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Symptoms and syndromes in diseases of internal organs

Manual for the third-year students of the international faculty

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The textbook is devoted to the discipline definition, the problems of diagnosis, and fundamentals of diagnostic process: history taking, inspection, and physical examination of the respiratory, cardiovascular, digestive systems.

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Topic 1. Mitral Valvular and Aortal Valvular Diseases of the Heart: the Main Syndromes and Symptoms on the Basis of Clinical and Instrumental Methods of Investigation

Heart Valvular Diseases. Rheumatic disease of the heart: classification**,** the clinical picture, and etiology factors. The main cause of acquired incompetence the mitral valve and mitral stenosis. Haemodynamics. Kitaev's reflex. The main complaints of the patients with incompetence of the mitral valve and mitral stenosis. External examination, palpation, percussion, auscultation of the patients with incompetence of the mitral valve and mitral stenosis. X-ray studies. Echocardiography. ECG. Phonocardiogram. Prolaps of the mitral valve.

Etiology factors and mechanism of development of aortic insufficiency, aortic stenosis. Haemodynamics. The main complaints of the patients with aortic insufficiency, aortic stenosis. External examination, palpation, percussion, auscultation of the patients with aortic insufficiency, aortic stenosis. X-ray studies. Echocardiography. ECG. Phonocardiogram.

HEART VALVULAR DISEASES

Stable pathological changes in the structure of the heart that interfere with its normal function are called heart disease. Congenital and acquired diseases of the heart are distinguished. The incidence of acquired heart diseases is much higher.

Congenital diseases of the heart arise due to abnormal development of the heart and the great vessels during the intrauterine growth of the foetus with preservation of the intrauterine character of circulation after birth. Endocarditic, and especially rheumatic endocarditis, is the main cause of acquired heart defects. Less frequently heart disease is the result of sepsis, atherosclerosis, syphilis, injuries, etc. Inflammatory processes occurring in the valve cusps often end in their sclerosis: deformation and shortening. An affected valve does not close completely to cause valvular incompetence. The cusps of the valves may adhere to one another because of inflammation to narrow the orifice they close. This narrowing is called stenosis.

ACUTE RHEUMATIC FEVER

Rheumatic fever is a general infectious in which connective tissues, mainly of the cardiovascular system, are affected by inflammation; joints, serous membranes, internal organs, and the central nervous system are often. Rheumatism is a collagenous disease, i.e. a disease characterized by a systemic and progressive derangement of connective tissue.

Rheumatism was classified as an independent disease with typical affections not only of the points but also mainly have the heart in 1835 by a French clinicist Bouillaud and in 1836 by the Russian physician Sokolsky. Until that time rheumatism had been considered a disease of joints.

Etiology

The epidemiology of acute rheumatic fever is identical to that of group A streptococcal upper respiratory tract infections. As is the case for streptococcal sore throat, acute rheumatic fever most often occurs in children: the peak age-related incidence is between 5 and 15 years. Most initial attacks in adults take place at the end of the second and beginning of the third decades of life. Rarely, initial attacks occur as late as the fourth decade and recurrent attacks may be seen even later; attacks have been documented in the fifth and sixth decades.

Epidemiologic risk factors classically associated with individual attacks and especially with outbreaks of acute rheumatic fever include lower standards of living, especially crowding; the disease has been more common among socially and economically disadvantaged populations. However, the outbreaks in the United States in the late 1980s and early 1990s cannot be explained entirely by these factors. The large Utah outbreak of almost 300 cases during 7 years affected patients in primarily middle-class families with ready access to medical care. Therefore, one can conclude that the organism itself as well as the degree of host/herd immunity to the prevalent serotypes in an affected community is equally important risk factors.

Studies have shown that approximately 3 percent of individuals with untreated group A streptococcal pharyngitis will develop rheumatic fever. The epidemiology of rheumatic fever is also

influenced by the serotypes of group A streptococci present in a population. The concept of "rheumatogenecity" of specific strains is largely based upon epidemiologic evidence associating certain serotypes with rheumatic fever. Mucoid or highly encapsulated strains have been associated with rheumatic fever.

Pathogenesis

More than half a century ago the pioneering studies of Lancefield differentiated beta-hemolytic streptococci into several serologic groups. This ultimately led to the association of infection by the group A organism of the oropharynx (not of other sites) and the subsequent development of acute rheumatic fever. However, the mechanism(s) responsible for the development of rheumatic fever after an infection remains elusive. Historically, approaches to understanding the pathogenesis of rheumatic fever have been grouped into three major categories:

1) direct infection by the group A streptococcus;

2) a toxic effect of streptococcal extracellular products on the host tissues;

3) an abnormal or dysfunctional immune response to one or more as yet unidentified somatic or extracellular antigens produced by all (or perhaps only by some) group A streptococci.

There is insufficient evidence to support direct infection of the heart as the inciting event. Additionally, while toxins such as streptolysin O and others have been postulated to be responsible for this sequel, there is relatively little convincing evidence at the present time. Major efforts have focused on an abnormal immune response by the human host to one or more group A streptococcal antigens. The hypothesis of "antigenic mimicry" between human and bacterial antigens has been studied extensively and has concentrated on two interactions. The first is the similarity between the group-specific carbohydrate of the group A streptococcus and the glycoprotein of heart valves; the second involves the molecular similarity between either streptococcal cell membrane or streptococcal M protein and sarcolemma or other moieties of the human myocardial cell. The possibility of a predisposing genetic influence in some individuals is one of the most tantalizing of the incompletely understood factors that might contribute to the susceptibility to rheumatic fever. The precise genetic factors influencing the attack rate have never been adequately defined. Observations have been described that support the concept that this nonsuppurative sequel to a group A streptococcal infection results from an abnormal immune response by the human host. Thus differences in immune responses to streptococcal extracellular antigens have been reported, with a unique surface marker on non-T lymphocytes of rheumatic fever patients.

Classification

1. Acute rheumatic fever
2. Rheumatic disease of heart (Rheumatic disease of heart – with defect or vice of heart, valvular heart disease).

The Jones Criteria for Rheumatic Fever, Updated 1992

A. Major Criteria:

1. Carditis
2. Polyarthritis
3. Chorea minor - hyperkinesia (abnormal movements of the extremities, the trunk, and the facial muscles).
4. Annular erhytema
5. Rheumatic subcutaneous nodule

B. Additional (minor) Criteria:

Fever
Pain in the joints
C-reactive increased
Increased the erythrocyte sedimentation rate

The *minor criteria* are nonspecific and may be present in many clinical conditions. To fulfill the Jones criteria, either two major criteria, or one major criterion and two minor criteria, plus evidence of an antecedent streptococcal infection are required. The latter may be provided by recovery of the organism on culture or by evidence of an immune response in one of the commonly measured group A streptococcal antigens (e.g. anti-streptolysin O, anti-deoxyribonuclease B, anti-hyaluronidase). Since the accurate diagnosis of rheumatic fever has future medical.

Clinical features

The clinical picture of rheumatism is quite varied and depends mostly on the localization of the inflammatory changes in connective tissues of various organs and on acuity of the rheumatic process. As a rule, the disease develops in 1-2 weeks after a streptococcal infection (e.g. tonsillitis, pharyngitis). Most patients develop subfebrile temperatures 3 weeks), new symptoms a heart. The patient complains of palpitation and intermissions the work of the heart, the feeling of heaviness or pain in the heart, and dyspnoea. Less frequently the onset of the disease is acute. Remitting temperature develops (38-39°C), which is accompanied by general asthenia, fatigue, and perspiration.

Heart affections may be the only clinical manifestation of rheumatism. On the other hand, practically all-rheumatic patients have their heart muscle affected rheumatic myocarditis. **Rheumatic myocarditis** is characterized by dyspnoea, the feeling of heaveness and pain in the heart, palpitation, and intermissions in the heart work. In addition, certain objective signs are found: enlargement of the heart, decrease heart sounds (especially the first sound); gallop rhythms develop in severe affection of the myocardium. A soft systolic murmur can he hear all the heart apex. It is associated with relative incompetence of the valve affection papillary muscles. The pulse of small and soft; tachycardia are frequent. Arterial pressure is usually decreased. Circulatory insufficiency rapidly develops in grave diffuse myocarditis. Myocardial cardiosclerosis develops in benign outcome of the disease.

Rheumatic myocarditis usually concurs with **rheumatic endocarditis** (rheumocarditis). Early endocarditis signs are not pronounced (symptoms of myocarditis prevail). Further development of the heart disease proves the presence of endocarditis. At earlier stages of endocarditis systolic murmurs are coarser than in myocarditis; the murmur becomes louder after exercise; in some cases it becomes "musical". Diastolic murmur may be heard as well. It is probably explained by deposition of thrombotic mass on the valve cusps, which produces turbulence in the blood flow as it passes from the atrium to the ventricle. These thrombotic deposits on the valves can leave their seat and become the cause of embolism or infarctions in various organs (e.g. the kidney or the spleen). The mitral valve is mostly affected on endocarditis. Next in incidence follows the aortic valve; the tricuspid valve is affected still less frequently. If early attacks of rheumatic endocarditis are treated timely, development of the valvular heart disease may be prevented.

In a grave course of rheumatism the affection of the myocardium and endocardium may combine with rheumatic pericarditis. Pericarditis may be dry or exudative.

Simultaneously (or several days later) the patient feels pain in the joints (mostly in large joints, such as the ankle, knee, shoulder, elbow joints, and in hands and feet). Affections of the joints are usually multiple and symmetric. The migrating character of pain is also characteristic: pain disappears in one joint and develops in others. **Rheumatic polyarthritis** is usually benign. Acute inflammation subsides in a few days, although dull pain in the joints may persist for a long time. Abatement of inflammation in the joints does not mean recovery because other organs become involved in the pathological process. The cardiovascular system is mostly involved, but the skin, lungs, liver, kidneys, and the nervous system may also be affected.

Examination of the patient with acute rheumatic fever reveals of skin (even at elevated temperature) and increased perspiration. In some patients, the skin of the chest, neck, abdomen and the face affected by **annular erythema** (pale-pink painless rings not elevating over the surrounding skin). In other cases nodular erythema develops: circumscribed indurated dark red foci on the skin varying in size from a pea to a plum; they are usually found on the lower limbs. In rare

cases, **rheumatic subcutaneous nodules** (firm, painless formations varying in size) can be palpated, mostly on the extensor surfaces of the joints find along the course of tendons. Lungs are affected in very rare cases. This is specific rheumatic of pneumonia. Dry pleurisy or pleurisy with effusion are more common.

The nervous system often involved in rheumatism. This is due to either rheumatic vasculitis (attended by small hemorrhages or thrombosis of cerebral vessels) or inflammation of the brain and the spinal cord. Children would develop encephalitis with predominant localization in the subcortical nodes (**chorea minor**). It is manifested by emotional liability and hyperkinesia (abnormal movements of the extremities, the trunk, and the facial muscles).

The alimentary system is rarely affected. Acute pain in the abdomen (the abdominal syndrome) associated with rheumatic peritonitis (mostly in children) sometimes occurs. Affections of the kidneys also common. Protein or red blood cells can befound in the urine due to affections of the renal vessels and frequently.

Additional methods of examination

Clinical blood analysis: leucocytosis, shift in the leucocytic formula to the left, eosinophilia, mono- and lymphacytosis may further develop and accelerated ESR.

Biochemical analysis of blood. Special laboratory tests help diagnose rheumatism.

- Dysproteinaemia characteristic: the albumin content drops below 50 per cent, the γ-globulin increases, and the albumin-globulin factor decreases below unity. A proteinogram shows increased α_2- and γ- globulin fractions;
- Fibrinogen content 0.6-1 per cent (normally it does not exceed 0.4 per cent).
- The C-reactive protein, which is absent in healthy individuals.
- The titres of antistreptolysine O, antistreptohyaluronidase, and antistreptokinase increase significantly.
- Increased levels of sialic acids, seromucoid, and gaptoglobin.

ECG: premature contraction, atrial fibrillation or flatter, decreasing of ECG voltage, depression of ST-segment, appearance of negative, asymmetrical T-wave is possible; elevation of ST-segment due to pericarditis or subepicardial damages of myocardium; different degrees of AV-blockade.

X-ray of heart and Echo-CG indicates enlargement of heart and its chambers.

MITRAL REGURGITATION

Mitral regurgitation develops due to incomplete closure of the left atrioventricular valve during systole. As a result, the blood is regurgitated from the left ventricle to the left atrium.

Mitral regurgitation may be organic and functional. Organic regurgitation arises as a result of rheumatic endocarditis. Connective tissue develops in the cusps of the mitral valve, which then contracts to shorten the cusps and the tendons. The edges of the affected valve do not meet during systole and part of the blood is regurgitated through the slit into the left atrium from the ventricle during its contraction.

In functional (relative) regurgitation the mitral valve is not altered but the orifice, which it has to close, is enlarged and the cusps fail to close it completely. Functional incompetence of the mitral valve may develop because of dilatation of the left ventricle (in myocarditis, myocardial dystrophy, or cardiosclerosis) and weakening of the circular muscle fibres that form the ring round the atrioventricular orifice. Affection of papillary muscles may also cause functional mitral regurgitation. Functional regurgitation thus depends on dysfunction of the muscles responsible for the closure of the valve.

Etiology

- rheumatic fever;
- bacterial endocarditis;
- atherosclerosis;
- congenital heart defects;

- mitral valve prolaps;
- perforation, rupture of the mitral valve, trauma of mitral cusps.

Disorders of hemodynamics

Disorders of hemodynamic occur because the bicuspid valve fail to close adequately and during systole of the left ventricle part of blood is regurgitated into the left atrium where added to the normal blood amount delivered from the pulmonary veins. This mitral regurgitation produces volume overload of the left atrium. Pressure in the left atrium increases (in normal 5-7 mm Hg), the atrium becomes hypertrophied. During diastole the amount of blood that is delivered into the left ventricle from the overfilled left atrium exceeds normal. The left ventricle has to perform excess work and become hypertrophied. In late stages of the disease, when the contractile power of the myocardium of the left ventricle weakens, diastolic pressure in it increases and this in turn increases significantly pressure in the left atrium, consequently overfills pulmonary veins, and develops hypertension in the lesser circulation and reflective contraction of the arterioles in the lesser circulation. The raised atrial and pulmonary venous pressure leads to pulmonary edema. Together with the spasm in the arterioles pressure in the pulmonary artery increases significantly. The right ventricle can therefore be hypertrophied. In case of progression of disease, the right ventricle is dilated and tricuspid regurgitation occurs.

Clinical features

Clinical features appear when near 10 ml of blood returns from the left ventricle into the left atrium. Most patients have no complaints for a long time and feel like healthy people. Than congestion in the lesser circulation develops, patient feels fatigue, exhaustion, palpitations of the heart, cough, exertional and nocturnal dyspnea.

Objective examination. *The patient's condition* is from satisfactory to grave. Consciousness is clear. Posture is active. In case of development of heart failure with congestion in lesser circulation the posture is active with restriction due to the dyspnea. In late stage may be forced posture - orthopnea. Acrocyanosis is determined.

Examination of respiratory system. Intermediate percussion sound, decreased vesicular breathing and fine bubbling rales, even crepitation are revealed over the low lobes of lungs due to the congestion as a signs of raised pulmonary capillary pressure and chronic pulmonary congestion.

Examination of cardiovascular system. In inspection of heart region the diffuse apex beat is determined, displaced to the left in V, sometimes VI intercostals space.

During palpation: the apex beat is diffuse, intensified and resistant due to hypertrophy of the left ventricle.

In percussion reveals displacement of the upper border of the relative cardiac dullness upward, left border to the left. In the late stage of disease the right border of *relative* cardiac dullness is displaced to the right due to hypertrophy of the right ventricle. The configuration of the heart becomes mitral with indistinct waist of the heart.

In auscultation reveals decreased first heart sound at the apex because the mitral valves never closed completely. In the late stage, when the blood pressure rises in the lesser circulation, the second heart sound is accentuated and may be splitted over the pulmonary trunk. Blood pressure does not change in compensated mitral incompetence. The characteristic sign of the mitral regurgitation: blowing, decreasing murmur, which is heard at the heart apex it synchronous with the first heart sound. Murmur arises during systole when the stream of blood passes a narrow slit leading from the left ventricle to the left atrium. Murmur can be transmitted in the left axillary region and along the left edge of the sternum, it becomes more intensive after physical exertion, in lying position on the left side during deep expiration.

Complications of mitral regurgitation, acute pulmonary edema, atrial fibrillation/flutter very rare, chronic left ventricular and atrial failure, chronic right ventricular heart failure and chronic total ventricular heart failure.

Additional methods of examination

X-ray examination: smoothed of the left border due to protrusion of the left atrium auricle, moderate enlarging of the pulmonary trunk, protrusion of the left low arch, narrowing of the retrocardial space in the second oblique position, declining of the esophagus on the radius, signs of pulmonary venous hypertension.

ECG: signs of hypertrophy of the left atrium and left ventricle.

Phonocardiogram taken at the apex shows diminished amplitudes of the first sound; the amplitude of the second sound over the pulmonary artery increases compared with that over the aorta; decreasing systole murmur at the heart apex it synchronous with the first heart sound.

Echo-CG: dilatation of the left parts of heart, excursion of the atrioventricular partition and back wall of the left ventricle, different direction of the diastolic motion of mitral valve, unclosing them during systole. Four degrees of mitral regurgitation are distinguished (from 2 up to 5 cm and above).

MITRAL STENOSIS

Mitral stenosis develops due to narrowing of left atrioventricular orifice.

Etiology

- Rheumatic heart disease;
- Bacterial (infectious) endocarditis.

Disorders of hemodynamics

Disorders of hemodynamics: due to pathological process, the adhesion of the mitral cusps, it consolidation, thickening and shortening narrow the left atrioventricular orifice. In patient with mitral stenosis orifice becomes 1.5 sm^2 and less instead of normal 4-6 sm^2. Narrowing of an orifice is a mechanical obstacle for a flow of blood from the left atrium to the left ventricle during diastole. The part of blood remains in the left atrium. Besides blood from pulmonary veins comes into the left atrium. In the left atrium the volume of blood is increased (in norm 50-60 ml, at narrowing 100-2000 ml), pressure raises (in norm - 5-7 mm Hg, at narrowing - 20-25 mm Hg). So the left atrium hypertrophies. However the muscle of a hypertrophied left atrium weak, therefore its contractile function reduces soon. It leads to dilation of the left atrium and increasing of venous pressure in pulmonary veins and capillaries. Increased pressure elevates in the pulmonary veins leads to irritation of baroreceptors, and causes reflex contraction of the arterioles in the lesser circulation (Kitaev's reflex), so pressure in the pulmonary trunk considerably rises, so called pulmonary hypertention. Pulmonary hypertension leads to a hypertrophy of the right ventricle, and subsequently and to its dilation. The left ventricle receives less blood in diastole, its size a little decreases and diastolic dysfunction develops.

Clinical features

The specific complaints of the patients with mitral stenosis: exertional and nocturnal dyspnea, cough, palpitation, pain in the heart. Symptoms secondary to arterial/venous emboli are hemoptysis, chest pain. Symptoms of diminished cardiac output are fatigue, tiredness.

Objective examination. In general inspection patient looks younger his age, the mitral face is observed. The characteristic of face: the cyanotic blush on the cheecks.

Examination of the respiratory system reveals the congestion in lesser circulation - moist rales in low lobes of lungs.

Examination of the cardiovascular system In inspection of heart region the spread pulsation in the III-IV intercostals space along left edge of sternum with synchronous pulsation in the epigastric region are detected. During palpation apex beat is of normal location, area, height and strength. Cat's purr symptom is characteristic for mitral stenosis. Diastolic thrill is palpated at the apex.

In percussion relative cardiac dullness is displaced to the right and upward, protrusion of the upper part of the left contour, indistinct waist of the heart, increasing of absolute cardiac dullness area.

In auscultation the first heart sound at the apex becomes loud and snapping, because the left ventricle receives little amount of blood and fast closing of fibrous cusps of the mitral valve. An additional sound due to the opening of the mitral valve, which would be explained by sclerosed and connected among themselves cusps. The loud first heart sound, second sound with the sound of opening of the mitral valve give a specific melody of mitral stenosis so called triple rhythm at the apex. The second sound becomes accentuated and splitted over pulmonary artery. At some patients with mitral stenosis cardiac rhythm is irregular, because mitral stenosis is often complicated with atrial fibrillation.

Diastolic murmur at the apex is sign of the mitral stenosis because the orifice from the left atrium to the ventricle during diastole is narrowed. This murmur can be heard to follow the mitral valve opening sound in early diastole (protodiastolic murmur - noise of filling) because the velocity of the flow in early diastole is higher due to the decreased pressure difference in the atrium and the ventricle. The murmur can be heard at the end of diastole, immediately before systole (presistolic). It arises during acceleration of the blood flow at the end of ventricular diastole.

Pulse on the radial arteries may be asymmetrical (p. differens) because the left subclavia artery is compressed by considerable hypertrophy of the left atrium. Blood pressure usually remains normal.

Complications of mitral stenosis: atrial fibrillation, flutter, arterial or venous emboli with massive pulmonary, cerebral, peripheral thromboembolism, acute pulmonary edema, chronic left atrial heart failure, right ventricle heart failure.

Additional methods of examination

X-ray examination: disappearing of the heart waist, enlarged of the left atrium auricle, enlarged of the right ventricle, protrusion of the pulmonary trunk. Narrowing of the retrocardial space in the first oblique position, declining of the esophagus on the small radius and congestion changes are revealed.

ECG: hypertrophy of the left atrium and right ventricle.

Echo-CG:

- the unidirectional movement both cusps of the mitral valve in diastole;
- change of flow character through the mitral orifice in diastole (a turbulent stream);
- narrowing of the orifice of the left atrioventricular valve. At the healthy middle-aged person diameter and square of mitral orifice is from 4 up to 6 cm^2 and from 2 up to 3 cm^2 accordingly;
- thickened immobile cusps of mitral valve;
- reduced rate of diastolic filling,
- reduced valve area.

