimson-cyanotic streaks of stretch on the skin of the thighs and abdomen.

At the initial lesion of the adrenal cortex with hyperproduction of glucocorticoids, *Itsenko-Cushing's syndrome* occurs.

**Diabetes insipidus (DI)** is a disease caused by absolute (loss of secretion of antidiuretic hormone by the hypothalamus (vasopressin)) or relative deficiency of antidiuretic hormone (insensitivity to vasopressin by the epithelium of the renal tubules).

*Etiology*:

- tumors, inflammation, trauma to the pituitary gland;
- lesions of the hypothalamus (supraoptic and paraventricular nuclei).

Pathogenesis and clinical and morphological manifestations:

- vasopressin deficiency causes a decrease in reabsorption of water in the distal tubules of the nephron and the release of large amounts of unconcentrated urine;
- polyuria leads to dehydration - deficiency of intracellular and intravascular fluid;
- the development of plasma hypoosmolarity irritates the osmoreceptors of the hypothalamus – there is thirst.

*Polyuria, dehydration, thirst* – the main manifestations of vasopressin deficiency.

## Diseases of the thyroid gland

***Diseases of the thyroid gland:***

- goiter,
- thyroiditis,
- tumors.

**Goiter** – pathological enlargement of the thyroid gland.

*Etiology:*

- lack of exogenous iodine;
- congenital disorder of thyroid hormone synthesis;
- autoimmune diseases;
- pathology of the pituitary gland.

*Classification:*

*By morphological features*:

- diffuse,
- nodal,
- diffuse nodular (mixed) goiter.

*By histological structure:*

- Parenchymal goiter is characterized by proliferation of the epithelium of follicles, which grows in the form of solid structures with the formation of small follicle-like formations without colloid or with a small amount. The function is increased.
- Colloidal goiter is built of follicles of different sizes, filled with colloid:
  - macrofollicular,
  - microfollicular,
  - macro-microfollicular.

*By function:*

- hypothyroid;
- euthyroid;

- hyperthyroid.

*By epidemiology, cause, functional and clinical features:*

- endemic (specific to a certain area – the Carpathians);
- sporadic;
- Graves' disease Toxic (Bazedov's goiter).

*Graves' disease (diffuse toxic goiter, Bazedov's goiter)* is a thyrotoxic goiter caused by autoimmunity (antibodies stimulate thyroid cell receptors).

*Morphological features of diffuse toxic goiter:*

- transformation of the prismatic epithelium of follicles into cylindrical;
- proliferation of the epithelium with the formation of papillae that branch inside the follicles;
- vacuolation and change of tinctorial properties of colloid due to its liquefaction and reduction of iodine content;
- lymphoplasmacytic infiltration of the stroma.

*Visceral manifestations of diffuse toxic goiter:*

- left ventricular hypertrophy, serous edema and lymphoid infiltration of the stroma (toxic myocarditis), resulting in diffuse sclerosis;
- serous edema and fatty degeneration in the liver (toxic hepatosis);
- dystrophic changes of nerve cells, perivascular cellular infiltrates in the diencephalon and medulla oblongata;
- enlargement of the thymus;
- hyperplasia of lymphoid tissue;
- atrophy of the adrenal cortex;
- exophthalmos.

**Thyroiditis** – a group of inflammatory diseases of the thyroid gland, among which are important:

- Hashimoto's thyroiditis (goiter);
- Chronic fibrous thyroiditis (Riedel's goiter).

***Hashimoto's thyroiditis*** is a true autoimmune disease with the formation of antibodies to thyrocyte antigens and thyroglobulin while preserving the function of the gland.

*Morphological changes*:

- diffuse infiltration of glandular tissue by lymphocytes and plasma cells with the formation of lymphoid follicles;
- replacement of the gland parenchyma with connective tissue.