Phonocardiogram taken at the apex shows the high amplitude of the first sound; the second sound is followed by the mitral valve opening sound and diastolic murmur; the amplitude of the second sound over the pulmonary artery increases compared with that over the aorta. If PCG and ECG are taken synchronously, attention should be paid to the length of the interval Q-I sound (from the beginning of the *Q* wave on the ECG to the first sound on the PCG) and the second sound - OS interval.

AORTIC STENOSIS

Aortic stenosis develops due to the narrowing of the aortic orifice resulted from different origin.

Etiology:

- bacterial endocarditis;
- atherosclerosis,
- congenital aortic stenosis (subvalvular and supravalvular);

- muscular obstructive hypertrophic cardiomyopathy.

Disorders of hemodynamics

At the expressed narrowing of the aorta orifice, when its area decreases up to 1.0-0.75 cm^2 (in norm 3 cm^2) during systole left ventricle does not empty completely. The gradient of systolic pressure between the left ventricle chamber and an aorta is increased. It exceeds 20 mm Hg. sometimes 100 and more.

At narrowing of aortic orifice the minute volume of blood is reduced. In diastole to this remained blood in the ventricle the normal amount of blood from the left atrium is added that lead to overfilling of left ventricle with blood and to increase of pressure in it. Systolic pressure in the left ventricle raises proportionally degrees of narrowing of the aorta orifice (in norm 120 mm Hg, at narrowing raises in 1.5-2 times in comparison with a normal amount and may reach 250-300 mm Hg). This disorders of heart hemodynamics is compensated by the strengthened work of the left ventricle and causes its hypertrophy. Coronary blood flow may become inadequate.

Due to good compensatory abilities of the left ventricle asymptomatic course of this disease may last 10-15 years. At reduction contractile abilities of myocardium develops dilatation of the left ventricle, later relative insufficiency of the mitral valve adds, with regurgitation of blood in the left atrium. First there is an intimate insufficiency in the lesser, and then in the lager circulation.

Clinical features

Patient complains on pain in the heart (angina type pain) due to the considerable insufficient blood ejection into the arterial system which upset normal blood supply to the hypertrophied myocardium of left ventricle. Disordered blood supply to the brain is manifested by giddiness, headache, and tendency to fainting. During sudden decrease of contractile ability of left ventricle may occur acute left ventricles heart failure with clinical signs of cardiac asthma and even pulmonary edema.

Objective examination. In general inspection the patient is pallid.

Examination of the cardiovascular system. The apex beat is displaced to the left, less frequently interiorly, it is diffuse, high and resistant. Systolic thrill (cat's purr symptom) can be palpated over the aorta. Percussion reveals displacement of the left border to the left, the heart configuration is "aortic" due to considerable hypertrophy of the left ventricle.

Auscultation of the heart at apex reveals diminished first heart sound due to the overfilling of the left ventricle and prolongation of systole.

The second sound is diminished over the aorta because the aortic cusps adhere and are immobile, the second sound can be inaudible.

Rough systolic murmur over the aorta is characteristic. This murmur is generated by the blood flow through the narrowed orifice. It is conducted by the blood on the a. carotis and can sometimes be heard in the interscapular space.

The pulse is small, slow and rare, since the blood slowly passed into the aorta and its volume is decreased.

Systolic blood pressure is usually diminished, while diastole remains normal or increased.

Complications: sudden cardiac death, cardiac asthma, pulmonary edema, heart failure due to "mitralization" of aortic stenosis.

Additional methods of examination

X-ray examination shows hypertrophied left ventricle, "aortic" configuration of the heart and post-stenotic dilatation of the ascending aorta, the cusps of the aortic valve are often calcified on lateral view.

The phonocardiograph shows the specific changes in the heart sounds diminished amplitudes of the first sound at the heart apex and of the second sound over the aorta. Systolic murmur over the aorta is typical; its oscillations are recorded in the form of specific diamond-shaped figures.

EchoCG: Great number of echo-signals into the aorta space that is related to deformation and quite often calcinosis of aorta valve cusps. Dilation of the left ventricle, enlarging of its back wall and interventricular septum are determined. Doppler-cardiography reveals high-speed flow in stenotic orifice (flow speed may reach 200-500 cm/sec), and also allows to measure a gradient of pressure through aortic orifice.

AORTIC REGURGITATION

Aortic regurgitation is defined as incomplete closing of aortic valve during diastole that lead to retrograde blood flow from the aorta into the left ventricle.

Etiology

- bacterial endocardidis;
- rheumatic endocarditis;
- syphilis of the aorta;
- atherosclerosis of the aorta;
- Marfan's syndrome.

Disorders of hemodynamics

During diastole the blood is delivered into the left ventricle not only from the left atrium but also from the aorta due to regurgitation, thus the left ventricle during diastole overfills. The amount of returning blood can reach from 5 up to 50 % of volume of the left ventricle. There is a significant overload of the left ventricle with volume (systolic volume may reach 200 ml and more). During systole the left ventricle has to contract with a greater force in order to expel the large volume of blood into the aorta. Insufficiency of the aortic valve for a long time may be compensated by the strengthened work of hypertrophied powerful left ventricle. In case of intense regurgitation of the blood that moves aside the mitral valve is formed functional mitral stenosis. During progression of disease increased systolic volume at left ventricle causes its dilation. At longstanding course the disease may be accompanied by functional incompetence of mitral valve with regurgitation of blood in left atrium, which is hypertrophied as response to overloading. This is mitralization of aortic regurgitation.

Clinical features

Patient complains on pain in the heart is due to the relative coronary insufficiency because of pronounced hypertrophy of the myocardium and inadequate filling of the coronary artery under low diastolic pressure in the aorta. Dizziness, headaches, syncope are the results of deranged blood supply to the brain.

In condition of decreased contractile ability of left ventricle the attacks of cardiac asthma occur. The signs of "mitralization" of cardiac regurgitation are dyspnea, cough.

Objective examination. In general inspection may observe such signs:

- the skin of the patient, especially on face, is pallid due to the insufficient filling of the arterial system during diastole, pulsation of the peripheral arteries (carotid, subclavian, brachial, temporal) as a result of marked variation blood pressure in the arterial system during systole and diastole;
- rhythmical movement of the head synchronous with the pulse (de Musset's sign).
- rhythmical change in the color of the nail bed under a slight pressure on the nail end, so-called capillary pulse - Quincke's pulse;
- rhythmical reddening of the skin after rubbing.

Objective examination of the cardiovascular system:

- the apex beat is almost always enlarged and shifted to the left and inferiorly;
- the apex beat is palpable in the sixth and sometimes seventh intercostals space, outside the left midclavicular line, even till the axillary line;
- the apex beat is diffuse, intense, rising like a dome due to the significant enlargement of the left ventricle.

In percussion - the border of the cardiac dullness can be found shifted lo the left. The heart becomes "aortic" with pronounced waist of the heart.

In auscultation reveals decreased first heart sound at the apex because the period when the valves are closed is absent. The second sound on the aorta is also weak due to the damage of the valve. Protodiastolic murmur is heard over the aorta and at the Botkin-Erb's listening point.

Murmurs of functional etiology can also be heard in aortic incompetence at the heart apex. If the left ventricle is markedly dilated, relative mitral incompetence develops and systolic murmur can be heard at the heart apex. Diastolic murmur (presystolic or Austin Flint murmur) can sometimes be heard. It arises due to an intense regurgitation of the blood that moves aside the mitral valve cusp to account for functional mitral stenosis. At auscultation of femoral artery double Traube's tone is heard due to rapid systolic tension and dilation of artery. In case of pressure femoral artery by stethoscope double Vinogradov-Duroziez's murmur can be heard - femoral bruit ("pistol shot").

Blood pressure: systolic pressure rises, diastolic decreased, pulse pressure is therefore high.

Pulse - fast, high large volume (pulses celer and altus).

Complications: cardiac asthma, pulmonary edema, chronic heart failure due to the "mitralization" of aortic regurgitation.

Additional methods of examination

ECG: hypertrophy of the left ventricle: the electrical axis is deviated to the left, the S-wave in the right chest leads are deep and the amplitude of the R-wave is higher in the left chest leads, relative coronary insufficiency: depressed of the ST-interval, inverted T-wave.

X-ray: protrusion of the left ventricle arch, heart apex rounding, marked heart waist, (heart configuration is duck-like), narrowing of the retrocardial space in the second position.

The phonocardiograph shows the specific changes in the heart sounds diminished amplitudes of the first sound at the heart apex and of the second sound over the aorta. Protodiastolic murmur over the aorta and at the Botkin-Erb's listening point is typical.

Echo-CG: dilated left ventricle, retrograde blood flow through the aortic valve into the left ventricle during diastole.

Topic 2. The Main Syndromes and Symptoms of Arterial Hypertension. Hypertenic Crisis.

Arterial hypertension (WHO/1999), essential hypertension, secondary hypertension. The risk main factors of arterial hypertension and mechanism of the development. Modern classification of arterial hypertension. The main complaints of the patients with arterial hypertension, external examination, palpation, percussion, auscultation of the patients with arterial hypertension. ECG-signs of the changes in myocardium in the patients with arterial hypertension. Secondary hypertension. Hypertonic crisis.

SYNDROME OF THE ARTERIAL HYPERTENSION

Arterial hypertension is defined as elevation systolic blood pressure (SBP) to 140 mmHg and higher and diastolic blood pressure (DBP) to 90 mmHg and higher in case of stable elevation confirming on repeating measurement blood pressure (2-3 times in different days during 4 weeks).

Classification on etiology:

1. Secondary (symptomatic) hypertension.
2. Essential arterial hypertension.

Symptomatic arterial hypertension

Symptomatic arterial hypertension causally related to the diseases with damages of some organs, participating in regulation of arterial pressure.

Causes of secondary hypertension

1. Renal diseases:

- parenchymal and interstitial diseases of kidneys (glomerulonephritis, chronic pyelonephritis, diabetic nephropathy, amyloidosis, hydronephrosis, postradiation nephrosclerosis):

- *renovascular* pathology (atherosclerosis of kidney artery, fibromuscular dysplasia, aortoartentis, vasculitis, endarteritis, thrombosis, embolism, aneurysm of kidney artery, stenosis and thrombosis of veins, trauma of kidney vessels);

- *anomalies* of kidney and urinary tract (polycystosis, hypoplasia, anomalies of urinary system);

- *secondary damage* of kidneys at tuberculosis, bacterial metastases and diffuse diseases of connective tissue (lupus, system sclerodermia).

2. Endocrine hypertension:

phaeochromocytoma;
primary hyperaldosteronism (Conn's syndrome);
idiopathic hyperplasia adrenal cortex (pseudoprimary hyperaldosteronism);
Cushing's disease (syndrome);
hyperparathyroidism;
acromegaly;
climacteric hypertension.

3. Hemodynamic hypertension:

atherosclerosis of aorta;
stenosis of carotid and vertebrobasilar arteries;
coarctation of aorta;
aortic regurgitation;
rheological hypertension (polycythemia vera).

4. Neurogenic hypertension:

vascular diseases and tumors of brain;
inflammatory diseases (encephalitis, meningitis, polyomyelitis);
trauma of brain (postcontusional syndrome);
polyneuritis.

5. Special forms of second hypertension (after taking some medicines: anabolic steroids and mineralocorticoids, oral contraceptives, containing progesterone and estrogen, sympathomimetic agents, indometacin and other).

Clinical features

Among all hypertensive states secondary arterial hypertension make approximately 20 %.

Chronic glomerulonephritis meets more frequent in young and middle ages. In anamnesis is acute glomerulonephritis. Clinical features of the glomerulonephritis - proteinuria more than 1 g/day, hematuria, impairment of renal function (early onset with hypo- and isostenuria) and hypertension (mostly increasing of diastolic pressure). Angina pectoris, myocardial infarction and stroke are rare. Rethinopathy develops comparatively lately, arteries are only slightly narrowed, veins are normal. But anemia, which atypical for essential hypertension, is often marked. Final establishment of diagnosis based at the result of isotopic renovasography and biopsy of kidneys, which finds out fibrioblastic, proliferative, membranouse and sclerotic changes in glomerules, tubes and vessels of kidneys.

Chronic pyelonephritis - is a chronic interstitial nephritis resulting from urinary tract infection associated with vesico-uretric reflux. In anamnesis are nephrolitiasis, pyelitis, anomalies of development at kidneys and other diseases of urinary tract. The most important among the morphological features is presence of coarse scars, which is associated with contraction of the related papilla and dilatation of the corresponding calyx. In the half of cases pyelonephritis is accompanied by arterial hypertension. Difficulty of diagnostics of chronic pyelonephritis consists of that in 1/3 cases the signs of inflammatory process in urinary ways are not observed. Diagnosis based at the following signs: hypostenuria, polyuria, pyuria, proteinuria, information of isotopic reno-, urography, ultrasound examination (diminishing of sizes of kidneys, deformation of the tubular

system), biopsy of kidneys and angiography. From the general features of course of disease: young age, primary increase of diastolic pressure, absence of coronary and cerebral complications.

Diagnostic criteria of the renoparenhimal hypertension: pointing in anamnesis on the previous pyelonephritis, glomerulonephritis, nephropathy at pregnant, nephrolytiasis and other diseases of kidneys; characteristic changes of laboratory, instrumental and morphological examination of kidneys and also positive hypotensive effect from specific therapy of kidney disease.

Diagnostic criteria of the renovascular hypertension: high systolic hypertension, refractory to treatment; in auscultation - systolic murmur over the abdominal aorta and especially in the area of projection of kidney arteries; small sizes of one kidney (ultrasound and urography); disorders of contrast distribution at kidney (at intravenous urography); high level of renin in plasma of blood; narrowing of the (one or both) kidney arteries (angiography).

Phaeochromocytoma - is a rare tumor of the chromaffin tissue which secretes catecholamines and is responsible for less than 0,1 % of causes of hypertension. The tumors are usually benign (10 % malignant) and may arise from any part of the sympathetic chain. In over 90 % of causes the tumor is found in the adrenal medulla.

Clinical features: hypertension usually paroxysmal.

Diagnostic criteria of the phaeochromocytoma: transitional arterial hypertension with the signs of activation of the sympathetic nervous system (excitation, trembling, increasing of body temperature), leucocytosis, hyperglicemia. Stable character of arterial hypertension does not exclude phaeochromocytoma; negative effect from therapy with beta-blockers; positive provocative tests (histamine, injected intravenously in a dose 0,05 mg in 0,5 ml of isotonic solution, causes an increase blood pressure on 60/40 mmHg during the first 4 min; palpation of kidney region provokes hypertensive crisis) and test with alpha-adrenoblockers; enlargement of adrenal glands from data of ultrasonic research, computer tomography; finding out the high level of adrenalin, noradrenalin. Tumor of adrenal gland found out by the instrumental methods.

Primary hyperaldosteronism *(Conn's syndrome)* is characterized by overproduction of aldosterone, the main salt-retaining hormone, may be due to a primary abnormality in the zone glomerulosa or secondary to stimulation of aldosterone secretion by angiotensin II following activation of the renin-angiotensin system.

Diagnostic criteria of the primary hyperaldosteronism (Conn's syndrome): high blood pressure; muscular weakness and neuro-muscular disorders (paraestesia, occasionally tetany because of the metabolic alkalosis with low ionized calcium, transient para- and tetraplegia); polyuria, nicturia, thirst; hypokaliemia, hypernatriemia, increase of potassium level in blood after the test with veroshpiron; alkaline reaction of urine; the low level of plasma renin; diminishing of tolerance to glucose, rarer is obvious diabetes mellitus; finding out the tumor at the adrenal gland by ultrasonic investigation, computer tomography, radioisotope scanning of adrenal glands; level of the aldosteron in blood and urine (their increase to 100 mg/ml and to 150 mg/day, respectively).

Cushing's syndrome — is defined as the symptoms and signs associated with prolonged inappropriate elevation of free corticosteroide level. Patients with Cushing's syndrome can be classified into two groups on the basis of whether the condition is adrenocorticotropic hormone (ACTH)-depended or independed:

1. *ACTH-depended:*
   - iatrogenic (ACTH-therapy);
   - pituitary-depended bilateral adrenal hyperplasia (Cushng's disease);
   - ectopic ACTH syndrome (benign or malignant non-endocrine tumour).
2. *non-ACTH-depended:*
   - iatrogenic (prednisolone therapy);
   - adrenal adenoma;
   - adrenal carcinoma.

Diagnostic criteria of the dishing s syndrome: general inspection: persons with overweight, obesity, thinning hair, hirsutism, acne, plethora, moon face, presence of purple-violet striates on the

skin of abdomen, thighs, in area of armpits; examination of organs and systems: arterial hypertension, psychosis, cataracts, peptic ulcer, osteoporosis, exuberant callus with fractures, wasting and weakness of the proximal thigh muscles, menstrual disorders; disorder of tolerance to glucose, hyperglycemia; changing in the normal day's rhythm of secretion of ACTH and Cortisol (in a norm in the morning higher, than in the evening), increasing the level of Cortisol and 17-OKS is in blood.

Hemodynamic arterial hypertension is associated with demanding of the heart and large vessels and subdivides into:

- systolic hypertension at atherosclerosis, aortic regurgitation;
- regional hypertension at aorta caorctation;
- hyperkinetic circulatory syndrome at arteriovenouse fistulas.

Diagnostic criteria of the hemodynamic arterial hypertension: Arterial hypertension as a result of atherosclerosis of aorta is diagnosed on the basis of the followings signs: elderly patients, accented of second heart sound and its metallic tint over the aorta, systolic murmur over the aorta, increased systolic arterial pressure, presence the signs of atherosclerosis of peripheral arteries; expansion of aorta detected by ultrasound and X-ray examination.

Arterial hypertension under aortic regurgitation characterized by increased of systolic blood pressure and the decreased diastolic with high pulse pressure.

Arterial hypertension as a result of aorta coarctation is characterized by increasing of blood pressure at the upper extremities and it's decreasing at the lower extremities. In palpation - over the intercostal arteries intensification of pulsation is marked, loosening the pulsation at the peripheral arteries of lower extremities is observed; in auscultation - rough systolic murmur is heard at heart base, over the pectoral aorta (at the anterior chest wall and in interscaspular region), irradiated along the large vessels (carotid, subclavia).

ESSENTIAL HYPERTENSION

Essential hypertension (hypertension) is a disease of the cardiovascular system, which develops due to primary dysfunction of the vascular regulatory centers and subsequent involment of neurohumoral and kidney mechanisms, characterized by arterial hypertension, functional, and at the expressed stages - by the organic changes of kidneys, heart and central nervous system. The essential hypertension can be diagnosed after exception of symptomatic (secondary) hypertension.

Predisposing factors: genetic factors; disorders of the nervous and endocrine systems, obesity; alcohol; smoking; hypodynamia; elderly age; professional factors: noise and vibration; hormonal factors: increased renin, reduced nitric oxide release.

Etiology

Acute and chronic psychoemotional stress, permanent mental overstrain, hypoxia of brain of any origin, age related neuroendocrine rebuilding (climacterium), salt abuse.

Pathogenesis

Elevation of blood pressure arise due to the imbalance between pressor and depressor factors which lead to development of changes in arterioles and precapillares, changing structure and function of cellular membranes, including smooth muscular cells of arterioles, disorders of activity of sodium-calcium pumps, increasing concentration of the ionized calcium in cytoplasm and finally excessive vascular resistance.

Classification

Classification of hypertension according to blood pressure level

Category	SBP(mmHg)		DBP(mmHg)
Optimal	< 120	and	< 80

Normal BP	120-129	and/or	80-84
High normal	130-139	and/or	85-89
Grade I hypertension	140-159	and/or	90-99
Grade II hypertension	160-179	and/or	100-109
Grade III hypertension	≥180	and/or	≥110
Grade IV hypertension	≥140	and	< 90

Classification of hypertension by extent of organ damage

Stage I	No objective signs of organic changes
Stage II	At least one of the following signs of organ involvement without symptoms or dysfunction: - left ventricular hypertrophy (electrocardiogram, ultrasound); - generalized and focal narrowing of the retinal arteries; - proteinuria and/or slight elevation of plasma creatinine concentration (1,2- 2,0 mg/dl or to 177 mmol/1); - ultrasound or radiological evidence of atherosclerotic plaque (carotid arteries, aorta, iliac and femoral arteries).
Stage III	Both symptoms and signs have appeared as result of organ damage. These include: - heart (myocardial infarction, heart failure); - brain (stroke, transient ischemic attack, encephalopathy, vascular dimension); - optic fundi (retinal hemorrhages and exudates with or without papillodema); - kidney(plasma creatinine concentration more than 2,0 mg/dl or 177 mmol/1); - vessels (dissecting aneurysm, symptomatic arterial occlusive diseases).

Clinical features

Complaints: pain at the heart, palpitation, headache, dizziness, disorder of vision. At the expressed left ventricular failure - attacks of dyspnea.

Objective examination. *General patient condition* is usually satisfactory. On progression of disease and appearance of complication general patient's condition may be from middle grave to grave (hypertension crisis, acute and chronic heart failure and cerebral attacks).

The color of the skin may be hyperemic. As usually the patients are overweight. At development of heart failure acrocyanosis and peripheral edema are observed.

Objective examination of the cardiovascular system. Apex beat is displaced to the left and downwards, diffuse, high. Displacement of the left border of the relative cardiac dullness to the left is observed. Increased loudness of the first heart sound at the heart apex and accentuated second heart sound over aorta are heard. At the presence of heart failure the gallop rhythm is heard. Blood pressure > 140/90 mm Hg. Pulse is firm tension (p. durus).

Protocol of diagnostic procedures for patients with hypertension I-II stages

Obligatory examination:

- inquiry;
- physical examination: measurement of blood pressure on both hands, measurement of blood pressure on lower extremities at persons younger 45 years; measurement of body weight of and waist circumference;
- laboratory routine examination hemoglobin and hematocrit, clinical urine analysis, Nechiporenko's test, Zemnicky's test, biochemical blood analysis: serum creatinine, serum potassium, serum total cholesterol, serum low density lipoprotein (LDL) cholesterol, serum high density lipoprotein (HDL) cholesterol, fasting serum triglycerides;
- ECG in 12 standard leads;
- echocardiography;
- fundoscopic examination.