***Riedel's thyroiditis (Riedel's goiter)*** is the primary growth in the gland of coarse fibrous connective tissue ("iron", "stone" goiter), which leads to atrophy of the follicular epithelium.

## Diseases of the parathyroid glands

**Hyperparathyroidism** is a syndrome of parathyroid gland hyperfunction, the morphological manifestation of which is hyperplasia or tumor (adenoma) of these glands.

*Hyperplasia of the parathyroid glands*:

- primary (adenoma of the gland) leads to the development of parathyroid osteodystrophy;

- secondary – reactive, compensatory hyperplasia due to the accumulation of calcium in the body during bone destruction (myeloma, bone metastases, rickets) and kidney disease (chronic renal failure).

***Parathyroid osteodystrophy (fibrous osteodystrophy)*** – a disease that occurs in hyperfunction of the parathyroid glands and is characterized by impaired metabolism of calcium and phosphorus from bone remodeling.

*Macroscopically*: bones are deformed, especially bones that perform a significant mechanical load (bones of the limbs, pelvis, spine, ribs).

*Microscopically*: bone remodeling – massive osteoclastic resorption of bone substance in some areas and its formation in others; endosteal growth and the formation of cellular fibrous tissue resembling fibrous tissue. Foci of tumor-like formations with giant cell granulomas, accumulation of erythrocytes and hemosiderin.

## Adrenal diseases

**Addison's disease (bronze disease)** is a bilateral impression of mainly the adrenal cortex with the exception (acorticism) or a decrease (hypoadrenocorticism) in the production of its hormones.

*Etiology:*

- adrenal tuberculosis;
- bilateral primary tumors or metastases to the adrenal glands;
- epinephropathic amyloidosis;
- lymphogranulomatosis;
- histoplasmosis;
- necrosis due to vascular thrombosis;
- autoimmune diseases.

*Clinical and morphological manifestations*:

- hyperpigmentation of the skin (melanoderma) and mucous membranes due to increased melanin production;
- brown myocardial atrophy;
- hypotension, lethargy;
- hypoglycemia due to adaptive hyperplasia of the islets of Langerhans;
- atrophy of the gastric mucosa.

*Complications:* cachexia (suprarenal), cardiovascular failure.

## Diseases of the endocrine part of the pancreas

***Diabetes mellitus (DM)*** is a disease that is caused by absolute or relative insulin deficiency.

*Classification*. There are the following types of diabetes:

- spontaneous,
- secondary,
- diabetes of pregnant women,
- latent (subclinical).

*Etiopathogenetic risk factors for diabetes mellitus*:

- genetically determined disorders of β-cell function and number (decreased insulin synthesis, impaired conversion of proinsulin to insulin, abnormal insulin synthesis);

- environmental factors that disrupt the integrity and functioning of β-cells (viruses, autoimmune reactions; nutrition that leads to obesity; increased activity of the adrenergic nervous system).

*Insular insufficiency leads to:*

- impaired glycogen synthesis;
- increase in blood sugar (hyperglycemia);
- the appearance of sugar in the urine (glucosuria).

*Spontaneous diabetes* is an independent disease, which can be of two types:

- type I diabetes (juvenile diabetes);
- type II diabetes (adult diabetes).

*Macroscopically:* the size and weight of the pancreas are reduced, the pattern of the gland in the section is changed due to lipomatosis and/or sclerosis.

*Microscopically:*

- degranulation and death of β-cells;
- atrophy and hyalinosis of the islets of Langerhans;
- compensatory hypertrophy of preserved islands;
- multiple sclerosis, lipomatosis.

*Changes in the blood vessels that develop in diabetes:*

Diabetic macroangiopathy is an atherosclerosis of the arteries of the elastic and muscular-elastic types.

Diabetic microangiopathy (lesions of the vessels of the microcirculatory tract):

- plasmorrhagia through the walls of capillaries;
- proliferation of perithelium, capillary endothelium and arterioles;
- sclerosis, hyalinosis of these vessels.