Special examination:

- determination of microalbuminuria;
- daily proteinuria;
- ambulatory blood pressure measurement using monitor;
- ultrasound examination of kidneys.

Protocol of diagnostic procedures for patients with hypertension III stages

Obligatory examination:

- inquiry;
- physical examination: - measurement of blood pressure on both hands, measurement of blood pressure on lower extremities at persons younger 40 years;
- measurement of body weight and waist circumference;
- laboratory routine examination hemoglobin and hematocrit, clinical urine analysis, Nechiporenko's test, Zemnicky's test, biochemical blood analysis: serum creatinine, serum potassium, serum total cholesterol, serum low density lipoprotein (LDL) cholesterol, serum high density lipoprotein (HDL) cholesterol, fasting serum triglycerides;
- ECG in 12 standard leads;
- echocardiography;
- examination of the eyes;
- X-ray examination of the chest;
- ultrasound examination of kidneys.

Special examination:

- ambulatory blood pressure measurement using monitor;
- doppler-ultrasound scanner of extracranial vessels;
- computer tomography and magnitoresonance tomography of head;
- in case of coronary heart diseases - cardioventnculography.

Additional methods of examination

Clinical blood analysis: at the prolonged course of hypertension occur hypertensive polycytemia - increased hemoglobin and hematocrit are possible.

Biochemical blood analysis: at development of kidney failure there is increasing level of creatinine.

Clinical urine analyses: at development of nephroangiosclerosis and renal failure - proteinuria, microhematuria, hypo-, isostenuria in Zimnitsky's test.

ECG: the left ventricle hypertrophy, depressed ST-segment, inverted or two-phase T-wave in the 1st and 2nd standard, V_5-V_6 chest leads.

X-ray examination of heart. In the initial period of hypertrophy, rounding of apex of the left ventricle is find out. All chambers of heart are dilated in the late stages.

Echocardiography: hypertrophy of the interventricular septum and the back wail of the left ventricle, decrease of contractility of the myocardium, increase end systolic and diastolic dimensions of the left ventricle.

Ophthalmoscopy is revealed angioretinopathy.

Topic 3. **Ischemic Heart Diseases, Main Symptoms and Syndromes at Angina pectoris and Myocardial infraction.**

Determination of Ischemic Heart Diseases. Main pathogenesis mechanisms of Ischemic Heart Diseases, Basic risk factors of Ischemic Heart Diseases. Modern classification of Ischemic Heart Diseases. Determination and main symptoms of angina pectoris. Functional classes of angina pectoris. Objective diagnostic methods of angina pectoris (ECG, Monitor- controlling 24 hours – ECG, Exercise test, Scintigraphy of heart, Coranarigraphy). Unstable angina pectoris, definition of unstable angina pectoris and main clinical signs and symptoms of unstable angina pectoris. Determination of acute coronary symptoms. Determination of main clinical signs of acute

myocardial infraction. Physical examination methods of patients with acute myocardial infraction. Stages of myocardial infraction. ECG-changes in different forms of myocardial infraction. Modern bio-markers of necrosis of myocardium.

ISCHEMIC HEART DISEASE

Ischemic (coronary) heart disease (IHD)- define as acute and chronic heart damage, caused due to diminishing or stopping blood delivery to myocardium. Disease of the coronary arteries is almost always due to atheroma and its complications, particularly thrombosis.

Etiology and pathogenesis

Atherosclerosis of coronary arteries; the degree of its expression is different -from small wall affection to complete occlusion of vessel.

Spasm of coronary arteries develops, as a rule, on a background of atherosclerosis of coronary arteries. The physical overloading, mental stress provokes the development of clinical features of IHD.

The main pathophysiological mechanism of IHD is imbalance between the demand myocardium in oxygen and possibilities of coronary arteries satisfied the myocardium by adequate amount of blood.

The followings mechanisms are involved in pathological process:

- mechanical occlusion of coronary arteries due to an atherosclerotic process;
- dynamic occlusion of coronary arteries due to coronarospasm;
- activation of thrombocytes aggregation with development of microagregates in microcirculation;
- promotion of production the pro-coagulating factors, insufficiently level of prostacyclin and endothelin- derived relaxing factor;
- increasing of demand myocardium in oxygen under influencing of the intensive physical loading, mental stress, resulting in the high level catecholamines in blood caused cardiotoxic action;
- insufficiency of collateral circulation of blood;
- activation of the lipid peroxidation;
- activation of immune mechanisms.

Thus the pathological substrate of IHD is almost atheroma narrowing of the coronary arteries. Atheroma or atherosclerosis is a focal disease of the arterial intima. There are some stages of evolution of atherosclerotic process. Initial stage is fatty streaks, which develop as circulating monocytes migrate into the intima take up oxidized low density lipoprotein from the plasma and become lipid foam cells. As these foams cells die extracellular lipid pools appear. Smooth muscle cells then migrate into and proliferate within the plaque. A mature fibrinolipid plaque has a core extracellular lipid, separated from the lumen by a thick cap of a collagen-rich fibrous tissue. Such plaque may narrow the lumen of the vessel and often precipitate local vasospasm and thrombosis. The luminal diameter of a coronary artery must be decreased by at least 50 % to 70 % before blood flows becomes inadequate to meet the metabolic demands of the heart during exercise or stress.

The evolution of the atheromatous plague corresponds with clinical forms of IHD. The principal cause of *stable angina* is atherosclerosis involving at least one large epicardial artery that limited coronary flow under some condition. Stable angina is related to a fixed obstruction and it is usually precipitated by an increase in myocardial oxyden demand (demanded ischemia).

Unstable angina is defined as an obstruction of at least one major epicardial artery that occupies at least 70 % of the artery's cross-sectional diameter or an obstruction of the left main coronary artery that occupies at last 50 % of its diameter. Episodes of myocardial ischemia are due to abrupt reduction in coronary blood flow results from plaque rupture, rapid growth of the lesion or incomplete occlusion of the vessel. Unstable angina is a transitory condition. A platelet rich thrombus forms rapidly around the site of the rupture, reducing, but not usually occluding the blood flow in the vessel.

Myocardial infarction is almost always due to the formation of occlusive thrombus at the site of rupture of an atheromatous plaque in a coronary artery. The affected artery is more commonly completely occluded, usually by a fibrin-rich "red" thrombus.

Sudden death in most cases is attributable to IHD and is usually due to arrhitmia or asystole (ventricular fibrillation, sinoatrial block, complete AV-block) related to acute coronary syndrome, heart failure or scarring from a previous myocardial infarction.

Classification of ischemic heart disease (IHD)

1. Sudden cardiac death.
2. Angina pectoris:
stable angina pectoris;
vasospastic angina (Princmetala's);
unstable angina.
3. Myocardial infarction (Ml):
acute Q-wave Ml;
acute non-Q-wave MI;
-subendocardial MI;
acute MI (undetected);
- recurrent MI (3-28 days);
- repeated MI (after 28 days).
4. *Postinfarction cardiosclerosis faction.*
6. Cardiac arrhythmia.
7. Painless form of the IHD.

STABLE ANGINA

The 2002 American College of Cardiology/American Heart Association (ACC/AHA) guideline update defined chronic stable angina as a clinical syndrome characterized by discomfort in the chest or adjacent areas caused by myocardial ischemia typically aggravated by exertion or emotional stress and relieved by rest or by nitroglycerin. Patients often describe their symptom as discomfort rather than pain.

Clinical features

The main parameters of pain in patients with stable angina are: location, character, intensity, duration, frequency, radiation, associated symptoms and cause of onset, aggravating and relieving factors. The typical location of angina is mid or lower part of sternum. Less typically, discomfort may occur in the epigastric area. The discomfort is usually described as pressure, tightness, heaviness, strangling, constricting, burning, squeezing, suffocating and crushing.

The severity of the discomfort varies greatly. The pain may radiate in arm to the wrist and fingers, lower jaw or teeth, throat, between the shoulder blades. The duration of the discomfort is brief, not more than 10 min in the majority of cases and more commonly even less. Angina equivalents are common and include dyspnea, faintness, and syncope. Chest discomfort may be accompanied by less specific symptoms such as nausea, burping, restlessness, or a sense impending doom. Frequency of the pain may be different.

An important characteristic is the relation to exercise, specific activities, or emotional stress. Symptoms classically triggered by increased levels of exertion, such as walking up an incline or against a breeze, and rapidly disappear within a few minutes, when these causal factors abate. Exacerbations of symptoms after a heavy meal or work are classical features of angina. Buccal or sublingual nitrates rapidly relieve angina.

For patient with stable angina it is useful to classify the symptoms using a grading system which was devised by the Canadian Cardiovascular Society, based on the severity of the angina stressor.

Canadian Cardiovascular Society classification of stable angina

Class	Severity of exertional stress including angina	Limitation ordinary activity
I	Strenuous rapid or prolonged exertion	None

	at work or recreation	
II	Walking or climbing stairs rapidly, walking uphill, walking or stair climbing	Slight
III	Walking one to two blocks on the level and climbing one flight of stairs in normal condition and at a normal pace	Marked
IV	Symptoms may be present at rest	Discomfort in all activity performed

Objective examination. During the attack of stable angina the patient's condition is moderate, clear consciousness, standing up right position (if the patient walking), or sitting position with hand placed over sternum. Patient's face is pale with cyanotic tint. Arcus senilis, xanthelasma are revealed. Extremities are cold.

In auscultation of lung may be detected bilateral basal rales. Apex beat displaced outside. The left border of relative cardiac dullness displaced. Both heart sounds are decreased, paradoxically split S, and sometimes may be arrhythmia. premature beat, atrial fibrillation. The clinical features of stable angina are abnormal carotid pulse, decreased peripheral pulse, jugular venous distension. In some patients observe hepatomegaly, pedal edema.

Additional methods of examination

Clinical blood analysis is without change.

Biochemical analysis in patients with stable angina may show elevated level of cholesterol, triglycerides, decreased high density lipoprotein cholesterol and increased low density lipoprotein cholesterol. Biochemical markers of myocardial damage in stable angina are in a normal range.

X-ray examination in stable angina does not provide specific information for diagnosis.

Resting ECG may show evidence of previous myocardial infarction, left ventricular hyperthrophy, bundle branch block, preexcitation, arrhythmias, or conduction defects, but is normal in most patients. Since 12-lead ECG is normal in 50 % of patients with chronic stable angina it cannot exclude 1HD. During chest pain the ECG becomes abnormal in half of the angina patients with a normal resting ECG. ST-segment and T-wave depression or inversion on the resting ECG and their pseudo normalization during pain are observed. Sinus tachycardia is common, bradyarrhythmia less go. These findings indicate that resting ECG should be performed during episode of chest pain.

Exercise ECG is more sensitive and specific than the resting ECG for detecting myocardial ischemia. Exercise tolerance test is usually performed using a standard treadmill or bicycle ergometer protocol to ensure a progressive and reproducible increase in work load while monitoring the patient's ECG, blood pressure and general condition. Planar and down sloping ST-segment depression of 1 mm or more is indicative of ischemia; up sloping ST-depression is less specific and often occurs in normal individuals. An exercise test should be carried out only after careful clinical evaluation of symptoms and a physical examination including resting ECG. Exercise ECG testing is not of diagnostic value in the presence of left bundle branch block, paced rhythm, and Wolff-Parkinson-White syndrome in which cases the ECG changes cannot be evaluated. Additionally, false positive results are more frequent in patients with abnormal resting ECG in the presence of left ventricular hypertrophy, electrolyte imbalance, intraventricular conduction abnormalities, and use of digitalis. Exercise ECG testing is also less sensitive and specific in women.

Resting two-dimensional and Doppler echocardiography is useful to detect or rule out the possibility of other disorders such as heart valve disease or hypertrophic cardiomyopathy as a cause of symptoms and to evaluate ventricular function. For diagnostic purposes, Echo-CG is useful in patients with clinically detected murmurs, history and ECG changes compatible with hypertrophic cardiomyopathy or previous myocardial infarction and symptoms or signs of heart failure. Tissue Doppler imaging allows regional quantification of myocardial motion and strain rate, imaging allows

determination of regional deformation thus improve to detect ischemia earlier in the ischemic cascade.

Stress testing in combination with imaging are used in the diagnosis of stable angina. The most well-established stress imaging techniques are echocardiography and perfusion scintigraphy. Both may be used in combination with either exercise stress. Exercise stress echocardiography has been developed as an alternative to "classica" exercise testing with ECG and as an additional investigation to establish the presence or location and extent of myocardial ischaemia during stress. A resting echocardiogram is acquired before a symptom-limited exercise test is performed, most frequently using a bicycle ergometer, with further images acquired where possible during each stage of exercise and at peak exercise.

Exercise testing with myocardial perfusion scintigraphy is required. Thallium-201 and technetium-99m radiopharmaceuticals are the most commonly used tracers, employed with single-photon emission computed tomography in association with a symptom-limited exercise test on either a bicycle ergometer or a treadmill. With this technique myocardial hypoperfusion in patients with stable angina is characterized by reduced tracer uptake during stress in comparison with uptake at rest.

Pharmacological stress testing with imaging techniques. Pharmacological stress testing with either perfusion scintigraphy or echocardiography is indicated in patients who are unable to exercise adequately or may be used as an alternative to exercise stress. Two approaches may be used to achieve this: infusion of short-acting sympathomimetic drugs such as dobutamine in an incremental dose protocol which increases myocardial oxygen consumption and mimics the effect of physical exercise or infusion of coronary vasodilators (adenosine and dipyridamole).

Cardiac magnetic resonance stress testing in conjunction with a dobutamine infusion can be used to detect wall motion abnormalities induced by ischemia or perfusion abnormalities.

ACUTE CORONARY SYNDROME

Acute coronary syndrome (unstable coronary artery disease) includes both ***unstable angina*** and ***non-Q-wave myocardial infarction.***

Clinical features

- increased severity or frequency of the patient's pre-existing angina within the last month;
- rapidly worsening chronic stable angina (crescendo angina);
- new onset of angina pectoris;
- angina at rest;
- post-infarction angina (more than 24 hours after myocardial infarction);
- non-Q-wave myocardial infarction.

Objective examination. During attack of chest pain the patient's condition is grave, forced sitting position, the face is pale with acrocyanosis. The border of relative cardiac dullness displaced outside.

In auscultation both heart sounds are decreased, S_3 or S_4 gallop may be detected during an episode of pain. Mitral regurgitation murmur appears. Arrhythmia is often observed. Blood pressure tends to have less level, than in period free of pain. The signs of congestion failure present: enlarged liver, pedal edema.

Additional methods of examination

Clinical blood analysis is without change, seldom may be slight leukocytosis.

Biochemical blood analysis: commonly there are the signs of disorders of lipid profile: increased level total cholesterol, triglycerides, low density lipoprotein cholesterol.

Small rises in the serum levels of biochemical markers of cardiac injury (creatine kinase, creatine kinase MB), troponin-T or troponin-I reflect the development of small foci of myocardial necrosis, minor creatine kinase, creatine kinase MB, which are usually accompanied by elevated troponin-T levels, indicate an increased risk of future events, despite stabilization of their clinical condition. Cardiac troponin-I is not detectable in the absence of cardiac injury. Because of the lag

period before a rise becomes detectable, at least two samples, taken at an interval of 12-24 hours, should always be tested.

Elevated fibrinogen levels at the time of admission are associated with an increased risk of death, myocardial infarction or spontaneous ischemia in patients with unstable angina.

The acute-phase proteins C-reactive protein is sensitive, but non-specific, markers of inflammation. There is much evidence to suggest a role for inflammation in the etiology of unstable angina and myocardial infarction and level of this protein have been observed to be elevated in some patients with acute coronary syndrome. C-reactive protein levels >3 mg/1, as detected by means of sensitive radioimmunoassay, indicate an increased risk of subsequent cardiac events m patients with acute coronary syndrome.

Instrumental examination. ECG monitoring is regarded as an essential part of routine management. All patients with suspected acute coronary syndrome should be admitted to the coronary unit for 12-24 hours of ECG monitoring (Holter monitoring). Admission ECG finding in acute coronary syndrome: ST-segment depression, ST-segment elevation (transient), T-wave inversion, normal ECG.

A normal ECG recorded when the patient is pain free not exclude the diagnosis of acute coronary syndrome, although a normal ECG recorded during an episode of pain makes the diagnosis unlikely, and is associated with an excellent prognosis. Following abnormalities of ECG support a diagnosis of acute coronary syndrome: ST-segment depression >0,5 mm, ST-segment elevation >1mm, T-wave inversion. Transient elevation of the ST-segment which settles, either spontaneously or in response to nitrate treatment, is fully consistent with the diagnosis acute coronary syndrome. Isolated T-wave inversion on the initial ECG is a relative by benign sign, and is associated with a low risk of future myocardial infarction or death. A total of more than 60 minutes of ischemia during Holter monitoring is associated with a poor prognosis. However, T-wave inversion and change of ST-segment must be considered in the context of the whole clinical picture taking into account the patient's age, presence of other risk factors, levels of biochemical markers of cardiac injury. Exercise testing undertaken either before or shortly after hospital discharge, is a minimum requirement for patients. Once the patient has been pain-free for 24-48 hours and the ECG stable the risks associated with performing an exercise test are very low. Severe ischemia and low exercise tolerance in a patient who has had either unstable angina or non-Q-wave myocardial infarction is associated with a poor short-term prognosis.

Echocardiography should be performed in all patients in order to evaluate the left ventricular function.

Stress echocardiography can be performed either during or immediately after dynamic exercise or under pharmacological stress administration of dipyridamole or dobutamine. Patients who are unable to perform an exercise test can be usefully assessed by pharmacological induced stress echocardiography.

Myocardial perfusion scintigraphy (tallium or technetium scan) may be particularly valuable in patients who are unable to exercise. Such techniques can outline perfusion defects.

Unstable angina

Classification of unstable angina was proposed by E. Braunwald.

Braunwald classification system for unstable angina (UA)

Patients are assessed according to each of the following sets of criteria:

Severity of angina

Class I - New onset of severe angina or increased frequency of attacks

No rest pain

Class II- Angina at rest, sub-acute

Angina at rest within the past month, but not within the preceding 48 hours

Class III-Angina at rest, acute

Angina at rest during the preceding 48 hours

Clinical circumstances

Class A -- Secondary UA

Symptoms secondary to an identified condition reducing myocardial oxyden suplly or increasing demand

Class B - Primary UA

Class C - Post-infarction UA

Intensity of treatment

Class I - Minimal or no therapy

Class II - Therapy for chronic stable angina

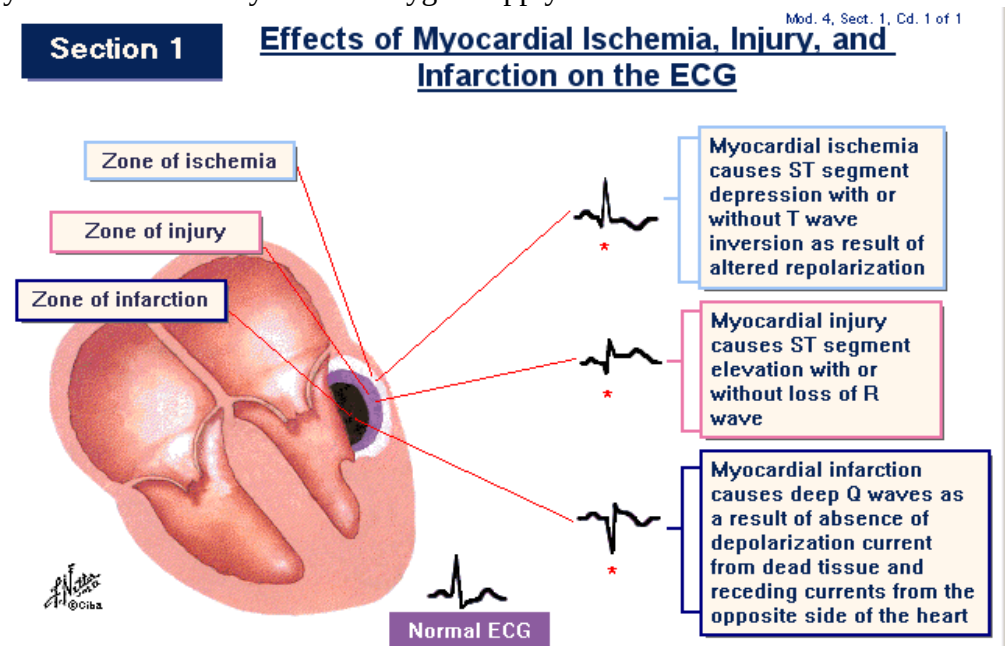
Class III - Maximum anti-anginal therapy, including intravenous nitrates

ECG changes

Presence or absence of transient ST, T abnormalities

MYOCARDIAL INFARCTION

Myocardial infarction is formation of necrotic foci in the heart muscle due to imbalance between upset coronary circulation and myocardial oxygen supply.



There are three pathophysiological events in development of myocardial infarction: rupture of an atheromatous plaque in a coronary artery, thrombus at a site of ruptured or intact plaque, local or generalized vasoconstriction. In myocardial infarction thrombus as a rule is occlusive. Under condition of complete occlusion of coronary artery the myocardial change occur after 20 minute and necrosis is formed for 6 hours. The time of formed necrosis is individual process which depends on presenting collateral circulation.

Diagnostics of myocardial infarction based on clinical features, ECG data and markers of tissue damage.

Clinical features

There are some clinical variants of myocardial infarction: angina (status anginous), abdominal variant, asthmatic variant, arrhythmic variant, cerebral variant, peripheral variant, painless or "silent" variant, combined variant.

Pain is the cardinal symptom of myocardial infarction. The pain resembles angina pectoris in patients with status anginous, but it usually more severe and often described as tightness, squeezing, pressing heaviness or constriction in the chest. The pain is characterized by inconstant character,

lasts longer than angina, more than 20-30 minutes, some hours and even days. The pain irradiates in the left arm, throat, teeth, ear, under the left shoulder blade, sometimes in epigastrium. The chest pain is not relieved at rest or taking nitroclycerin. The pain is accompanied by feeling of fear, impending death, excitation, weakness, sweating and palpitation.

Objective examination. The patient's condition is severe, may be forced sitting position, consciousness is clear, pallor, excessive perspiration, cold peripheries, acrocyanosis. At second-third days of pain the temperature elevation till subfebril or febril level is observed. In percussion of the lung the intermediate sound is revealed in posterior part. Lung crepitation is heard. The borders of cardiac dullness correspond with preceding disease. Tachycardia is appeared as sign sympathetic activation. Decreased first heart sound or decreased both sounds are heard. At mostly patients presystolic and protodiastolic gallop rhythms occur. At 90-95 % of patients the extrasystoles are appeared. In the first listening point is heard loud pansystolic murmur which is explained by sudden onset of severe mitral incompetence with regurgitation due to the myocardial dysfunction or rupture of papillary muscle. A new loud pansystolic murmur may have another origin and caused by rupture of the interventricular septum with left-right shunting through a ventricular septal defect. Temporary, pericardial friction sound may appear at acute period of myocardial infarction as a rule in case of damage of anterior wall of the left ventricle.

Blood pressure can elevate in the period of pain attack. Sign of impaired myocardial function are hypotension, small pulse (pulses porous), oliguria. Sudden death, presumably from ventricular fibrillation or asystole, may occur immediately, within the first hour of chest pain.

According to clinical features and results Additional methods of examination five periods of myocardial infarction are distinguished: very acute, acute, subacute, recovery, stabilization. Acute period lasts approximately two days and characterized by diminished or disappeared chest pain. Nevertheless at this period may be the complications such as acute heart failure, disorders of cardiac rhythm and conduction, cardiogenic shock.

At the peak of first day at patient develops the syndrome related to the resurbtion of necrotic tissue. This syndrome includes elevated temperature, leukocytosis and accelerated ESR.

In case of bening course of disease at the subacute period the patient's condition becomes better, chest pain as usually absent, the heart sound louder, blood pressure remove to normal level. The signs of resorbtion syndrome disappeared. Prolonged leukocytosis and accelerated ECR indicate on accompanied complication, such as postinfarction syndrome or presence of inflammatory process as pneumonia, thromboflibites. At the period of recovery and stabilization the myocardial scar is formatted. The patient's condition is satisfactory, temperature is normal, tolerance to exercise load and physical activity are increased. The loudness of cardiac sound is slight decreased or normal. Heart rate is normal. Arrhythmia may preserve, but a number life-threatening arrhythmia is diminished. Hypertrophy of left ventricle reflects the cardiac remodeling in post infarction period.

Laboratory findings are normalized.

Atypical variants of myocardial infarction are particularly common in elderly and diabetic patients.

Abdominal type variant is observed more frequently at posterior diaphragmal myocardial infarction. This variant is characterized by intenstive pain in the epigastrium or in the right hypochondrium, which associated with dyspeptic disorders such as nausea, vomiting, regurgitation by air. Altered intestinal motility leads to diarrhea or constipation, paresis of intestine. On examination there is tenderness of the abdominal wall. Dangerous complication is acute gastrointestinal lesion and ulcer which are responsible for acute hemorrhage. The bleeding is often recurrent and caused shock.

Asthmatic variant is characterized by severe difficulty in breathing, cough with a foamy pink sputum (cardiac asthma, pulmonary edema) and small intensity of chest pain. There gallop rhythm, arrhythmias, decreasing of blood pressure is present. As a rule, this variant is more frequently observed at repeated myocardial infarction, and also at myocardial infarction on background of severe cardiosclerosis and practically always at the myocardial infarction of papillary muscle resulted the relative mitral incompetence.

Arrhythmic variant of myocardial infarction is predominated with disorders of rhythm and cardiac conduction, with slightly pain syndrome. This variant is related mostly with supraventricular or ventricular paroxysmal tachycardia, less frequent - paroxysmal atrial fibrillation or complete atrioventricular block. Arrhytmic variant may be complicated by cardiogenic shock with fall of blood pressure and sharply diminished myocardial perfusion.

Cerebral variant is observed in elderly patients with cerebral atherosclerosis and diminished brain circulation. Simultaneously with myocardial infarction may be spasm or thrombous of cerebral arteries. According to decreased cardiac output relevant with myocardial infarction such symptoms and signs of cerebral ischemia appear: giddiness, nausea and vomiting central origin, syncope, bradycardia, cramps and even, coma. Affection of central nervous system may be in a form of psychomotor anxiety resembles the clinical features of meningitis, epilepsy, polyneuropathy.

Painless, or "silent" variant of myocardial infarction pass unrecognized and may reveal afterwards during ECG recording or Echo-CG examination.

Course and outcomes of myocardial infarction depends on accompanied *complications.* In acute period may be such complications: disorders of rhythm and conduction, acute left ventricular failure (cardiac asthma, pulmonary edema), cardiogenic shock, acute aneurysm of left ventricle, rupture of the ventricle with cardiac tamponade and is usually fatal, pericarditis, thromboembolism, acute lesions and ulcers of gastrointestinal tract. In subacute period may observe: disorders of rhythm and conduction, chronic heart failure, chronic aneurysm of left ventricle, post-infarction angina, thromboembolism, post-infarction remodeling, post-infarction syndrome (Dressler's syndrome).

Nearly all patients with different variants of myocardial infarction have arrhythmias, which may be mild with favorable outcomes, but sometimes cause life threatening events. Ventricular fibrillation occurs in about 5-10 % of patients with myocardial infarction and is the major cause of sudden death. Atrial fibrillation is frequently transient state. Heart block complicating infarction is usually temporary and removes after specific treatment. Heart block complicating arterior infarction has unfavorable prognosis, because asystole may suddenly appear.

Cardiogenic shock - the most severe complication of myocardial infarction. Diagnostic signs of cardigenic shock: deranged consciousness, fall systolic blood pressure less 90 mm Hg, peripheral vasoconstriction and decreased volume of urine less 20 ml/hour. According to the leading mechanism there are three kind of shock: reflectory, arrhythmic, and true cardiogenic shock. Reflectory shock develops at patients with status anginous as a hemodynamic reaction on pain. Arrhythmical shock is resulting from paroxysmal tachycardia or cardiac blockade. True cardiogenic shock is explained by damage of cardiomyocytes, disorders of microcirculation and pronounced decreasing of contractile ability of left ventricle.

Heart failure complicating acute myocardial infarction indicates a bad prognosis. Cardiac asthma and pulmonary edema develop due to the acute left ventricular failure at approximately in up 10-15 % of patients and often lead to death. Classification of the acute heart failure at patients with myocardial infarction was proposed in 1967 by Killip. Four classes of acute heart failure are distinguished: 1 class - absence of pulmonary rales and gallop cardiac rhythm, this class develops at 40-50 % of patients and mortality is till 10 %. 2 class - presence of rales in less 50 % of lung areas or gallop rhythm, this class develops at 30-40 % of patients, mortality is till 20 %. 3 class - presence of rales in more, 50 % of lung areas associated with gallop rhythm, this class develop at 10-15 % of patients, mortality is till 40 %. 4 class - presence of cardiac shock, develops at 5-20 % of patients, mortality is till 50-90 %.

In approximately 10% of patients full thickness myocardial infarction causes thinning of the infracted segment and develops the bulge at the left ventricle so called ***aneurysm,*** revealed during inspection of the heart region as weak restricted pulsation in the III-IV intercostals spaces somewhat laterally from the left sternal edge. ***Post-infarction angina*** occurs in up to 50 % of patients. ***Thromboembolism*** is determined in different vessel sites with clinical features of stroke, pulmonary infarction and ischemic limb. Primary thrombus forms on the endocardial surface of freshly infarcted myocardium and transformed to systemic embolism.

The post-infarction syndrome (Dressler's syndrome) is an autoimmune reaction to necrotic process in myocardium and is characterized by persistent fever, pericarditis and pleurisy. The Dressler's syndrome occurs a few weeks or even month after the myocardial infaction.

Additional methods of examination

Clinical blood analysis - leukocytosis with mild nuclear shift to the left occurs in a few hours after onset of chest pain, reached the peak at 2-4 days and normalized in a week. The degree of leukocytosis depends on amount of damaged myocardial tissue. Accelerated ESR is observed at 2-3 days from onset of chest pain, reached maximal level till 2 week and normalized at 3-4 weeks.

Markers of myocardial infarction are plasma enzymes, which are normally concentrated within cardiac cells. During the necrosis of cardiomyocytes their membranes destroyed and the enzymes released at first at microcirculation and later at systemic circulation. Thus myocardial infarction causes a detectable rise in the plasma enzymes which serve as laboratory markers of necrosis: creatine kinase, lactate dehydrogenase, aspartate aminotransferase, troponin T and I, myoglobin. Optimal time for estimation of myocardial markers of necrosis depicted at table.

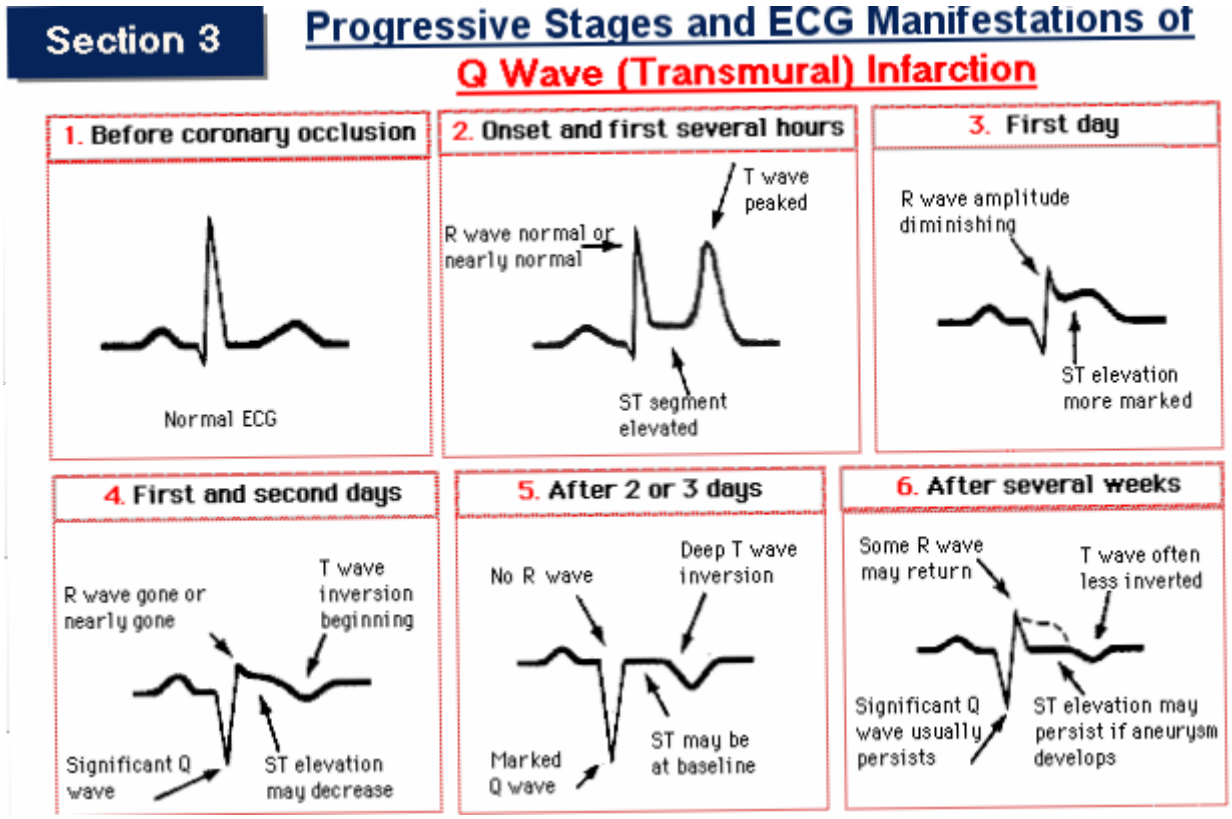
Optimal time for estimation of myocardial markers of necrosis

Markers	Optimal time for estimation of myocardial markers of necrosis
Myoglobin	In 1-2 hours after chest pain
Creatine kinase	Every 12 hours 3 time
Creatine kinase MB	In 60-90 minutes after chest pain, every 12 hours 3 time
Lactate dehydrogenase	In 24 hours after chest pain, one time
Troponin T	In 12 hours after chest pain, one time
Troponin I	In 12 hours after chest pain, one time

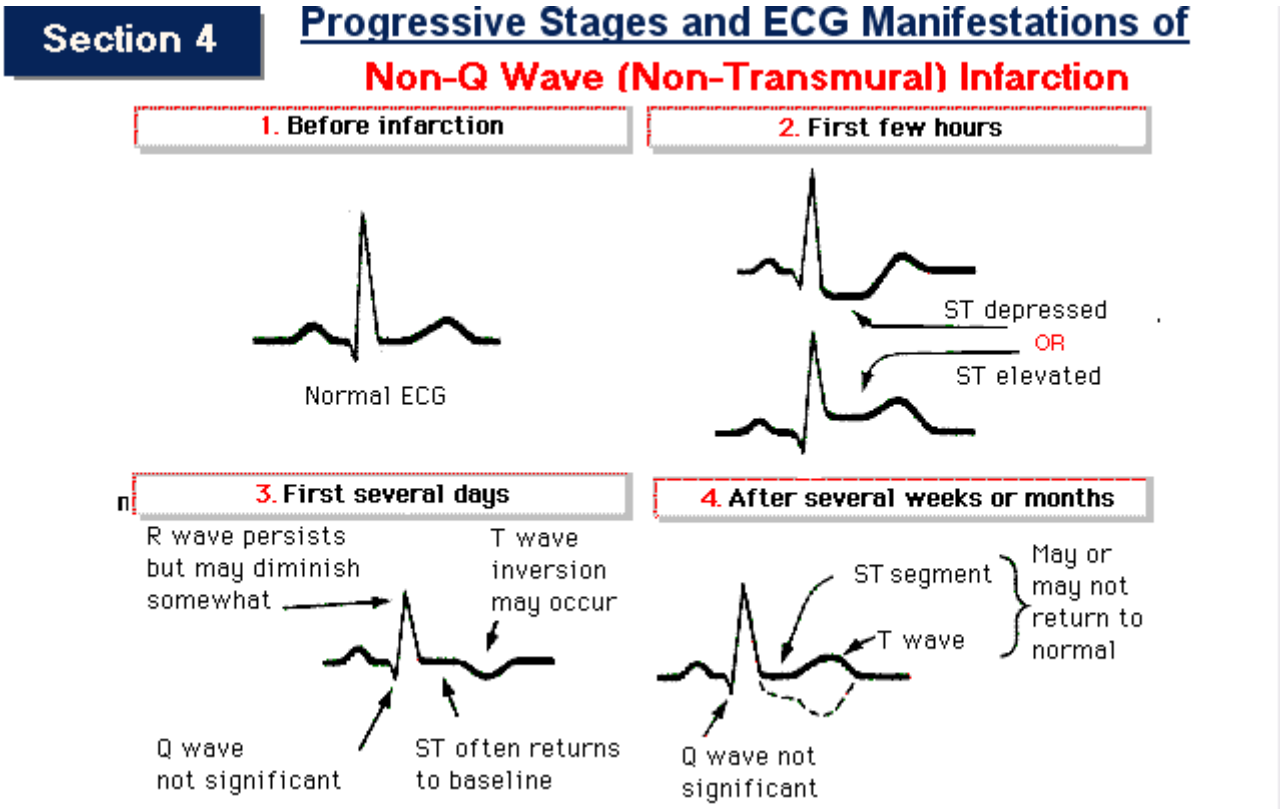
Baseline and peak elevation of markers of myocardial damage is different. Dynamic of laboratory markers of myocardial infarction is depicted at table

Dynamic of laboratory markers of myocardial infarction

Markers	Norma	Time from onset of myocardial infarction		
		Baseline elevation hours	Peak elevation hours	Normalization days
Creatine kinase MB	0-4 ME/L	3-6	12-24	1,5-3
Lactate dehydrogenase	15-30%	12-24	24-72	7-14
Aspartate aminotransferase	28-125 mmol/l	8-12	24-48	3-5
Troponin T, I	Less 0,1 mkg/1	3-12	12-48	3-16
Myoglobin	20-66 mkg/1	1-4	6-7	1



ECG: one of the most significant uses of a 12 lead ECG is to aid in determining whether a myocardial infarction has occurred.



The usual first finding in an infarction is elevation of the ST-segment, which occurs some hours after infarction. Hours to days later the T-wave inverts, diminution of the size of the R-wave and the Q-wave becomes deep and wide. The height of the R-wave is directly proportional to the amount of living tissue that escapes death. In case of full thickness myocardial infarction the R-wave

is disappeared. Days to weeks later the ST-segment returns to near normal isoilectric line position. Weeks to moths later the T-wave becomes upright again, but Q-wave may remain abnormal. As the infarction heals the Q-wave may remain as the only sign of an old coronary occlusion. Since a deep and wide Q-wave is often indicate of an old infarction. The Q-wave may considered abnormal if it is over 0,03 second wide and if it is greater in depth than one fourth the height of the R-wave.

Echo-CG: two-dimensional echocardiography may assess the cardiac structures, pericardium and ascending aorta, allows identification of regional wall motion abnormalities, valvular abnormalities, global left and right ventricular function and detecting important complications such as cardiac rupture, ventricular septal defect, mitral regurgitation and pericardial effusion.

Radioisotope scintigraphy by technetium-99m-pyrophosphate. Scintigraphy is generally used for the diagnosis of myocardial infarction in patients hospitalized late after the onset of symptoms in which cardiac enzymes are no longer elevated or are unreliable. Imaging is optimal 2-7 days after myocardial infarction. Focal increases in technetium pyrophosphate uptake are generally diagnostic of infarction. This technique is highly sensitive (>90 %) in detecting large transmural infarctien but is less reliable in the detection of small non-Q-wave myocardial infarction.

Radionuclide ventriculography allows to reveal right and left ventricular ejection fraction and assessment of regional wall motion abnormalities. Because radionuclide ventriculography provides less information regarding the cardiac structures, echocardiography is generally preferred in the initial evaluation of patients with myocardial infarction

Sudden cardiac death

Sudden cardiac death (SCD) is defined as follows: "Natural death due to cardiac causes, heralded by abrupt loss of consciousness within one hour of the onset of acute symptoms; preexisting heart disease may have been known to the present, but the time and mode of death are unexpected". The key concepts that are central in the definition of sudden death are the non-traumatic nature of the event and the fact that sudden death is unexpected and instantaneous.

The single most important cause of death in the adult population of the industrialized world is SCD due to *ischemic heart disease.* In patients with sudden cardiovascular collapse, the most often recorded rhythm shows that ventricular fibrillation is present in 75-80% of cases, whereas bradyarrhythmias are thought to contribute to a minority of SCD. In about 5% to 10% of cases, SCD occurs in the absence of coronary artery disease or congestive heart failure.

Hypertrophic cardiomyopathy is a relatively common cardiac disorder (adult prevalence about 1:500) in which sudden unexpected death is the most devastating outcome, occurring throughout life, but particularly in young, often asymptomatic patients.

Dilated cardiomyopathy is the most common cause of death in dilated cardiomyopaty especially in less advanced functional classes. Ejection fraction has been repeatedly identified as best predictor of outcome both with regards to SCD and death from heart failure; occurrence of syncopal events is another accurate indicator of risk of SCD.

Long QT syndrome is associated with high risk of SCD. Risk stratification is mainly based on history of syncopal events, Torsades de Pointe or cardiac arrest.

Brugada syndrome. Diagnosis of Brugada syndrome is established in the presence of spontaneous or induced ST-segment elevation in leads V_1-V_2 with/without right bundle branch block.

Aortic stenosis. SCD occurs in about 20 % of patients whose deaths are attributed to aortic stenosis. In the absence of cardiac symptoms, survival is excellent without valve replacement. The prognostic value of different hemodynamic and electrophysiologic testing is limited.

Wolff-Parkinson-White syndrome. In patients with Wolff-Parkinson-White syndrome natural history studies have reported SCD rate of 0,15 % /year due to ventricular fibrillation. SCD survivors tend to be symptomatic.

Bradyarrhithmias. It is estimated that 15-20 % of SCD may be attributed to bradyarrhithmias. Advanced AV block and intraventricular conduction disturbances represent a risk factor for bradyarrhithmic deaths.

Clinical features

Complains: giddiness, darkening in the eyes, sudden appearance of dyspnea.

Objective examination*:* grave condition, passive position, loss of consciousness expansion of pupils, appearance of pale-grey tint of skin, apnea, absence of heart sounds, absence of pulse on large arteries.

Program examination for the prevention of sudden coronary death:

Clinical examination of patients with IHD, detection of risk factors, reanimated in the acute period of MI with the heart failure; with angina pectoris at rest after the MI; with the complete blockade of bundle-branches block.

Clinical analysis of blood, urinalysis.

Biochemical analysis of blood: total protein, transaminases, creatin-phosphokinase, lactatdehydregenase, cholesterol, triglycerids, coagulogram.

ECG-Holter-monitoring.

Topic 4. The Basic Clinical Symptoms of Chronic Bronchitis and Bronchial Asthma. Chronic Obstructive Pulmonary Diseas.

Modern classification of chronic obstructive pulmonary disease. Definition and the basic mechanisms of the development of chronic bronchitis and bronchial asthma. Chronic bronchitis and bronchial asthma, the basic complaints and physical examination of the patients. A syndrome of bronchial obstruction, mucocellular insufficiency and the increased lightness of the lungs. The basic methods of instrumental diagnostics. Laboratory findings of bronchial asthma according to the general blood tests and sputum examination. Bronchiectasis, definition and the basic clinical syndroms.

CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

A disease characterized by chronic bronchitis or emphysema and airflow obstruction that is generally progressive, may be accompanied by airway hyperreactivity, and may be partially reversible.

Patients who have features of chronic bronchitis or emphysema without airflow obstruction have one or both of those diseases but not COPD. Most patients with COPD, who by definition have airflow obstruction, have features of both chronic bronchitis and emphysema. Patients whose asthma is characterized by incomplete reversibility of airway obstruction are considered to have a form of COPD (called asthmatic bronchitis or asthmatic COPD in the USA), because they often cannot be differentiated from those who have chronic bronchitis and emphysema with reversible airway obstruction and airway hyperreactivity. Those with completely reversible airflow obstruction without features of chronic bronchitis or emphysema have asthma but not COPD.

Etiology. Smoking is the dominant risk factor for the development and progression of COPD; however, not all smokers develop COPD, and COPD does occur in persons who have never smoked,1 suggesting that other factors are important in the etiology of COPD. α_1-antitrypsin deficiency is an important cause of COPD in a very small percentage of cases. Other undefined genetic factors certainly play an important role in COPD development. The role of infections in both the development and progression of COPD is receiving increased attention, including the role of adenoviral infections in emphysema and the role of intracellular infections (eg, mycoplasma) in asthma. Occupational and environmental exposures to various pollutants (eg, particulate matter, agricultural dusts) are also important factors in the development of COPD.

Classification of Chronic Obstructive Pulmonary Disease by Severity

Stage	Characteristics
I (mild COPD)	Chronic symptoms (cough, sputum production) FEV1/FVC < 70% FEV1 ≥ 80% of predicted
II (moderate COPD)	With or without chronic symptoms FEV1/FVC < 70% 50% of predicted ≤ FEV1 < 80% of predicted
III (severe COPD)	With or without chronic symptoms FEV1/FVC < 70% 30% of predicted ≤ FEV1 < 50% of predicted
IV (very severe COPD)	With or without chronic symptoms FEV1/FVC < 70% FEV1 < 30% of predicted or < 50% of predicted plus the presence of respiratory failure or clinical signs of right heart failure increase.

FEV_1 - forced expiratory volume in 1 second; FVC - forced vital capacity.

Clinical features

Patients who have smoked > 20 cigarettes per day for > 20 yr may develop a productive cough in their 40s or early 50s. Exertional dyspnea usually does not become severe enough to warrant a visit to a physician until COPD patients are in their 50s lo mid-60s. Sputum production is insidious in onset, initially occurring only in the morning. Daily volume rarely exceeds 60 mL. Sputum is usually mucoid but becomes purulent during an exacerbation.

Acute chest illnesses-characterized by increased cough, purulent sputum, wheezing, dyspnea, and occasionally fever-may occur from time to time. (A history of wheezing and dyspnea may lead to the erroneous diagnosis of asthma.) As COPD progresses, the intervals between acute exacerbations tend to become shorter. Late in the disease, an exacerbation may cause severe hypoxemia with cyanosis, which is accentuated if erythrocytosis is present. Morning headache may indicate hypercapnia. Hypercapnia with more severe hypoxemia, sometimes with erythrocytosis, is common in end-stage disease. Weight loss occurs in some patients.

Objective examination. Early in COPD, physical examination of the chest may not be remarkable except for auscultation of expiratory wheezes. As airway obstruction progresses, hyperinflation of the lungs becomes evident. The anteroposterior diameter of the chest in creases because the lungs are near full inspiration and because emphysema increases total lung capacity. The diaphragm is depressed, and its motion limited. Breath sounds are decreased, and heart sounds become distant. Signs of pulmonary hypertension and right ventricular hypertrophy are usually not detectable because emphysematous lung tissue is interposed between the heart and anterior chest wall. A few coarse crackles are often heard at the lung bases. An enlarged, tender liver indicates heart failure. Neck vein distention, especially during expiration, may occur in the absence of heart failure because of increased intrathoracic pressure. Asterixis may accompany severe hypercapnia.

The patient with end-stage COPD is often a dramatic sight - standing before a counter leaning forward with arms outstretched and weight supported on the palms. The accessory respiratory muscles of the neck and shoulder girdle are in full use. Expiration often occurs through pursed lips. The chest appears overinflated, often with paradoxic in drawing of the lower interspaces. Cyanosis may be present.

Additional methods of examination

Clinical blood analysis: without significant changes, sometimes secondary erythrocytosis; in progression assess leukocytosis, neutrophilia, accelerated ESR.

Sputum analysis: sputum in patients with stable chronic bronchitis is mucoid. During an exacerbation, sputum usually becomes purulent, with an influx of neutrophils.

X-ray examination: in severe disease, persistent, marked overdistention of the lungs is indicated in the frontal view by a low, flat diaphragm and in .the lateral view by widening of t he retrosternal airspace and an increase in the angle formed by the sternum and diaphragm from acute to ≥ 90°. The heart shadow tends to be long and narrow.

Test of ventilatory function (spirometric recording and pneumotachymetry): pulmonary function tests are helpful in diagnosing COPD, in assessing its severity, and in following its progress. Forced expiratory spirometry quantifies airway obstruction. Airflow obstruction is an important indicator of symptomatic respiratory insufficiency and of the likelihood of blood gas abnormalities. The FEV_1 and the FEV_1/FVC fall progressively as the severity of COPD increases. The FEV_1 is less variable than other measurements of airway dynamics and can be predicted more accurately from age, sex, and height. Functional residual capacity and residual volume are increased; vital capacity is decreased. Roughly comparable information can be obtained from the forced expiratory flow-volume loop.

ECG: diagnosing pulmonary hypertension and cor pulmonale in COPD is difficult without right-sided heart catheterization. On the ECG, an R or R' wave as large as or larger than the S wave in lead V_1 and R wave smaller than the S wave in lead V_6 and right-axis deviation >110° without right bundle branch block support the diagnosis of cor pulmonale.

Echocardiography: especially with an esophageal transducer, and pulsed Doppler techniques to estimate mean pulmonary arterial pressure can be used to assess pulmonary hypertension and right ventricular function. Left ventricular size and performance are generally normal inpatients with COPD and no other associated cardiac abnormalities. The right ventricular ejection fraction is frequently abnormal, especially during exercise.

Blood gas analysis: arterial blood gas measurements detect hypoxemia and hypercapnia and determine their severity. In the early stages of COPD, measuring arterial blood gases reveals mild or moderate hypoxemia without hypercapnia. As the disease progresses, hypoxemia becomes more severe and hypercapnia supervenes. Hypercapnia occurs with increasing frequency as the FEV_1 falls below 1L. Blood gas abnormalities worsen during acute exacerbations and may worsen during exercise and sleep. .

CHRONIC BRONCHITIS

Chronic bronchitis is chronic inflammation of the bronchi and bronchioles.

Etiology

- smoking, pollution of the environment by products of incomplete fuel substances combustion, organic and inorganic dust;
- infection (bacterial, viral, micoplasms, fungus);
- congenital occurrences in lesser circulation on heart failure;
- exposure of metabolic products on renal failure;
- result of acute bronchitis.

Classification of chronic bronchitis (by N.R Paleev, 1990)

I. According to the character of inflammatory process:

- simple (catarrhally);
- purulent;
- muco-purulent;
- special forms: hemorrhagic and fibrinous.

//. According to the presence of bronchial obstruction:

- obstructive bronchitis (stages: I, II, III; duration: simple, moderate grave, grave);
- non obstructive bronchitis.

III. According to the level of bronchi injury:

- proximal;
- distal;
- diffuse.

IV. According to the duration:

- latently;
- with infrequent aggravations;
- with frequent aggravations;
- continuously progress.

V. According to the phases:

- progress;
- remission.

VI. According to the complications:

- emphysema of the lungs;
- hemoptysis;
- pneumonia;
- respiratory failure;
- "Cor pulmonale".

Pathogenesis. *On chronic bronchitis occurs development of classic pathogenetic triad:*

- hypercrinia (mucous hyperproduction);
- dyscrinia (increased sputum viscosity);
- mucostasis (overcrowding of the sputum in bronchi).

Approaching to the bronchi of infection agent leads to the sensebilization and autosensebilization of the organism.

There are the next mechanisms of the bronchial obstruction development:

- brochospasm;
- inflammatory edema and bronchial wall infiltration;
- hyper- and dyscrinia;
- hypotonic dyskinesia of large bronchi;
- collapse of small bronchi during expiration;
- mucus lays hyperplasic reaction.

Clinical features

The main complaints in patients with chronic bronchitis are moist cough, general weakness, perspiration and dyspnea in cause of bronchium obstruction.

Cough is commonly periodic, moist with difficult sputum expectoration.

Sputum expectoration is the most important symptom of chronic bronchitis. On early stages of the disease the sputum may be mucous, tenacious consistency, glass-like, for the period of progression becomes mucopurulant or purulent. The 24-hours amount of sputum is usually 50-70 ml, due to development of bronchiectasis significantly increase to 100-200 ml.

Dyspnea - commonly has expiratory character and its appearing indicates presence of bronchial obstruction and emphysema.

Objective examination. *General patient's condition* is usually satisfactory. On progression and complications advance general patient's condition may be from middle grave to grave. Due to gradual chronic hypoxia and intoxication possibly will be observed perspiration and subfebrile or febrile temperature.

The posture of the patients is frequently active. On progression and complications advance is forced in form of orthopnea - sitting position fixing the shoulder girdle in order to reduce dyspnea via assists the accessory muscles and diaphragm to take part in respiration.

The color of the skin and visible mucous depends on the stage and variant of obstruction. In initial stage the color of the skin and visible mucous is without any particularities. Due to the chronic bronchitis progression observe diffuse cyanosis with peripheral edema via to the "cor pulmonale" development. In obstructive emphysema bronchi spasm occurs during expiration therefore alveolar air is a little change and in spite for constant dyspnea the skin and visible mucous cyanosis isn't specific. In purulent chronic bronchitis detect the form of the Hippocratic nails.

The data of chest inspection, palpation and percussion include clinical features of bronchium obstruction: emphysematous form of the chest with accessory respiratory muscles participation in

the breathing act, decreased excursion of the chest, badly transmitted vocal fremitus and generalized bandbox sound over the lungs during percussion.

Auscultation of the lungs. Auscultative data in patients with chronic bronchitis is characterized by sibilant and sonorous dry rales of different tone and intensity over the pathologically increased vesicular breathing. In localized affection of medium and large bronchi insignificant amount of low pitched and soft rales are heard. Accumulation of the viscous secret in bronchi via active inflammation, are accompanied by coarse and medium bubbling rales that can be altered by coughing or deep inspiration.

Additional methods of examination

Clinical blood analysis: without significant changes, sometimes secondary erythrocytosis; in progression assess leukocytosis, neutrophilia, accelerated ESR, eosinophilia (allergic reaction).

Sputum analysis: the character of the sputum depends on the stage of disease: in initial stage the sputum is mucous; in progression or later stage - muco-purulant, tenacious or tenacious thick consistency, glass-like or with yellow traces, odorless and absent of layersness. In microscopic study are revealed a lot of columns ciliated epithelium, leucocytes, alveolar macrophages, eosinophils, fibrin fibers, Charcot-Leyden crystals and large amount of microorganisms (bacterial flora).

X-ray examination: augment and deformity of lung picture over increased in transparent lung tissue.

Test of ventilatory function (spirometric recording and pneumotachymetry): in patients with no obstructive bronchitis results of spirometric recording is comparable with healthy subjects; in patients with bronchial obstruction assess decreased respiratory reserve (75 % of maximum lung ventilation and lower), and decreased Votchal-Tiffeneau index.

ECG: deviation of electric axis of the heart to the right, P-pulmonale in II, III, AVF leads.

BRONCHIAL ASTHMA

A pulmonary disease characterized by reversible airway obstruction, airway inflammation, and increased airway responsiveness to a variety of stimuli. Obstruction persisting for days or weeks is known as status asthmaticus.

In the base of the disease lays chronic inflammatory process in bronchi due to the bronchi smooth muscles spasm (acute obstruction), mucus edema (subacute obstruction) and bronchi obstruction by tenacious secret (chronic obstruction). On longterm duration of disease via fibrosis in bronchial wall develops sclerotic obstruction**.**

Etiology

/. *The risk factors:*

- genetic factors;
- atopia (ability of the organism to the increased production of IgE owing to the allergens);
- bronchi hyperreactivity.

//. *The cause factors:*

- allergens;
- endogenous factors;
- impaired arachidonic acid metabolism;
- bronchi hyper reactivity to physical load;
- nervous and psychological factors;
- dyshormonal state.

///. *The initiate factors:*

- respiratory infections;
- airs pollutants;
- smoking.

Classification

Bronchial asthma is classificated according to the complex of clinical and functional signs of bronchial obstruction.

Category	**Symptoms**	**Pulmonary Function**
Mild intermittent	Symptoms ≤ 1 times a week No symptoms and normal PEF between exacerbations Exacerbations brief (from a few hours to a few days); intensity may vary Nighttime symptoms ≤ 2 times a month	FEV1 or PEF ≥ 80% predicted PEF variability < 20%
Mild persistent	Symptoms > 1 times a week but not daily Exacerbations that sometimes limit activity Nighttime symptoms > 2 times a month	FEV1 or PEF ≥ 80% predicted PEF variability 20-30%
Moderate persistent	Daily symptoms Daily use of inhaled short-acting β2-agonist Exacerbations that limit activity Exacerbations ≥ 2 times a week; may last days Nighttime symptoms > 1 time a week	FEV1 or PEF > 60% predicted PEF variability > 30%
Severe persistent	Continual symptoms Limited physical activity Frequent exacerbations Frequent nighttime symptoms	FEV1 or PEF ≤ 60% predicted PEF variability > 30%

FEV_1 - forced expiratory volume in 1 second; PEF - peak expiratory flow.

Classification of the bronchial asthma aggravations (according to the anamnesis, intensity of the clinical signs, respiratory and cardiovascular dysfunction):

Degree I- effortless;

Degree II- moderate grave;

Degree III - grave;

Degree IV- risk of breathing stop.

Symptoms	Effortless	Moderate grave	Grave	Risk of breathing stop
Dyspnoea	At walking	At speaking	At rest	-
Conversation	Sentences	Phrases	Words	-
Consciousness	Normal	Exiting	Exiting	Deranged
Breathing rate	Increase	Increase	>30/min	-
Participation of the additional muscles	Absent	Present	Present	Paradox thoracoabdominal breathing
Whistling breathing	At the end of expiration	Loud	Loud	Absent
Pulse/min.	<100	100-120	>120	Bradycardia
FEV_1 after taking broncholytic, % from normal level	> 80 %	60-80 %	< 60 %	Absent
PaO_2	Normal	>60 mm Hg	<60 mm Hg	-
$PaCO_2$	<45 mm Hg	<45 mm Hg	>45 mm Hg	-

Clinical features

The main complaints in patients with bronchial asthma are bronchial asthma attacks: dyspnea, asphyxia, episodic breathlessness and cough. In attacks development there are divide 3 periods: prodromal, manifestation, reverse.

/. *The prodromal period:* starts at several minutes, hours or sometimes days before asthma attack and characterized by sneezing, itchiness of the skin and eyes, hypersecretion from nose, paroxysmal coughing, breathlessness, headache, weakness and changes of mood.

//. *The period of clinical manifestation (bronchial asthma attack):* appears feeling of difficult breathing, significant dyspnea (expiratory type) with changes in respiratory rate (tachypnea), depth (shallow respiration) and noisy distant rales. *General patients condition* is from middle grave to extremely grave. Due to the acute hypoxia may be observed depressed or exited deranged consciousness. During asthma attack the patients take the *forcedposture* in form of orthopnea - sitting position fixing the shoulder girdle in order to reduce dyspnea. *The color of the skin* is pale with central or diffuse cyanosis. The form of the chest is emphysematous with accessory muscles participate in the breathing act, observed decreased excursion of the chest. The vocal fremitus is badly transmitted and generalized bandbox sound assessed over the lungs during percussion. *Anscultative data* are characterized by sibilant and sonorous dry rales over the pathologically decreased vesicular breathing.

III. The period of asthma attack reverse: the duration of attack is differing and its final may come quickly without any complications through sputum discharge; or may continue for several hours or days accompanied by permanent dyspnea, headache and weakness.

In severe causes bronchial asthma attacks may transform at asthmatic status -lingering bronchial asthma attack that characterized by shallow quick respiration (significant tachypnea), constant dyspnea and formation of "dumb lung". Severity of asthmatic status is characterized by degree of respiratory failure, acidosis, hypercapnia, level of hypoxemic coma and respiratory center paralysis.

In period of stable remission the general patients condition commonly satisfactory or middle grave, however the clinical signs of emphysema are stay be present, particularly in causes of long disease duration and recurrently asthma attacks.

Additional methods of examination

Clinical blood analysis: secondary erythrocytosis; eosinophilia, accelerated ESR.

Sputum analysis: the character of the sputum is mucous, tenacious or tenacious thick consistency, glass-like color and odorless. In microscopic study are revealed columns ciliated epithelium, leucocytes, alveolar macrophages, eosinophils, Charcot-Leyden crystals and Kurshman spirals.

X-ray examination: in initial stages the specific data are absent. During asthma attack and according to the repeatedly periods of progression assess transparent lung tissue, horizontal position of the ribs, dilation of the intercostals spaces, low diaphragm position. In cause of inflammatory and allergic etiology of bronchial asthma observed augment and deformity of lung picture.

Test of ventilatory function (spirometric recording and pneumotachymetry): assess decreased respiratory reserve (75 % of maximum lung ventilation and lower), and decreased Votchal-Tiffeneau index.

Dynamic lung volumes and capacities are reduced but return toward normal after inhalation of an aerosolized bronchodilator. In patients with mild asymptomatic asthma, results may be normal. Because expiratory flow is determined by the diameter of the airways and by the elastic recoil forces of the lung, flow at large lung volumes exceeds flow at small lung volumes. Tests that measure flow at relatively large lung volumes (the forced expiratory volume during the first 1 sec (FEV_1) and peak expiratory flow) are largely effort-dependent and are less satisfactory than tests that measure flow over a range of lung volumes. Expiratory flow measurements at large lung volumes are insensitive to changes in peripheral airway resistance and reflect abnormalities principally in central airways. Early in an acute attack, forced expiratory flow between 25 and 75% of the vital capacity (FEF25-75%) may decrease only modestly. As the attack progresses, the FVC

and FEV_1 progressively decrease; associated air trapping and increased residual volume result in hyperinflation of the lungs.

Allergen identification: Inhalational bronchial provocation testing can be used with allergens to establish the clinical significance of positive skin tests or with methacholine or histamine to assess the degree of airway hyperresponsiveness in known asthmatics. It also aids in diagnosis when the symptoms are atypical (a persistent cough but no wheeze, as in cough-variant asthma).

SYNDROME OF BRONCHIUM OBSTRUCTION (bronchospastic syndrome)

Bronchospastic syndrome - the grouping of symptoms that developed due to the impaired air entrance to the pulmonary tissue through bronchus and accompanied by decreased lung's ventilation, enlargement of residual air volume in them, clinically manifests by intensive cough and resulted in emphysema.

Etiology: spasm of the smooth muscles; inflammatory infiltration and edema of the tracheobronchial tree mucus; non-uniform swelling of the bronchial mucus due to the inflammation or viscous sputum narrows the lumen of bronchi; deformity of the bronchial tree; expiratory bronchi collapse; external compression of bronchi by diffuse peribronchial fibrosis.

Pathogenesis. In syndrome of bronchium obstruction at first modify air passage in small bronchi and bronchioles due to the inflammatory edema and swelling of their mucosa (chronic bronchitis), spasm in the smooth muscles (bronchial asthma) and the external compression by peribronchial diffuse fibrosis.

Affection of the air passage through the bronchi (in all causes and pathogenetic mechanisms) leads to the alveoli hypoventilation, hypoxemia, hypercapnia, pulmonary hypertension and "cor pulmonale" development.

Clinical features. The main complaints in patients with bronchium obstruction are dyspnea and cough. Dyspnea commonly has expiratory character, gradually increased (chronic obstructive pulmonary diseases) and frequently transformed to periods of asthma (bronchial asthma). Cough is commonly periodic, moist with difficult sputum expectoration that has mucous or mucopurulant character, tenacious consistency, glass-like or glass like with yellow- traces color.

Objective examination. General patients condition is from middle grave to grave. Due to the acute or gradual chronic hypoxia may be observed the deranged consciousness.

The posture of the patients is frequently forced in form of orthopnea - sitting position fixing the shoulder girdle in order to reduce dyspnea via assistance of accessory muscles and diaphragm to take part in respiration.

The color of the skin depends on the variant of obstruction. In chronic bronchitis observe diffuse cyanosis with peripheral edema due to the "cor pulmonale" development. In obstructive emphysema bronchi spasm occurs during expiration therefore alveolar air is a little change and inspite for constant dyspnea the skin and visible mucous cyanosis isn't specific.

The data of chest inspection, palpation and percussion include clinical features of bronchium obstruction complications: emphysematous form of the chest with accessory respiratory muscles participation in the breathing act, decreased excursion of the chest, badly transmitted vocal fremitus and generalized bandbox sound over the lungs during percussion.

Auscultative data are the main specific in patients with bronchospastic syndrome: they characterized by dry rales over the pathologically increased vesicular breathing. Moreover, the particularities of the rales give possibility to evaluate the cause of the obstruction, the size and depth of the affected bronchi:

- in localized affection of medium and large bronchi insignificant amount of low pitched and soft rales are heard;
- widespread bronchi inflammation or bronchospasm in asthma attack both sibilant and sonorous rales of different tone and intensity are heard;
- accumulation of the viscous secretions in the lumen of bronchi accompanied by dry rales that can be altered by coughing or deep inspiration.

Additional methods of examination

Clinical blood analysis: secondary erythrocytosis; leukocytosis, neutrophilia, accelerated ESR (during progression of chronic diseases), eosinophilia (bronchial asthma).