*Changes in the organs* in microangiopathy:

Kidneys – sclerosis and hyalinosis of the glomeruli and walls of the arterioles.

Liver – the disappearance of glycogen from hepatocytes, fatty liver disease.

Retina – sclerosis and hyalinosis of the retina.

*Complications*:

- renal failure (often chronic);
- diabetic coma (rare);
- associated with macroangiopathy (myocardial infarction, lower extremity gangrene, stroke, etc.);
- infectious complications (pneumonia, sepsis, tuberculosis).

### *Training macropreparations*

**Nodular goiter.** The thyroid gland is significantly increased in size, dense consistency, the surface of the humpback, in the section - multiple cavities of different sizes, filled with brown-yellow colloid.

**Diffuse goiter**. Enlarged thyroid, gray-pink, soft consistency. Training micropreparations

### *Training micropreparations*

**Colloidal goiter** (staining with hematoxylin and eosin). The follicles are enlarged, stretched, cystically dilated, lined with flattened epithelium, filled with oxyphilic colloid.

**Hashimoto's thyroiditis** (staining with hematoxylin and eosin). Parenchyma of the thyroid gland with atrophy, partially replaced by connective tissue. In the stroma -

infiltration of lymphocytes and plasma cells, the formation of lymphoid follicles with light growth centers.

**Atrophy of the pancreas** (staining with hematoxylin and eosin). In the tissue of the pancreas is determined by a small number of small sclerosed islets of Langerhans, lymphocytic infiltration.

### *Questions for self-control*

1. Diseases of the pituitary gland: causes and clinical and morphological characteristics of acromegaly and gigantism.
2. Itsenko-Cushing's disease: etiology, clinical and morphological manifestations; difference from Itsenko-Cushing's syndrome.
3. Definition, etiology, pathogenesis, clinical and morphological manifestations of diabetes mellitus.
4. Diseases of the thyroid gland. Definition and classification of oxen.
5. Graves' disease: etiology, morphological changes of the thyroid gland, visceral manifestations, complications.
6. Thyroiditis: etiology, pathomorphology of Hashimoto's and Riedel's thyroiditis.
7. Diseases of the parathyroid glands. Hyperparathyroidism: classification according to the cause. Pathomorphological changes of parathyroid osteodystrophy.
8. Diseases of the adrenal glands. Addison's disease: etiology, clinical and morphological manifestations, complications.
9. Etiology, classification, pathogenesis of diabetes.
10. Macro- and microangiopathy in diabetes: pathomorphology, changes in internal organs, complications.

### *Examples of tests*

1. The patient showed an increase in the thyroid gland in two. The palpatory gland is dense, the surface is unevenly tuberous. Histological examination revealed diffuse infiltration of glandular tissue with lymphocytes, plasma cells with the formation of follicles and increased connective tissue growth. Your diagnosis.

A. * Hashimoto's goiter.
B. Endemic goiter.
C. Sporadic goiter.
D. Diffuse toxic goiter.
E. Riedel's goiter.

2. A patient from a mountainous region of Central Asia was diagnosed with an enlarged thyroid gland, which made it difficult to swallow. There was an increase in body weight, inhibition, drowsiness, swollen face. At microscopic research in a thyroid gland - follicles of different sizes with hypochromic colloid. Which of the diagnoses is most likely?