Sputum analysis: the character of the sputum is mucous or muco-purulant, tenacious or tenacious thick consistency, glass-like or glass like with yellow traces color, odorless and absent of layers ness. In microscopic study are revealed columnar, ciliary epithelium, leucocytes, alveolar macrophages, eosinophils, fibrin fibers, Charcot-Leyden crystals and large amount of microorganisms (bacterial flora).

X-ray examination: augment and deformity of lung picture over increased in transparent lung tissue.

Test of ventilatory function: Forced expiratory spirometry quantifies airway obstruction. The FEV_1 and the FEV_1/FVC fall progressively as the severity of bronchium obstruction increases. The FEV_1 is less variable than other measurements of airway dynamics and can be predicted more accurately from age, sex, and height. Roughly comparable information can be obtained from the forced expiratory flow-volume loop. These tests cannot distinguish between chronic bronchitis and emphysema. Arterial blood gas measurements detect hypoxemia and hypercapnia and determine their severity.

SYNDROME OF INCREASED AIRINESS OF THE PULMONARY TISSUE

The syndrome of increased airiness of the pulmonary tissue is based on the protracted enlargement of residual air volume in the lung that clinically manifests by emphysema.

Etiology: chronic bronchial obstruction; decreased of the pulmonary tissue elasticity; compensatory reaction on the advance of destructive process in the lung and diffuse fibrosis.

Pathogenesis. Depending on the character and mechanism there are the next forms of increased airiness of the pulmonary tissue:

I. *According to the widespread*:

- local (one sided injury);
- diffuse (both lungs injury).

II. *According to the development*:

- destructive (chronic obstructive lung diseases, bronchiectatic disease);
- nondestructive (bronchial asthma).

Usually of bronchial obstruction has diffuse character, lung emphysema is most frequently bilateral process and assessed as complication of chronic lung diseases.

Clinical features. The main complaints in patients with increased airiness of the pulmonary tissue are dyspnea and cough. Dyspnea - has expiratory or mixed character and increased during physical activity. Cough - commonly dry and has reflex character, on destructive processes - with purulent sputum discharge.

Objective examination. General patient's condition may be satisfactory (early stage of the disease, the stage of remission); may be middle grave, moderate grave or grave (progression of bronchiectatic disease, destructive process in the lung, bronchial asthma attacks). Due to the acute or gradual chronic hypoxia may be observed the deranged consciousness.

The posture of the patients is frequently active. May be observed the forced posture m form of orthopnea (spasm of bronchi, attacks of bronchial asthma, decreasing the breath surface).

The color of the skin is characterized by central or diffuse cyanosis due to the accumulation of the carbon dioxide and reduced restored hemoglobin.

Inspection of the chest may reveal barrel-like (emphysematous) form of the chest with protruded supra- and subclavicular fosses, horizontal direction of the ribs, smoothed and narrow intercostals spaces, increased anteroposterior diameter. As usual the chest is symmetrical, the type of respiration is mixed or thoracic, accessory respiratory muscles active participate in the breathing act. especially m. sternocleidomastoideus and m. trapezius with evident elevation and lowering of the entire chest during breathing. May be observed tachypnea with shallow respiration depth.

Palpation of the chest. Elasticity of the chest is decreased (rigid chest), the chest is painless. Vocal fremitus is badly transmitted.

Percussion of the lungs. In comparative percussion of the lungs generalized hyperresonance (bandbox sound) may be heard over the hyperinflated lungs of emphysema. In topographic percussion of the lungs is observed bilateral lowering of the lower lungs edges, respiratory mobility of the lower borders of the lungs is decreased.

Auscultation of the lungs. In auscultation of the lungs may be observed pathologically decreased vesicular breathing and dry rales.

Additional methods of examination

Clinical blood analysis: secondary erythrocytosis; leukocytosis, neutrophilia, accelerated ESR (during progression of chronic diseases), eosinophilia (bronchial asthma).
Sputum analysis: data depends on the main disease.
X-ray examination: the signs of increased airiness of the pulmonary tissue, low diaphragm's position.
Spirometry shows decreased vital lung capacity.

***Topic 5*. Pneumonias: Symptoms and Syndromes on the Basis of Clinical - Instrumental and Laboratory Methods of Examination. Pneumosclerosis. Tumors of the Lungs**. **The Basic Symptoms and Syndromes in Dry Pleurisy and Pleural Effusion. Syndrome of Respiratory Failure in the Pathology of Broncho-Pulmonary System**.

Definition and modern classification of pneumonias (hospital-acquired, non-hospital-acquired, aspiration, pneumonia at immunodeficiency persons), classification by character of affection of the lungs (pleuropneumonia, bronchopneumonia, interstitial pneumonia). The basic etiology factors of pneumonias. Lobar and bronchopneumonia: complaints and physical methods of examination of the patients. Criteria of heavy current of pneumonia. Instrumental diagnostics of consolidation of pulmonary tissue. Laboratory findings of an inflammatory syndrome at pneumonias. Principal causes of development of pneumosclerosis. Pneumosclerosis, physical and instrumental examination of a patient. The basic clinical forms of tumors of the lungs: clinical features in the central and peripheral localization of tumor. A syndrome of consolidation of pulmonary tissue. The reasons of the development of inflammation of the pleura. Ways of occurrence and circulation of intrapleural fluid both in norm and pathologies. Complaints of a patient in dry pleurisy and pleural effusion, differences of the results of physical examination (palpation, percussion, auscultation of the lungs). Syndromes of accumulation of fluid and air in the pleural cavity. Opportunities of instrumental diagnostics. Pleural puncture: pleural fluid examination. Differences between exudates and transudates due to the results of physical and laboratory examination. The basic clinical syndromes and stages of the syndrome of respiratory failure in lung diseases.

PNEUMONIA

Pneumonia – acute inflammatory lung disease with obligatory alveoli involment and exudative formation in them.

Classification

I. *Acceding to the particularities of infection*:
- nonhospital pneumonia;
- pneumonia in outpatients;
- pneumonia in innnpatients;
- intrahospital pneumonia;
- asperities pneumonia;
- pneumonia at severe immunodeficiency persons.

II. *The category of the patients with nonhospital pneumonia*:

1 category – pneumonia in patients without associated pathology and other modified factor;

2 category – pneumonia in patients with associated pathology and/or other modified factor;

3 category – pneumonia that needs hospitalization (without intensive treatment);

4 category – severe pneumonia that needs intensive treatment (reanimation).

III. *The groups with intrahospital pneumonia*:

1 group (A) – patients with mild or moderate pneumonia severity (without risk factors) that develops in different period of hospitalization or grave pneumonia with early manifestation (less than 5 days of hospitalization);

2 group (B) – patients with slight or moderate pneumonia severity (with specific risk factors) that develops in different period of hospitalization or grave pneumonia with early manifestation (less than 5 days of hospitalization);

3 group (C) – patients with grave in presence risk factors) or pneumonia with late manifestation (more than 5 days of hospitalization).

Nonhospital pneumonia means pneumonia that develops outside from hospital (in conditions of life).

Intrahospital pneumonia means pneumonia that develops in first 48-72 hours after hospitalization in condition of reject infectious in incubation period on the moment of admission to the hospital.

The main risk factors:

- smoking;
- taking of alcohol;
- chronic left ventricular heart failure;
- chronic obstructive pulmonary disease;
- influence of toxic ecologic and professional factors;
- innate defects of bronchopulmonary system;
- chronic infection in nosepharynx;
- the state of immunodeficiency and treatment with immune depressants;
- the status after operation;
- general exhaustion;
- long confinement to bed;
- old age.

The main pathogenic links:

- entrancing of the pathologic agent to the pulmonary tissue;
- impaired local bronchopulmonary resistance;
- development of the local inflammatory process and its overspreading in lung tissue;
- sensebilization advance to infectious agents and input of proinflammatory reactions;
- impaired microcirculation;
- activation of oxidative stress and proteolysis in lung tissue;
- antibody and immune complexes formation.

ACUTE LOBAR PNEUMONIA

All authors who studied the etiology of acute lobar pneumonia (pleuropneumonia, croupous pneumonia), discovered Frenkel pneumococci (mostly types I and II, less frequently types III and IV) in about 95 per cent of cases. Fridlaender diplobacillus, streptococcus, staphylococcus, etc. are found less frequently.

Acute lobar pneumonia occurs mostly after severe overcooling. The main portal of infection is bronchogenic, less frequently lymphogenic and haematogenic. Congestion in the lungs in cardiac failure, chronic and acute diseases of the upper airways, avitaminosis, overstrain and other factors promote the onset of pneumonia. Acute lobar pneumonia is relatively frequent in patients who had pneumonia in their past history (it recurs in 30- 40 per cent of cases which is another evidence of the hyperergic character of the disease).

Pathological anatomy: Four stages are distinguished in the course of acute lobar pneumonia. The stage of *congestion* is characterized by acute hyperemia of the lung tissue, exudation, obstruction

of capillary patency, and stasis of the blood. It lasts from 12 hours to 3 days. The stage of *red hepatization* continues from 1 to 3 days. The alveoli are filled with plasma rich in fibrinogen and erythrocytes. The stage of *grey hepatization* is characterized by cessation of erythrocyte diapedesis; the erythrocytes contained in the exudate decompose and their hemoglobin converts into haemosiderin. The alveoli (containing fibrin) become filled with leucocytes. The lungs become grey. The stage lasts from 2 to 6 days. The last stage is *resolution.* Fibrin is liquefied by proteolytic enzymes and exudate is gradually resorbed.

Clinical features

The onset of the disease. Typical acute lobar pneumonia begins abruptly with shaking chills, severe headache, and fever, to 39-40°C. The chills usually persist for 1-3 hours, then pain appears in the affected side; sometimes it may arise below the costal arch in the abdomen to simulate acute appendicitis, hepatic colics, etc. (this usually occurs in inflammation of the lower lobe of the lung, when the diaphragmal pleura becomes involved in the process). Cough is first dry and in 1-2 days dusty sputum is expectorated.

Objective examination: the patient's general condition is grave. General examination shows hyperemia of the cheeks, more pronounced on the affected side, dyspnea, cyanosis, often herpes on the lips and nose; the affected side of the chest lags behind in the respiratory act. Vocal fremitus is slightly exaggerated over the affected lobe. Sounds over the lungs are quite varied and depend on the distribution of the process, the stage of the disease, and other factors. At the onset of the disease, shortened percussion sound can be heard over the affected lobe, often with tympanic effect because liquid and air are simultaneously contained in the alveoli; the vesicular breathing is decreased while bronchophony is increasing; the so-called initial crepitation (crepitus indux) is present.

The height of the disease (classified by pathologists as the red and grey hepatization stages) is characterized by the grave general condition. It can be explained not only by the size of the affected area of the lung which thus does not take part in respiration but also by general toxicosis. Respiration is accelerated and superficial (30-40 per min) and tachycardia (100-200 beats per min) is characteristic. Dullness is heard over the affected lobe of the lung; bronchial respiration is revealed by auscultation. Vocal fremitus and bronchophony are exaggerated. Vocal fremitus is in some cases either absent or enfeebled (in combination with pleurisy with effusion, and also in massive acute lobar pneumonia, in which the inflammatory exudate fills large bronchi); bronchial breathing is inaudible. Before the antibiotic era, the patient with acute lobar pneumonia would often develop vascular failure with a marked drop in the arterial pressure due to toxic sis. Vascular collapse is attended by general asthenia, drop of temperature, increased dyspnea, cyanosis and accelerated small pulse. The nervous system is also affected (sleep is deranged; hallucinations and delirium are possible, especially in alcoholic patients). The heart, liver, kidneys and other organs are also affected. Fever persists for 9-11 days if antibiotics are not given. The temperature then drops abruptly during 12-24 hours or lytically during more than 2-3 days. Resolution stage. The exudate thins, air again fills the alveoli to decrease dullness of the percussion sound, tympany increases, and bronchial breathing lessens. Crepitation is heard again (crepitus redux) because the alveolar walls separate as air fills them. Moist rales are heard. Exaggerated vocal fremitus, then bronchophony, and finally bronchial breathing disappear.

Additional methods of examination

General blood analysis. The leukocyte count in the blood increases to 15-25 x 10^9 per liter (15000-25000 per microlitre); neutrophils account for 80-90 per cent of the leucocytes; a shift to the left with the appearance of juvenile forms is sometimes observed. The number of eosinophils increases and they can disappear completely in grave cases. Relative lymphopenia and monocitosis are observed. The ESR increases, the red blood does not change.

Sputum is tenacious during the congestion period; it is slightly crimson and contains much protein, a small number of leucocytes, erythrocytes, alveolar cells, and macrophages. In the stage of red hepatization sputum is variant and rusty; it contains fibrin and a higher number of formed elements. In the stage of grey hepatization leucocyte count in the sputum increases significantly; the

sputum becomes mucopurulent. In the resolution stage, leucocytes are converted into detritus, which is found in the sputum; many macrophages are also found. Pneumococci, staphylococci, Friedlaender diplobacilli can be detected in the sputum.

X-Ray changes in the lungs depend on the stage of the disease. The lung pattern is first intensified, then dense foci develop, which later fuse. The shadow usually corresponds to the lung lobe. The lungs become normally clear in two or three weeks. Dynamics of the X-ray changes spends on the tune when the therapy is begun.

BRONCHOPNEUMONIA (FOCAL PNEUMONIA)

Separate lobules of the lungs are affected in bronchopneumonia, hence another name, lobular pneumonia. Inflammatory foci may be multiple, or they may fuse (confluent pneumonia); the foci may be located in various parts of both lungs simultaneously (mostly in the lower parts of the lungs).

Quite varied bacterial flora would be normally found in bronchopneumonia. The importance of pneumococcus has significantly decreased while the role of other microorganisms, especially of streptococci and staphylococci, has increased. Acute pneumonia is caused in many cases by viruses (in influenza, ornithosis, and psittacosis).

Development of bronchopneumonia is associated with the extension of the inflammatory process from the bronchi and bronchioles to the pulmonary tissue (hence another name of bronchopneumonia - catarrhal pneumonia, which reflects the transition of inflammation and infection with the mucous secretion from the inflamed bronchi into the alveoli). Infection gets inside the pulmonary tissue via the bronchi, and more frequently peribronchially, i.e. by lymph ducts and interalveolar septa. Local atelectasis that occurs in obstruction of the bronchus by a "mucopurulent plug" is important in the pathogenesis of bronchopneumonia. Obstruction of bronchial patency can be caused by a sudden bronchospasm and edema of the bronchial mucosa, inflammation (bronchitis), etc. Recently bronchopneumonia occurs mostly in children and the aged, usually during cold seasons (spring, autumn, winter).

Clinical features

The onset of the disease is usually overlooked because the often develops against the background of bronchitis or catarrh of the up air airways. But if a patient with clinical signs of acute bronchitis develops high temperature and has symptoms of a more severe disease, he should be considered to have bronchopneumonia. The most typical signs of bronchopneumonia are cough, fever and dyspnea. If the inflammatory focus at the periphery of the lung and the inflammation involves the pleura pain in the chest during coughing and deep breathing may occur. Fever may persist for various terms in bronchopneumonia. Usually fever is remittent and irregular. The temperature is often subfebrile or it may even be normal in the middle-aged or old patients.

Objective examination can sometimes reveal moderate hyperemia of face and cyanosis of the lips. Respiration accelerates to 25-30 per min; respiratory lagging of the affected side of the chest may be observed. Percussion and auscultation may prove ineffective if the inflammatory foci are small and deeply located. In the presence of a large focus, especially if it is located at the periphery of the lung tissue, and also in confluent pneumonia, the percussion sounds lose resonance (or become completely full), and auscultation reveals vesiculobronchial or bronchial breathing. Vocal fremitus and bronchophony are characteristic of such cases. Dry and moist rales are frequent, but consonating moist rales and crepitation that are heard over a limited part of the chest are especially informative.

Additional methods of examination

Clinical blood analysis: leukocytosis, neutrophilia, shift of leukocyte formula to the left, accelerated ESR.

Sputum analysis: in focal pneumonia the sputum is mucopurulant, tenacious or tenacious thick consistency, glass-like with yellow traces color, odorless. In microscopic study are revealed a lot of columns ciliated epithelium, leucocytes, alveolar macrophages.

X-ray examination: in focal pneumonia- the signs of focal pulmonary tissue consolidation (darkening limited by the lung's segment).

TUMORS OF THE LUNGS

Tumors of the lungs may be benign or malignant primary tumors or metastases from primary cancers of many other organs and tissues. Primary lung tumors include bronchogenic carcinoma (the most common type of lung cancer), bronchial carcinoid, and a number of rarer types.

Bronchial carcinoid (formerly called bronchial adenoma) may be benign or malignant and occurs equally in both sexes. Its course is prolonged. The endobronchial portion of the tumor may obstruct the lumen of major bronchi. Risk bleeding from the overlying mucous membrane often occurs. Recurrent pneumonia within the same lung zone and localized overlying pleural pain are common. Metastases are uncommon but may occur to regional lymph nodes.

Etiology: Cigarette smoking is the principal cause of bronchogenic carcinoma, accounting for >90% of cases in men and > 80% of cases m women, with 87% of all lung cancers attributed to tobacco exposure. A strong dose-response relationship occurs in the three most common types of bronchogenic carcinoma: squamous cell, small cell, and adeno carcinoma; the slope of the curve is steepest for small cell carcinoma and least steep for adenocarcinoma. A small proportion of lung cancers (15% in men and 5% in women) are related to occupational agents, often overlapping with smoking: asbestos, radiation, arsenic, chromates, nickel, chloromethyl ethers, mustard (poison war) gas, and coke oven emissions. The exact role of air pollution is uncertain.

The TNM (tumor, node, metastasis) system is a standard staging classification for non-small cell carcinoma. Small cell carcinoma has usually metastasized by the time it is diagnosed; it is staged as either limited (confined to one hemithorax with or without involvement of mediastinal and ipsilateral supraclavicular lymph nodes) or extensive (spread beyond this point).

Clinical features

Manifestations depend on the tumor's location and type of spread. Because most *bronchogenic carcinomas* are endobronchial, patients typically present with cough, with or without hemoptysis. In patients with chronic bronchitis, increased intensity and intractability of preexisting cough suggest a neoplasm. Sputum arising from an ulcerated bronchial tumor usually is not excessive (although occasionally sputum may be profuse and watery with bronchioloalveolar carcinomas), but it contains inflammatory exudate and is often blood-streaked. Hemoptysis is uncommon in small cell carcinoma. Copious bleeding is uncommon and strongly suggests invasion of large underlying blood vessels. Bronchial narrowing may cause air trapping with localized wheezing and commonly causes atelectasis with ipsilateral mediastinal shift, diminished expansion, dullness to percussion, and loss of breath sounds. Infection of an obstructed lung produces fever, chest pain, and weight loss. Persistent localized chest pain suggests neoplastic invasion of the chest wall.

Peripheral nodular tumors are asymptomatic until they invade the pleura or chest wall and cause pain or until they metastasize to distant organs. Late symptoms include fatigue, weakness, decreased activity, worsening cough, dyspnea, decreased appetite, weight loss, and pain. Malignant serosanguineous pleural effusions are common and are often large and recurrent. *Horner's syndrome* (due to invasion of the cervical thoracic sympathetic nerves) consists of enophthalmos, miosis, ptosis, and ipsilateral facial anhidrosis. *Pancoast syndrome* (due to infiltration of the brachial plexus and neighboring ribs and vertebrae) consists of pain, numbness, and weakness of the affected arm. The two syndromes may coexist. A tumor may extend directly into the esophagus, producing obstruction, sometimes complicated by a fistula. Phrenic nerve invasion usually causes diaphragmatic paralysis. Clinical features of cardiac involvement include arrhythmias, cardiomegaly, and pericardial effusion. *Superior vena cava obstruction* and left recurrent laryngeal nerve paralysis (causing hoarseness) are produced by direct extension of the tumor or by extension of the tumor from neighboring lymph nodes. In the superior vena cava syndrome, obstruction of venous drainage leads to dilation of collateral veins in the upper part of the chest and neck; edema and plethora of the face, neck, and upper part of the torso, including the breasts; suffusion and edema of the conjunctiva; breathlessness when supine. Intrapulmonary spread of primary or secondary cancer may cause lymphangitic carcinomatosis with subacute cor pulmonale, worsening

hypoxemia, and severe dyspnea. Secondary hematogenous nodular metastases within the lungs are common, but secondary bronchial invasion is rare. Hematogenous metastatic spread to the liver, brain, adrenals, and bone is common and may occur early, resulting in symptoms at those sites before obvious pulmonary symptoms.

Paraneoplastic syndromes of lung cancer, which are numerous, are extrapulmonary, remote effects of tumors. They lead to metabolic and neuromuscular disturbances unrelated to the primary tumor or metastases. They may be the first sign of occurrence or recurrence, but they do not necessarily indicate that a tumor has spread outside the chest In hypertrophic pulmonary osteoarthropathy (the best known), clubbing of the fingers and toes and periosteal elevation of the distal parts of long bones occur. Hematologic disorders, including thrombocytopenic purpura, leukemoid reaction, myelophthisic anemia, polycythemia, and marantic thrombosis, may also occur.

Additional methods of examination

X-ray. The principal sources of diagnostic information are the history, which raises the suspicion of tumor and provides early localizing information, and the chest x-ray, which shows the lesion, its location, and its anatomic effects. However, large-scale studies at several cancer centers did not demonstrate any advantages for lung cancer screening using chest x-rays and sputum sample analysis. Although cancers were occasionally detected earner using these methods, early detection did not appear to affect the overall survival of patients.

Bronchoscopy is used to visualize and biopsy bronchial tumors. With a flexible bronchoscope, the subsegmental bronchi can be explored to demonstrate and to sample tumors by washings, brushings, and biopsy. Many surgeons perform a preoperative mediastinoscopy to evaluate the mediastinal and hilar lymph nodes, to confirm the diagnosis, and to separate operable from inoperable tumors.

Exploratory thoracotomy is required in < 10% of cases to establish the diagnosis and resectability of lung cancer. Contraindications include distant or mediastinal metastases and cardiorespiratory insufficiency. Exploration is unnecessary when metastases are demonstrated by mediastinoscopy, by parasternal mediastinotomy (which has largely replaced scalene node exploration), or by pleural or liver biopsy. Palpable lymph nodes and metastatic skin nodules provide important diagnostic material.

PLEURISY

Most diseases of the pleura (pleurisy included) are secondary to disease of the lung. Pleurisy usually develops as a reaction of the pleura to pathological changes in the adjacent organs, in the lungs in the first instance, and less frequently as a symptom of a systemic disease. Serous pleurisy often arises as an allergic reaction. Purulent pleurisy is often a complication of bronchopneumonia: inflammation may extend onto the pleura, or an inflammatory focus may turn into an abscess, which opens into the pleural cavity. Inflammation of the pleura is always attended by markedly increased permeability of the wall of the affected capillaries of the pulmonary pleura.

In the presence of purulent processes in the lungs or adjacent organs (pericarditis, perioesophagitis, etc.), purulent pleurisy often develops abruptly. The affection of the pleura in tumours, which in most cases are metastatic (less frequently primary), decreases its absorptive function to promote accumulation of pleural effusion (haemorrhagic effusion in most cases).

DRY PLEURISY

Dry pleurisy (adhesive, fibrinous) is the pathology of the respiratory system that characterized by bands and commissures formation between pleural layers and increase of their thickness due to the inflammation.

Etiology

- infection (tuberculosis, bacterial infection, fungus, viral infection);
- dissemination of the tumor cells to pleura;
- reactive pleuritis (uremia);
- dehydrotation (profuse bleeding, vomiting, diarrhea).

Pathogenesis

- dilation of lymphatic capillaries;
- increased vessels penetration;
- pleural inflammation;
- pleural infiltration;
- fibrin accumulation on visceral and parietal pleura;
- fibrosis development;
- anatomic and functional block of resorbtion apparatus;

Clinical features Intensity of clinical features depends on the pathologic process spreading. The main complaints in patients with dry pleurisy are: cough, pain in the chest and dyspnea.

Cough - most commonly dry and has reflectivity character.

Pain in the chest - connecting with pleura injury, occurs suddenly on the affected side, intensive and increases during deep inspiration or coughing.

Dyspnea - intensity depends on process spreading.

Objective examination. *General patient's condition* may be from middle grave to grave.

The posture of the patients is forced (lie on the affected side in order to relieve the pain).

The color of the skin and visible mucosa is without changes.

In inspection occur superficial, rapid breathing (via intensive pain); participation of the accessory respiratory muscles in the breathing act or even mixed type of respiration. In static inspection as usual the chest is symmetrical, on dynamic - detect poor movement of the chest expansion on one side.

In palpation the chest is painful on the damage side, elasticity is saved, vocal fremitus is equal transmitted.

In comparative percussion of the lungs may be observed dull sound over pathological region.

In topographic percussion of the lungs the normal lower borders are revealed, respiratory mobility of the lower border on the affected side is decreased.

In auscultation of the lungs over the region with decreased vesicular breathing detect pleural friction sound.

Additional methods of examination

Clinical blood analysis: leukocytosis, neutrophilia, shift of leukocyte formula to the left, accelerated ESR.

X-ray examination: - the signs of pleura injury and fibrin deposition.

PLEURISY WITH EFFUSION

Pleurisy with effusion is characterized by the presence of exudate in the pleural cavity, mostly in the outer costal-diaphragmatic sinus. Parietal, supradiaphragmatic and interlobar pleurisy also occur. After abatement of inflammation, effusion (serous, serofibrinous, haemorrhagic, purulent) usually resolves but the pleura remains thickened, its membranes adhere to one another, and the pleural cavity is completely obliterated in some cases. Effusion sometimes remains between adhesions to stimulate encapsulated pleurisy.

Etiology

- infection (tuberculosis, bacterial infection, fungus, viral infection);
- dissemination of the tumor cells to pleura;
- allergic and autoimmune pleurisy;
- pleurisy in diffuse connective tissue pathology;
- posttraumatic pleurisy.

Pathogenesis

- direct pleura injury (trauma, operation, tumor, infection through lymph or blood);
- contact way of process spreading;
- infection and allergic mechanism;
- inflammatory exudation to the pleural cavity;

- impaired lymph and blood circulation;
- oncotic pressure disturbance;
- impaired resorbtion;
- fluid accumulation in pleural cavity.

Clinical features

Intensity of clinical features depends on the pathologic process spreading, etiology, amount and character of exudates. The main complaints in patients with exudative pleurisy are: cough, dyspnea, pain and feeling of heaviness in the chest, supplementary - general weakness, hyperthemia, loss of appetite and perspiration.

Cough - most commonly in initial stage dry and has reflectivity character, along disease progression becomes moist.

Pain in the chest - one of the fist symptoms and connecting with pleura injury, may be different in its intensity (from moderate to acute) and increases during deep inspiration or coughing. In cause of diaphragmatic pleurisy localization the pain can irradiate to the upper abdominal region or via the n. diaphragmatic to the neck. For the period of exudates volume intensity the pain becomes duller but dyspnoea increase.

Dyspnea - has mixed character and its intensity depends on the exudates volume and speed of its accumulation, degree of affected lung ventilation via compression by fluid and mediastenum organs displacement.

Objective examination. *General patient's condition* may be from middle grave to grave.

The posture of the patients is forced (lie on the affected side in order to revile the pain).

The color of the skin and visible mucosa are characterized by diffuse cyanosis. In case of mediastenum fluid localization observed edema of the face and neck, dysphagia and voice changes.

In inspection observe superficial, rapid breathing (via intensive pain); mixed type of dyspnea. In static inspection as usual the chest is asymmetrical, on dynamic - detect poor movement of the chest expansion on the affected side.

In palpation the chest is painful, rigid with badly vocal fremitus transmission on the damaged side.

In comparative percussion of the lungs detect dull sound over the pathological region.

In topographic percussion of the lungs the lower edge on the affected side is elevated, respiratory mobility is increased. In large exudates amount over the lung there are 5 clinical-diagnostic zones (for more detail information seen syndrome of fluid accumulation in pleural cavity).

In auscultation of the lungs in the initial stage on the affected side over the region with decreased vesicular breathing detect pleural friction sound. In large exudates amount according to the five clinical-diagnostic zones there are distinguished: over exudates - the zone with significant decreased vesicular breathing or full absent of breathing sounds; over consolidate pulmonary tissue - the zone with pathological bronchial breathing; over the free from fluid and healthy side - the zone with increased vesicular breathing.

Additional methods of examination

Clinical blood analysis: leukocytosis, neutrophilia, shift of leukocyte formula to the left, accelerated ESR.

X-ray examination: - the signs of pleura affection, significant darkness with slanting upper border of the fluid and dislocation of mediastenum to the healthy side.

Pleural fluid analysis includes: assessment of macroscopic characteristics (character, transparency, color, consistency, odor, relative density); chemical study (protein, Rivalts's reaction); microscopic study (cellular composition); bacterioscopic study.

RESPIRATORY INSUFFICIENCY

The function of the external respiratory apparatus is to supply the body with oxygen and to remove carbon dioxide formed by exchange reactions. This function is realized firstly by ventilation, i.e. gas exchange between the outer and alveolar air. This insures the required oxygen and carbon dioxide pressure in the alveoli (an important factor is intrapulmonary distribution of the inspired air). Secondly, this function is realized by diffusion of carbon dioxide and oxygen through the walls of the alveoli and lung capillaries (oxygen is supplied from the alveoli to the blood and carbon dioxide is diffused from the blood to the alveoli). Many acute and chronic diseases of the bronchi and the lungs cause respiratory insufficiency (Wintrich, 1854). The degree of morphological changes in the lungs does not always correspond to the degree of their dysfunction.

Respiratory insufficiency is now defined as the condition with abnormal gas composition of the blood, or this abnormality is compensated for by intense work of the external respiratory apparatus and higher load on the heart. This decreases functional abilities of the body. It should be noted that the external respiratory function is closely connected with the blood circulatory function: the heart work is intensified during external respiratory insufficiency, which is an important compensatory element of the heart function.

Respiratory insufficiency is manifested clinically by dyspnea and cyanosis; at later stages, when cardiac failure joins the process, edema occurs.

The patient with respiratory insufficiency employs the same compensatory reserves as a healthy person does during heavy exercise. But the compensatory mechanisms of a sick person are actuated much earlier and it loads under which a healthy person would feel no discomfort (e.g. dyspnea and tachypnea can develop in a patient with lung emphysema given during slow walking).

Among the first signs of respiratory insufficiency are inadequate changes in ventilation (rapid and deep breathing) at comparatively light roads for a healthy individual; the minute volume increases. In certain bases (bronchial asthma, lung emphysema, etc.) respiratory insufficiency is compensated by intensified work of the respiratory muscles, i.e. by the filtered respiratory mechanics. In other words, in patients with pathology if the respiratory system, the external respiratory function is maintained at he required level by mobilizing compensatory mechanisms (i.e. by efforts greater than required for healthy persons), and by minimizing the respiratory reserves: the maximum lung ventilation decreases, the coefficient of oxygen consumption drops, etc.

Various mechanisms are involved gradually to compensate for progressive respiratory insufficiency depending on its degree. At the early stages of respiratory insufficiency the external respiratory function at rest is realized in normal way. The compensatory mechanisms are only actuated during exercise in a sick person. In other words, only reserves of the external respiratory apparatus are decreased at this stage. As insufficiency further progresses, tachypnea, tachycardia, and signs of intensified work of the respiratory muscles (during both inspiration and expiration), with involvement of accessory muscles, develop during light exercise and even at test. At the later stages of respiratory insufficiency, when the body compensatory reserves are exhausted, arterial hypoxaemia and hypercapnia develop. In addition to the growing vivid arterial hypoxaemia, signs of latent oxygen deficit also develop; underoxidized products (lactic acid, etc.) are accumulated in the blood and tissues.

Still at later stages, right ventricular incompetence joins pulmonary insufficiency because of the developing hypertension in the lesser circulation, which is attended by increased load on the right ventricle, and also because of dystrophic changes in the myocardium occurring as a result of its constant overload and insufficient oxygen supply. Hypertension in the vessels of the lesser circulation in diffuse affections of the lungs arises by reflex mechanisms in response to insufficient lung ventilation and alveolar hypoxia- the Euler-Liliestrand reflex (this reflex mechanism is an important adaptation means in focal lung affections; it limits blood supply to insufficiently ventilated alveoli). Further, in chronic inflammatory diseases of the lungs due to cicatricial and sclerotic changes in the lungs (and due to affections in the lung vessels) blood passage through the lesser circulation becomes even more difficult. Increased load on the myocardium of the right ventricle

stimulates gradual development of its insufficiency to cause congestion in the greater circulation (pulmonary heart).

Depending on the cause and mechanism of developing respiratory insufficiency, three types of disordered lung ventilation are distinguished: *obstructive, restrictive and mixed* (combined).

The obstructive type is characterized by difficult passage of air through the bronchi (because of bronchitis, bronchospasm, contraction or compression of the trachea or large bronchi, e.g. by a tumor, etc.). Spirography shows marked decrease in the MLV and PVC, the VC being decreased insignificantly. Obstruction of the air passage increases the load on the respiratory muscles. The ability of the respiratory apparatus to perform additional functional load decreases (fast inspiration, and especially expiration, and also rapid breathing become impossible).

The restrictive type of ventilation disorder occurs in limited ability of the lungs to expand and to collapse, i.e. in pneumosclerosis, hydro- and pneumothorax, massive pleural adhesions, kyphoscoliosis, ossification of the costal cartilages, limited mobility of the ribs, etc. These conditions are in the first instance attended by a limited depth of the maximum possible inspiration. In other words, the vital capacity of the lungs decreases together with the maximum lung ventilation), but the dynamics of the respiratory act is not affected: no obstacles to the rate of normal breathing and whenever necessary, to significant acceleration of respiration) are imposed.

The mixed or combined type includes the signs of the two previous disorders, often with prevalence of one of them; this type of disorder occurs in long-standing diseases of the lungs and the heart.

External respiratory dysfunction occurs also when the anatomical dead pace increases (in the presence of large cavities inside the lung, caverns, abscesses, and also in multiple large bronchiectasis). Similar to this type is the respiratory insufficiency due to circulatory disorders (e.g. in thromboembolism, etc.) during which part of the lung is excluded from gas exchange, while its ventilation is to a certain degree maintained. Finally, respiratory insufficiency arises during uneven distribution of air in the mgs (distribution disorders), when a part of the lung is not ventilated (in pneumonia, atelectasis), with preservation of blood circulation. Part of venous blood is not oxygenated before it enters pulmonary veins and the left chambers of the heart. Similar to this type of respiratory insufficiency with regard to pathogenesis) is the so-called vascular bypass or shunting (from right to left), during which part of the venous blood from the pulmonary artery system enters directly the pulmonary vein (bypassing the capillaries) to mix with oxygenated arterial blood. Oxygenation of blood in le lungs is thus upset but hypercapnia may be absent due to compensatory intensification of ventilation in the intact parts of the lung. This is partial respiratory insufficiency (as distinct from total insufficiency where hypoxemia and hypercapnia are present).

Respiratory insufficiency is characterized by upset gas exchange through the alveolar-capillary membrane of the lungs. It occurs when this membrane is thickened to interfere with normal gas diffusion through it he so-called pneumonoses, alveolar-capillary block). It is not accompanied by hypercapnia either since the rate of CO_2 diffusion is 20 times higher than that of oxygen. This form of respiratory insufficiency is, in the first instance, characterized by arterial hypoxaemia and cyanosis. Lung ventilation is intensified.

Respiratory insufficiency associated with toxic inhibition of the respiratory centre, anaemia, or oxygen deficit in the inhaled air, is not connected directly with the pathology of the lungs.

Acute and chronic respiratory insufficiencies are differentiated. The former occurs in attacks of bronchial asthma.

Three degrees and three stages of respiratory insufficiency are also distinguished. The degrees of respiratory insufficiency reflect the gravity of the disease at a given moment.

The first degree of respiratory insufficiency (dyspnea, in the first instance) becomes evident only at moderate or significant physical load.

Dyspnea develops during light exercise in *the second degree* of insufficiency; the compensatory mechanisms are involved when the patient is at rest and functional diagnosis can reveal some deviations from the normal indices.

The *third degree* is characterized by dyspnea at rest and cyanosis as a manifestation of arterial hypoxaemia; deviations from the normal indices during functional pulmonary tests are significant.

Stages of respiratory insufficiency in chronic diseases of the lungs reflect the changes occurring during the progress of the disease. Stages of latent pulmonary, pronounced pulmonary and cardiopulmonary insufficiency are normally differentiated.

Topic 6. Clinical, Instrumental and Laboratory Examination of the Patients with Chronic Gastritis, Gastric and Duodenal Ulcer and Diseases of the Intestine.

Definition and modern classifications of gastritis, gastric and duodenal ulcer. Etiology of these diseases. Epidemiology of Helicobacter pylori, conditions of damage of a mucosa of a stomach and duodenum. Main complaints of the patients with gastritis and peptic ulcer. Instrumental and laboratory examination of the patients. Complications of peptic ulcer disease. Acute upper gastrointestinal bleeding: clinical features. Main symptoms and syndroms in patients with enteritis and colitis: intestinal dyspepsia, symptoms of malabsorption. Irritable bowel syndrome.

SYNDROM OF FUNCTIONAL DYSPEPSIA

Syndrome of functional dyspepsia - the complex of the symptoms that includes the pain and feeling of the discomfort in epigastria, heaviness and feeling of overflow after meal, early saturation, swelling of a stomach, nausea, vomiting, eructation, heartburn and other signs at which it is not possible to reveal organic pathology.

Classification

I. *According to the type of dyspepsia there are distinguish:*

- the ulcer-like type;
- the dysmotor type;
- the nonspecific type.

II. *According to the stage of dyspepsia there are distinguish:*

- stage of aggravation;
- stage of unstable remission;
- stage of remission.

Clinical features

In patients with functional dyspepsia the clinical picture includes the general neurologic displays - sleeplessness, migraines, irritability, bad mood and special (gastric) that depend on a type of dyspepsia.

Ulcer-like type - is characterized by periodic pain in epigastria, the moderate intensity, as a rule without irradiation, arising on an empty stomach (hungry pains) or at night (night pains), relieved after reception of food and/or antacids.

Dysmotor type - is characterized by the feeling of early saturation, weight, overflow, a swelling in the epigastria; sensation of discomfort after meal; nausea, sometimes vomiting; decrease in appetite.

At a nonspecific type there can be various attributes, which difficultly carry to any of described variants.

For functional dyspepsia there are specific three attributes (according to Roman (III) diagnostic criteria):

- constant or recurrent dyspepsia (a pain or the discomfort localized in epigastria), which duration not less than 12 weeks for last 6 months (between aggravations there can be light intervals);

- on the basis of the anamnesis, endoscopic researches of the upper part of a gastrointestinal tract and ultrasound examination of abdominal cavity organs there are absent proofs of organic disease;

- absence of proofs, that dyspepsia is facilitated by defecation or connected with change of frequency of a stool.

Establishment of the diagnosis probably only by exception of disease with a similar clinical picture, especially that connected with the «symptoms of alarm» (a fever, an impurity of blood in stool, an anemia, accelerated ESR, unmotivated behaviors).

CHRONIC GASTRITIS

Chronic gastritis - chronic inflammatory-dystrophic process in the stomach mucous with recurrent duration that passing with cells regeneration disturbances, progressive atrophies of secretory epithelium, impairment secretory, motoric and incretory functions of the stomach.

Chronic gastritis is morphologic concept with stereotypic reactions in the stomach mucosa: inflammation, atrophy, impaired cells regulation with metaplasia and dysplasia.

Etiology

- the leading role in development of the chronic gastritis belongs to Helicobacter pylori;
- genetic predisposition;
- influence of other infectious factors (parasites invasions, virus infectious, fungus damage);
- autoimmune factors;
- particularities of nutrition;
- food allergy; influence of harmful factors of an environment;
- radiating irradiation;
- influence of drugs therapy.

Classification

The international classification of chronic gastritis, 1996

The type of gastritis	Synonyms	Etiologic factors
Non-atrophy	Type B Superficial Antral gastritis Chronic antral gastritis Hypersecretory	Helicobacter pylori Other factors
Atrophy	Type A Autoimmune Associated with pernicious anemia	Autoimmune Helicobacter pylori Particularities of nutrition Influence of harmful factors of an environment
The special forms		
Chemical	Type C Reactive reflux-gastritis	Contents of duodenum
Radiating		Radiating irradiation

Lymphocytary	Variolomorphy Associated with celiakia	Idiopathic mechanisms Autoimmune mechanisms Helicobacter pylori
Non-infective granulomatous	Isolated granulomatous	Crone's disease Sarcoidosis
Eoshynophily	Food allergy Other allergens	Allergic
Other infections		Bacteria Viruses Fungus Parasites

Clinical features

The signs of chronic gastritis are difficult to describe because the course and symptomatology of the disease are quite variable. Some patients do not complain of anything during remissions; the disease may also develop for a long time without any manifestations and it is therefore difficult to establish the time of its onset.

The main syndrome of chronic gastritis is gastric dyspepsia: heaviness in abdomen after the meal, earlier saturation, deterioration of appetite, nausea, eructation and vomiting. It may combine with intestinal dyspepsia characterized by meteorism, rumbling sounds in the abdomen, constipation, and diarrhoea.

Objective examination. *General patient's condition* is usually from satisfactory to moderate grave. The consciousness is clear, the posture active. The color of the skin and visible mucosa has corporeal color.

The data of inspection, palpation, percussion and auscultation of respiratory and cardiovascular systems are without peculiarities.

Palpation of the epigastrium is in most cases painless or may be distinguish moderate pain in epigastrium and umbilical regions.

Additional methods of examination

Gastric secretory function. The acid secretion may remain normal or it may decrease. Free hydrochloric acid may be absent from the gastric juice (achlorhydria).

Roentgenography is but of little use in the diagnosis of chronic gastritis.

Gastroscopy can give valuable diagnostic information, especially if it is combined with sighting biopsy.

Biopsy is important for the study of patients with chronic gastritis.

Detecting of Helicobacter pylori.

PEPTIC ULCER DISEASE (Gastric and Duodenal Ulcer)

Peptic ulcer is a general chronic and relapsing disease characterized by seasonal exacerbations with ulceration of the stomach wall or the duodenum. Approximately 10% of all adults have peptic ulcer at some time in their lives. Duodenal ulcer is more common 4 times than gastric ulcer. The male to female ratio for duodenal ulcer varies from 4:1 or 2:1. Gastric ulcer is more common in the older (over 50 year), and duodenal ulcer in those from 30-60 year. Duodenal ulcer is more common in male at age 30-55 years. 90-95% of duodenal ulcers occur in the first portion of duodenum. More than 90% of gastric ulcers occur in the lesser curvature.

Etiology

- associated with Helicobacter pylori;
- influence of drugs;
- results of pathological hypersecretion;
- mixed etiology.

Many ulcers are caused by a bacterium called Helicobacter pylori (H. pylori). Around 90% of duodenal ulcer patients and 70% of gastric ulcer patients are infected with H. pylori. Peptic ulcers frequently also can be caused by daily use of pain relievers called non-steroidal anti-inflammatory drugs (NSAIDs). The remaining 30% of gastric ulcers are due NSAIDs.

Having a close relative with peptic ulcer disease also increases your risk, as does smoking and alcohol use.

Pathogenesis

An ulcer forms when there is an imbalance between aggressive factors and defense factors. Aggressive factors: H. pylori infection, NSAIDs, acid and pepsin, smoking, alcohol and other factors. Defense factors: gastric mucosa, gastroprotective prostaglandins, mucus layer on epithelial cells, bicarbonate secreted by epithelial cells and adequate blood supply of gastric mucosa.

Cinical features

The leading symptom of peptic ulcer is abdominal pain. In peptic ulcer the pain is localized in epigastric region, may radiate to the back and is of variable quality: gnawing, burning, boring, or hunger like. The pain is intermittent, last from a few minutes to many hours, be worse when your stomach is empty. Food, antacids or other antisecretory drugs often bring relief. The seasonal character of pain is very typical of peptic ulcer disease.