A. * Endemic goiter.
B. Diffuse toxic goiter.
C. Hoshimoto's thyroiditis.
D. Sporadic goiter.
E. Riedel's goiter.

3. At the autopsy of a 45-year-old woman who suffered from upper obesity, steroid diabetes, hypertension, secondary ovarian dysfunction were found: hypertrichosis, hirsutism, stretch marks on the skin of the thighs and abdomen. In the anterior

pituitary there is a tumor (microscopically: basophilic adenoma); in the adrenal glands - hyperplasia of the bundle layer. Your diagnosis.
A. * Itsenko-Cushing's disease.
B. Itsenko-Cushing's syndrome.
C. Simmonds disease.
D. Adipogenital dystrophy.
E. Pituitary dwarfism.
4. The patient complains of poor sleep, general weakness, irritability, exophthalmos, tachycardia. The thyroid gland is enlarged. At the phenomena of increasing cardiovascular insufficiency the patient died. Histological examination of the thyroid gland - epithelial proliferation with papillary formation, colloid thinning, lympho-plasmacytic infiltration, formation of lymphatic follicles with embryonic centers. What is the name of this disease?
A. * Diffuse toxic goiter.
B. Endemic goiter.
C. Sporadic goiter.
D. Hashimoto's thyroiditis.
E. Benign thyroid tumor.
5. A 50-year-old patient suffered from parathyroid disease for a long time. At the phenomena of accruing renal failure the patient died. At autopsy: deformation of the bones of the extremities, spine, ribs. The bones are easily cut with a knife. The kidneys are wrinkled. Histologically: in the bone tissue foci of lacunar resorption. Giant cell granulomas, accumulation of erythrocytes and hemosiderin are found in the foci of tumors. Your diagnosis.
A. * Parathyroid osteodystrophy.
B. Multiple metastases of cancer to bone.
C. Chronic renal failure.
D. Paget's disease.
E. Myeloma.
6. Histological examination of the thyroid gland revealed moderate parenchymal atrophy, sclerosis, diffuse infiltration of the stroma by lymphocytes and plasma cells with the formation of lymphoid follicles. Your diagnosis.
A. * Autoimmune thyroiditis.
B. Parenchymal goiter.
C. Thyrotoxic goiter.
D. Thyroiditis.
E. Riedel's goiter.

## SYPHILIS

**Syphilis** is a chronic infectious venereal disease characterized by lesions of the skin, mucous membranes, internal organs, bones, nervous system with a consistent change in the stages of the disease.
*Etiology* and *pathogenesis*. The causative agent is Treponema pallidum. Entrance gate - damaged epidermis or epithelium of mucous membranes.
*Depending on the route of infection, there are*:

- Acquired syphilis
  - ✓ sexual infection,
  - ✓ asexual infection (household, occupational syphilis).
- Congenital syphilis – in fetal infection.

Syphilis *occurs in three periods*, which is determined by the reactivity of the organism:

- Primary period – increasing sensitization;
- Secondary period – immediate type of hypersensitivity reactions;
- Tertiary period – delayed type hypersensitivity.

*Pathological anatomy*.

***The primary period of syphilis*** is characterized by the formation of primary syphilitic affect – a solid chancre at the site of penetration of the pathogen.

*Macroscopically*: painless round ulcer with a smooth lacquered bottom and smooth, cartilaginous edges.

*Microscopically*: inflammatory infiltrate of lymphoid, plasma cells and a small number of neutrophils and epithelioid cells around small vessels, where endothelial proliferation is observed.

*Primary syphilitic complex* – solid chancre + lymphangitis + regional lymphadenitis. After 2-3 months, a small, unpigmented scar is formed at the site of primary affect, and sclerosis occurs in the lymph nodes.

***The secondary period of syphilis*** is characterized by the appearance of syphilides - numerous inflammatory foci on the skin and mucous membranes that contain treponema.

*Morphology*: roseola, papules, pustules. Focal edema of the skin and mucous membranes, loosening of the epithelial cover, redness of blood vessels with necrosis of the walls and perivascular infiltrates. In the lymph nodes – edema, hyperplasia, foci of necrosis, accumulation of treponemes.

Healing of syphilides occurs in 3-6 weeks from the beginning of the rash with the formation of pigment-free scars in their place.

***The tertiary period of syphilis*** occurs 3-6 years after infection and manifests itself:

- *Chronic diffuse interstitial inflammation* – endarteritis and lymphangitis with the formation along the vessels of lympho-plasmacytic infiltrates with the subsequent development of syphilitic sclerosis (lobular liver, etc.);
- *Formation of* ***gums*** (solitary or multiple) – syphilitic granulomas. Microscopically: the central part is represented by caseous necrosis, which has the form of glue (gummi - glue), surrounded by a cell wall of lymphoid, plasma, epithelioid cells and sometimes giant cells of Pirogov-Langhans, **endovasculitis.**

Visceral syphilis is a lesion of the internal organs that occurs more often in the tertiary period of syphilis.

Heart lesion is manifested by humus or chronic intermediate myocarditis with the development of cardiosclerosis.

Arterial lesions are manifested by productive arteritis with the development of arteriosclerosis.

Aortic lesions – syphilitic mesoarthritis.

*Localization:* ascending part (often above the valves), aortic arch.

*Macroscopically*: whitish nodules in the intima of the aorta with cicatricial indentations, resembling **shagreen skin**.
*Microscopically*: small foci of necrosis, accumulation of lymphoid plasma cells, giant Pirogov-Langhans cells, fibroblasts, destruction of elastic fibers with their replacement by connective tissue.
Decreased wall strength leads to the formation of a *syphilitic aortic aneurysm*.
Supravalvular aortic syphilis can turn into an aortic valve with the development of an inflammatory process in the cuspids, which results in *syphilitic aortic defect*:

- Stenosis of the aortic orifice – a heart defect characterized by narrowing of the left ventricular outflow tract in the aortic valve, resulting in obstruction of blood flow from the left ventricle to the aorta (fusion of valves).
- Aortic valve insufficiency – a heart defect characterized by incomplete closure of the valve cuspids during diastole and leads to reverse diastolic blood flow (regurgitation) from the aorta to the left ventricle. Main symptoms:
  - *Musset's symptom* – rhythmic rocking of the head back and forth synchronously with systole and diastole;
  - *Landolph's symptom* – systolic narrowing and diastolic dilation of the pupils;
  - *Mueller's symptom* – rhythmic pulsation and expansion of the tongue and tonsils;
  - *Quincke's symptom* – alternation of red and pale skin or visible mucous membranes, respectively, systole and diastole.

Lesion of the nervous system – ***neurosyphilis***. Forms:

- *gummatous* – the formation of solitary or diffuse gummas;
- *simple* – inflammatory lymphocytic infiltration of brain tissue;
- *vascular lesions* – obliterating endarteritis or endophlebitis;
- *progressive paralysis* – a decrease in brain mass, thinning of the convolutions, atrophy of the subcortical nodes and cerebellum due to inflammatory and dystrophic processes;
- *tabes dorsalis* – atrophy of the spinal cord, which begins mainly in the lumbar region, due to dystrophic and inflammatory changes (disintegration of myelin sheaths).

**Congenital syphilis** occurs during intrauterine infection of the fetus through the placenta from a mother with syphilis.
*Classification* of congenital syphilis:

- syphilis of stillborn premature fetuses;
- early congenital syphilis;
- late congenital syphilis.

*Syphilis of stillborn premature fetuses*: death of the fetus between 6 and 7 months of fetal development due to the toxic effects of treponema – premature birth with macerated fetus.
**Congenital syphilis** occurs in fetal infection through the placenta from a mother with syphilis.
*Classification* of congenital syphilis:

- syphilis of stillborn premature fetuses;
- early congenital syphilis;
- late congenital syphilis.

*Syphilis of stillborn premature fetuses*: fetal death between 6 and 7 months of fetal development due to toxic effects of treponema - premature birth with macerated fetus.

*Early congenital syphilis* is manifested in the first two months of life by the lesion:

- skin – syphilids (papules and pustules);
- lung – interstitial syphilitic pneumonia, which leads to compaction of lung tissue with the development of sclerotic changes – white pneumonia;
- liver – interstitial hepatitis with hepatocyte necrosis, intermediate round-cell infiltration, miliary gum formation and sclerosis;
- bone – syphilitic osteochondritis – inflammation and violation of calcification of the epiphyseal cartilage on the border of the diaphysis and the distal epiphysis of the thigh, ribs, sternum;
- CNS – syphilitic encephalitis and meningitis (formation of miliary gums).

*Late congenital syphilis* is characterized by the presence of the ***Hutchinson triad***:

1. Deafness,
2. Parenchymal keratitis,
3. "Hutchinson's teeth" – barrel-shaped deformation of the teeth (at the level of the neck teeth are wider than at the free edge), which is based on hypoplasia of the enamel and the formation of a crescent-shaped notch on the upper central incisors.

Changes in the internal organs are similar to the manifestations of acquired tertiary syphilis. In the thymus there are cavities filled with serous fluid with impurities of neutrophils and lymphocytes surrounded by a shaft of epithelioid cells - *Dubois abscesses.*

### *Training macropreparations*

**Syphilitic lobular liver**. The liver is enlarged in size, represented by a large number of different sized humps (rubber), in section is filled with adhesive masses.

### *Training micropreparations*

**Syphilitic granuloma (guma*)*** (staining with hematoxylin and eosin). The focus of necrosis is surrounded by an inflammatory infiltrate consisting of lymphocytes, plasma cells, epithelioid cells, surrounded by connective tissue with a large number of blood vessels, in some of which - endovasculitis.

### *Questions for self-control*

1. Etiology, routes of infection, pathogenesis of syphilis.
2. Pathomorphology of the primary period of syphilis.
3. Pathomorphology of the secondary period of syphilis.
4. Pathomorphology of the tertiary period of syphilis.
5. Pathomorphology of congenital syphilis.

### *Examples of tests*

1. An aneurysm of the ascending aorta was detected at the autopsy of a deceased man without a definite place of residence. Microscopically in the middle layer of the aorta revealed: inflammatory infiltrates of lymphocytes, plasma cells, fibroblasts with an admixture of giant Pirogov-Langhans cells, and the presence of vessels with endovasculitis. What disease should you think about?

A. *Syphilis.

B. Atherosclerosis.

C. Rheumatism.
D. Hypertensive disease.
E. Tuberculosis.
2. Patient M., 12 years old, was diagnosed with Hutchinson's triad: barrel-shaped teeth, parenchymal keratitis and deafness. Which disease is characterized by detected changes?
A. *Syphilis.
B. Opisthorchiasis.
C. Tuberculosis.
D. Toxoplasmosis.
E. Leprosy.
3. At the patient of 20 years inguinal lymph nodes are increased in the sizes, are not painful, are condensed. In the area of the mucous membrane of the genitals of small ulcers with sealed edges and "lacquered" bottom of gray-red color. Make a diagnosis.
A. *Syphilis
B. Trophic ulcer.
C. Mycosis.
D. Tuberculosis.
E. Gonorrhea.
4. When examining a 4-year-old boy, the dentist found: a saddle-shaped nose, a high palate, a buttock-shaped skull. Both front upper cutters are barrel-shaped with a crescent-shaped cut on the free edge. Lymph nodes are not changed. Your previous diagnosis?
A. *Late congenital syphilis.
B. Early congenital syphilis.
C. Tertiary syphilis.
D. Fluorosis.
E. Rickets.
5. At the autopsy of a 62-year-old man found supravalvular rupture of the aorta with cardiac tamponade. Histological examination of the ascending aorta in the outer and middle membranes - infiltrates of lymphoid, plasma, epithelioid cells, foci of necrosis in the middle membrane, proliferation of adventitial and endothelial cells of the outer shell. Changes in the aorta are characteristic of:
A. *Syphilitic aortitis.
B. Septic aortitis.
C. Rheumatic aorta.
D. Atherosclerosis.
E. Hypertension.

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