In patients with peptic ulcer the main complaints are abdominal pain and displays of dyspeptic syndrome. Heartburn, vomiting, belching, regurgitation, and salivation are frequent symptoms. Vomiting relieves pain of gastric ulcer and some patients force themselves to vomit after eating to relieve symptoms. Heartburn is a specific burning sensation behind the sternum, associated with regurgitation of gastric contens into the inferior portion of lie esophagus. The mechanism of heartburn is associated with motor dysfunction of the esophagus (in addition to the acid fact of the gastric contents, which was formerly believed to be decisive). Appetite is often increased. The intestinal symptoms of peptic ulcer disease are constipations, which are closely connected with the character of nutrition and bed-rest during exacerbations, and are mainly connected with reflex dyskinesia of the intestine.

Objective examination. *General patient's condition* is usually from moderate grave to extremely grave. The consciousness is clear, the posture usually active or may be forced in cause of complications development. *The color of the skin* and visible mucosa has corporeal color. With disease progression and prolonged duration may occurs pale color and loss of weight. The tongue is usually clean. The data of inspection, palpation, percussion and auscultation of respiratory and cardiovascular systems are without peculiarities.

In superficial tentative oriental palpation and percussion of the abdomen may be distinguish pain in epigastrium and umbilical regions with local muscular resistance.

Additional methods of examination

Endoscopy (fibroesophagogastroduodenoscopia) is the procedure of choice for diagnosis of peptic ulcer. Endoscopy with biopsy and the subsequent morphological research of a bioptates - confirms presence of ulcer defect and specifies of its localization, depth, the form, the sizes, condition of the bottom and edges of the ulcer.

Barium meal (or X-ray examination). A direct proof of peptic ulcer is a niche, which is found in 75-80 per cent of patients. The ulcer is usually located on the lesser curvature. In duodenal ulcer, the can be found inside the bulb or outside it (extrabulbar ulcer). Barium meal is less commonly used now. Endoscopy should be done if it shows gastric ulcer to rule out malignancy.

Gastric secretory function. The main method of study of gastric secretion is pH-measure (intragastral pH-metria). Normal basal pH in body stomach is 1.6-2.2. There is pH more than 2.2 – hyperacidity. There is pH less than 1.6 – hypoacidity. If the ulcer is found in the stomach, hydrochloric acid, pepsin, mucoprotein and albumin fractions of the gastric juice vary within normal limits. In duodenal ulcer all these indices significance exceed normal values.

Determining of Helicobacter pylori. *Blood test or Serological test* - determine antibodies of H. pylori in blood. *Breath test*. You drink a solution that contains a radioactive carbon atom. If H. pylori is in your body, it will break down the solution and release the carbon. Your bloodstream carries the carbon to your lungs, where it's exhaled and can be detected in your breath. *Stool test* – determine antigen of H. pylori in feaces. H. pylori can be detected *histologically* on biopsy of gastric mucosa.

Rapid urease activity test. Culture. Biopsies obtained can be cultured on special medium.

Clinical blood analysis. May be determining of the signs of ferric deficiency anemia at chronic or acute bleeding.

Examination of faeces. Latent haemorrihage is almost always revealed on examination of faeces during exacerbation of peptic ulcer.

Complications

Haemorrhage. This is the most frequent complication. It may be manifested by haematemesis (blood vomiting) and tarry faeces (melaena). Among other causes of gastric haemorrhagel peptic ulcer is accounted for 15-25 per cent of patients. The patient general condition depends on the length and intensity of bleeding.

Perforation. Free perforation into peritonial cavity occurs in approximately 2-3% of patients. Signs of perforation are a sudden stabbing pain, the reflex collapse, acute abdomen, and progressive peritonitis (unless a timely surgical aid is given to the patient). The pain is felt beneath the xiphoid process or in the right hypochondrium. The abdominal wall is tense. The patient assumes a forced posture on his back; the tongue is dry and coated. The pulse is retarded.

Penetration. Extension of the ulcer crater beyond the gastric or duodenal wall into contiguous structure e.g. pancreas especially if ulcer is in posterior wall of duodenum. Less commonly ulcer may penetrate into liver, biliary tract or colon.

Stenosis or pyloric obstruction. Ulcers heal to leave scars. If the ulcer was in the pylorus, the cicatricial tissue may narrow the lumen and interfere with free passage of he gastric contents into the duodenum. First the narrowing is compensated for by hypertrophy of the gastric muscles, but later the stomach becomes distended, food stays inside it for a longer period. Patient presents with abdominal bloating, nausea, vomiting and weight loss. Patients complain of permanent pain, eructation with rotten egg wind, and profuse morning vomiting with food that was ingested several days ago. Constipation is alternated with diarrhea. In the presence pyloric stenosis peristaltic and antiperistaltic movements of the epigastrium can be seen.

IRRITABLE BOWEL SYNDROME

Functional gastrointestinal disorders are defined as disorders of gut function in the absence of structural pathology. Irritable bowel syndrome is a function bowel disorder in which abdominal pain is associated with defaecation or a change in bowel habit with features of disordered defaecation and distension.

Irritable bowel syndrome encompasses a wide range of symptoms and single cause is unlikely. It is generally believed that most patients develop symptoms in response to psychosocial factors, altered gastrointestinal motility, altered visceral sensation or luminal factors.

Clinical features

The most common presentation is that of recurrent abdominal pain. This is usually colicky or “cramping”, is felt in the lower abdomen and is relived by defaecation. Abdominal bloating worsens throughout the day; the cause is unknown but it is not due to excessive intestinal gas. The bowel habit is variable. Most patients alternate between episodes of diarrhea and constipation. The constipated type tend to pass infrequent pellety stools, usually in association with abdominal pain. Those with diarrhoea have frequent defaecation but produce low-volume stools. Passage of mucus is common.

Despite apparently severe symptoms, patients do not lose weight and are constitutionally well. Many have other “functional” symptoms including dyspepsia, headaches, backache, poor sleep and chronic fatigue syndrome. Physical examination does not reveal any abnormalities.

Topic 7. Basic Symptoms and Syndroms in Biliary Diseases: Chronic Cholecystitis, Cholangitis, Cholelithiasis, Chronic Hepatitis and Hepatic Cirrhosis.

Definition and modern classifications of chronic cholecystitis and cholangitis. Biliary duct dyskinesia and its tapes. Main complaints of the patients with cholecystitis and cholangitis. Clinical, instrumental and laboratory examination of the patients for biliary disease. Study of duodenal contents and to analyze the results. Cholelithiasis.: main complaints and clinical features. Biliary pain (“biliary colic“). Jaundice and cholestasis, them laboratory findings.

Definition and modern classifications of chronic hepatitis and hepatic cirrhosis. Main causes of hepatitis and cirrhosis. The mechanisms of affection of liver in viral hepatitis. Main complaints and clinical features of the patients with chronic hepatitis and cirrhosis of liver. Hepatic histology and biochemical tests for hepatocellular damage. Child-Pugh classification and index of histological activity. Portal hypertension, liver failure and hepatorenal failure. Main complications of hepatic cirrhosis.

SYNDROME OF BILE DUCTS DYSKINESIA (dysfunctional bile tract disorders)

The syndrome of bile ducts dyskinesia is the complex of clinical symptoms which developing connects with moto-tonic dysfunction of gallbladder, bile ducts and sphincters. Dysfunctional bile tract disorders include not coordinated, untimely, insufficient or excessive reduction of a gallbladder and sphincters (Oddy, Lutkensa and Mirricy).

Classification

Depending on the etiological factor, localization and functional state there are the next forms of dysfunctional bile tract disorders:

I. *According to the etiology*:

1. Primary dysfunctional bile tract disorders (hereditary decrease of muscular tone, decrease of receptors apparatus sensitivity to neurohumoral stimulation).
2. Secondary dysfunctional bile tract disorders.

II. *According to the localization*:

1. Dysfunction of the gall bladder.
2. Dysfunction of the Oddy's sphincter.

III. *According to the functional state*:

1. Hyperfunction.
2. Hypofunction.

In hyperkinetic form of the gall bladder or/and bile ducts dysfunction the main complaints are: acute pain in the abdomen and clinical signs of neurotic syndrome.

Pain in the abdomen - is periodic, recurrent, colic like, localized in the right hypochondrial region with radiation to the back, right scapulae and right shoulder, aggravated more frequent at night-time after improper feeding, alcohol, augment physical or psychical activity.

In hypokinetic form of the gall bladder or/and bile ducts dysfunction the main complaints are: dull pain in the abdomen, clinical signs of neurotic and dyspeptic syndromes.

Clinical features

Pain in the abdomen is periodic, recurrent, has dull holding apart character with localization in the right hypochondrial region and radiation to the back, right scapulae and right shoulder, aggravated during bending of body and at night-time after improper feeding, alcohol, augment physical or psychical activity.

The clinical signs of neurotic syndrome include - irritability, fatigue, perspiration, tachycardia, and headache. The clinical signs of dyspeptic syndrome include - bitterness in a mouth, nausea, vomiting and difficult defecation.

Objective examination. *General patient's condition* as usual satisfactory, consciousness is clear, posture is frequently active or active with restriction in cause of intensive biliar colic.

The color of the skin and visible mucosa has corporeal color *(cutis colons so-matici),* without eruption, moderate moisture arid elasticity, preserved turgor, may observe transient subicteria of the skin.

The results of inspection, palpation, percussion and auscultation of respiratory and cardiovascular systems are without particularities.

In superficial tentative oriental palpation of the abdomen detect moderate pain in right hypochondria. Muscular resistance, diastases recti, and fluctuation symptoms are negative.

In penetrative palpation of the abdomen identify tenderness in gall bladder point (Ker point).

Additional methods of examination

Clinical blood analysis: without pathological changes.

Clinical urine analysis: without pathological changes.

Biochemistry blood analysis: increased activity of alkaline phosphotase and aspartate aminotransferases (more than in twice during two-multiple analisis), in combination with pancreatic ferments elevation (amylasa, lipasa), hyperbilirubunemia with predominance of bound fraction.

Medicament test (morphincholeretic test Debrea or morphinneostigmin test Nardy) - provocation of typical bile colic.

Ultrasound examination of the digestive organs. With obligatory evaluation of functional gall bladder state (use of bile discharge stimulated breakfast - 29g sorbitol in 100ml water) - specific constriction of gall bladder less than 40 %, increase of choledoch diameter more than after fat food.

Endoscopy. Endoscopic visualization of the biliary tree is now the best diagnostic procedure for stones, tumors, and strictures of the bile duct and is the only reliable means of diagnosing primary sclerosing cholangitis. Furthermore, it offers the therapeutic procedures of sphincterotomy, stone withdrawal, and the insertion of stents across strictures.

In patients with dysfunctional bile tract disorders the endoscopic sign are: edema and stricture of duodenal papilla.

Study of duodenal secretion. Reduction of gall bladder reflex (amount of bladder bile increase to 100-150ml in norm 30-70ml; the bile excreted by little portions; dilation of bile discharge more than 45min).

CHRONIC CHOLECYSTITIS

Cholecystitis is the inflammatory gallbladder. The incidence of the disease is rather high; women are mostly affected. Inflammatory response can be evoked by three factors: mechanical inflammation; chemical inflammation and bacterial inflammation. The disease can be provoked by gall stones, dyskinesia of the bile ducts, anatomical properties of the gall bladder and bile ducts, ptosis of the internal organs, pregnancy, inactive mode of life, rare meals, etc. Chronic cholecystitis may develop after acute cholecystitis but in most cases it develops gradually as an independent disease.

Clinical features

The patient complains of dull boring pain in the right hypochondrium which usually develops 1-3 hours after taking abundant specially fat and roasted food. The pain radiates upward to the region of the right shoulder, neck and the scapula. If cholecystitis concurs with cholelithiasis, sharp pain may arise (like in biliary colic).

Dyspeptic signs the also present: bitter and metallic taste in the mouth, eructation, nausea, abdominal flatulence, and alternation of diarrhoea with constipation. The disease is sometimes not attended by pain except that the patient feels heaviness in the epigastrium or right hypochondrium, and dyspepsia develops.

Objective examination. The temperature is often subfebrile. *Surface palpation of the abdomen* reveals sensitivity and sometimes tenderness in the region of gall-bladder projection. The Mussy's, Ortner's, Murphy's, and Vasilenko's symptoms are positive. The gall bladder is impalpable.

- *Vasilenko's symptom* (sharp pain in the region of the gall bladder when it is tapped over at the height of inspiration);
- *Murphy's symptom* (sharp pain in the right hypochondrium when the examiner's nandifpifess the gall bladder at the height of inspiration);
- *Ortner's symptom* (pain during tapping over the right costal arch by the edge of the hand). If inflammation extends onto the peritoneum overlying the gall bladder;
- *Shchetkin-Blumberg's* symptom is positive. In this case, in the presence of gangrenous cholecystitis (gangrene of the gall bladder) and possible perforation of the gall-bladder wall, a dangerous sign appears;
- In moderate tension of the abdominal muscles it is sometimes possible (especially in purulent cholecystitis) to palpate an enlarged and very tender gall bladder. The liver does not usually increase, but its tender edge can sometimes be palpated;
- *The Mussy's* symptom (tenderness at the point of the phrenicus nerve, between the heads of the sternocleidomastoid muscle) can often be positive.

Additional methods of examination

Clinical blood analyses. The blood changes (during exacerbation) are characterized by moderate leucocytosis and mildly increased ESR.

Signs of inflammation (mucus, leucocytes, desquamated epithelium) on be found in B bile. If inflammation involves bile ducts (cholangitis), C the contains the same signs of inflammation. The vesical reflex (B bile) is sometimes impossible to obtain even by repeated probing. This indicates disordered contractility of the gall bladder which is typical of chronic cholecystitis. Bacteriological studies of B bile reveal the character of microbial flora. Polarographic study of bile can reveal signs of inflammation.

Cholecystography shows changes in the configuration of the gall bladder and the absence of its distinct contours. This indicates upset concenting capacity of the gall-bladder mucosa. After taking a stimulating cal the gall bladder contracts insufficiently.

CHOLANGITIS

Cholangitis is caused by bacterial infection of bile ducts and occurs in patients with other biliary problems such as choledocholithiasis, biliary strictures or tumors.

Jaundice, fiver and abdominal pain are cardinal presenting features.

CALCULUS CHOLECYSTITIS (cholelitiasis)

Calculus cholecistitis (the stone of the gall bladder) is chronic disease that caused by impaired cholesterol exchange and/or bilirubin metabolism with stones formation in the gall bladder (cholelitiasis) and/or in the common bile duct (choledocholitiasis). Stones in the common bile duct occurs in 10-15% of patients with gallstones.

Etiology

- metabolic dysbalance (impaired cholesteric exchange, adiposity and increased estrogen development);
- hypodinamia;
- an irrational nutrition (high-caloric food, low contents of vegetative fibers in the meal);
- eldery;
- treatment by hyperlipidemic fibrates;
- diseases of the gastrointestinal tract, accompanied with acquire incompetence,
- biliary tract infections and bile;
- hemolytic anemias.

Pathogenesis

- stages of bilious stones formation;
- stage of saturation;
- stage of crystallization;
- stage of growth.

Cholesteric concrements in the gall bladder are formed at presence in it the bile overload by cholesterol. Thus in the liver the superfluous quantity of cholesterol and insufficient quantity of bilious acids is synthesized, including lecithin that is also is in the dissolved condition. As a result cholesterol drops out in a deposit. For the further formation of stones the condition contractivity functions of the gall bladder and presence of inflammatory mucous damage is of important sense. Under influence of nucleation factors (bile glicoproteins) from the dropped out crystals of cholesterol the first microlits appear. In condition of decreased evacuator functions they are start to grow.

Classification

The I stage - the stage of the beginning or prior to the stone formation;
The II stage - the stage of stones formation with indication;
The III stage - the stage of complications.

Clinical features

The most typical complaints are attacks biliary colic. Sudden obstruction of the cystic duct or common bile duct by a gallstone in biliary colic causes epigastric or right upper quadrant steady, aching pain (not colicky) that may radiate to the right scapula and shoulder. This pain is characterized by rapid onset over a few minutes, lasts one to several hours and subsides gradually. Anorexia, nausea, vomiting, restlessness often accompany the pain in biliary colic. Also the patients show complaints to the bitterness in a mouth, sub fibril temperature.

Objective examination. *General patient's condition* is from satisfactory to moderate grave. The consciousness is clear and the posture is active or forced. At survey - the raised weight of a body as a rule is defined.

The color of the skin and visible mucosa has corporeal color (cutis colons somatici), without eruption, moderate moisture and elasticity, preserved turgor, may observe transient subicteria of the skin or even yellow color due to obstruction - development of mechanical type of jaundice.

In superficial tentative oriental palpation of the abdomen detect moderate pain in right hypochondria. Muscular resistance, diastases recti, and fluctuation symptoms are negative.

In penetrative palpation of the abdomen identify tenderness in gall bladder point (Ker's point) and positive Kerras', Murphys', Ortners' and Mussis' symptoms.

Additional methods of examination

Clinical blood analysis - leucocytosis with shift of the formula to the left, accelerated ESR.
Biochemical blood analysis - increase of the common bilirubin due to direct fraction, increase of alanine aminotransferases and aspartate aminotransferases activity (at development of hepatitis and in the period biliary colic), increase activity of alkaline phosphotase and moderate increase of amylase, cholesterol and β-lipoproteins levels.
Ultrasound examination of the digestive organs - revealing the signs of cholecystitis and stones in the gall bladder.
Cholecyctography. About 80 to 85 per cent of gallstones are not radio-opaque and oral cholecystography remains the method of choice for examining the gall bladder with contrast medium to detect calculi when ultrasound is not available or is inconclusive.
Computed tomography - for the diagnosis verification and carrying out of differential diagnostics.

JAUNDICE

The syndrome of jaundice is one of the most widespread syndromes of the digestive system pathology that based on the significant hyperbilirubinemia and bilirubin accumulation in the tissue and skin.

Etiology

Depending on the etiological factor there are the next forms of jaundice:

A. Exogenic (false) jaundice or xanthosis.

B. Endogenic (true) jaundice:

I. Suprahepatic (hemolytic):

1. Hereditary hemolytic anemia (talassemia, Minkovskogo-Shofara).
2. Acquired hemolytic anemia (autoimmune, posthemotransfusion).
3. Increased erythrocytes hemolysis on different diseases:

- infections;
- burns;
- tumors;
- hemorrhages (hematoms, infarctions);
- on diseases with deranged erythropoesis (B_{12}-deficiency anemia, primary erythrocytosis, sideroplastic anemia).

II. Hepatic (parenchimatous):

1. Liver disease:

- different types of hepatitis;
- liver cirrhosis;
- tumor of the liver;
- Gilber's syndrome;
- Kriglera-Nayara syndrome;
- Dabina-Dgonsona syndrome;
- Rotor syndrome.

III. Subhepatic (mechanical):

1. Mechanical jaundice with tumor genesis:

- cancer of the pancreas;
- cancer of the major duodenal papilla;
- cancer of the bile bladder;
- cancer of the extra hepatic bile duels

2. Mechanical jaundice with non-tumor genesis:

- calculus cholecystitis.

Pathogenesis

Depending on the causes there are the next mechanisms of jaundice:

A. Exogenic (false) jaundice or xanthosis: xanthosis related with prolonged using of carotin (carrots), oranges, tangerines and administration of ethacridme lactate (rivanol), picric acid.

B. Endogenic (true) jandice:

I. ***Suprahepatic jaundice*** (icterus suprahepatica) occurs due to the excessive hemolysis of erythrocytes in the cells of the reticulohistocytic system (spleen, liver, bone marrow). Hemoglobin brakes down to the globin and hem. Bilirubin is formed from the released hem and accumulates in blood. Observe in malaria, sepsis, poisoning by hemolytic substances, inherited or acquired hemolytic anemia.

On suprahepatic jaundice - it is characterized by lemon-yellow tint, moderate intensity without itching of the skin and hematological signs of anemia and hyperbilirubinemia in suprahepatic jaundice: bilirubinemia - increased of total bilirubin mainly due to the unbound bilirubin.

II. ***Hepatic jaundice*** (icterus hepatica) occurs due to the damage of hepatocytes and disorders of their function (inversion of unbound bilirubin to bound), observe in acute and chronic hepatitis, poisoning and other liver diseases. On parenchymatous jaundice it is characterized by orange-yellow tint. In hepatic jaundice: bilirubinemia - increased of total bilirubin due to the unbound and bound fractions.

III. ***Subhepatic jaundice*** (icterus infrahepatica) occurs due to the accumulation of bilirubin (the product of gradual oxidation of bilirubin) resulted from partial or complete obstruction of the common bile duct in patients with stones in the gall bladder, cancer of the head of the pancreas, cancer of the major duodenal papilla. On obstructive jaundice - it is characterized by greenish-yellow tint, with early appearance of skin itching (may be before jaundice manifestation). In subhepatic jaundice - increased of total bilirubin mainly due to the bound bilirubin.

Additional methods of examination

Clinical blood analysis: anemia, leukocytosis, neutrophilia and accelerated ESR.

Clinical urine analysis: the color is greenish-yellow or greenish-brown (beerlike), odorless, bilimbinuria and urobilinogenuria.

Biochemical blood analysis.

In suprahepatic jaundice: bilirubinemia - increased of total bilirubin mainly due to the unbound bilirubin; dysproteinemia, positive thymol test; elevated aldolase; alanine aminotransferases;

In hepatic jaundice: bilirubinemia - increased of total bilirubin due to the unbound and bound fractions; dysproteinemia, positive thymol test; elevated prothrombin index (in significant degree of hepatic-cellular failure - decreased), decrease of total cholesterol, increased concentration of aldolase, alanine aminotransferases, aspartate aminotransferases, alkaline phosphatase, lactate dehydrogenase, cholinesterase, sorbitol dehydrogenase and ceruloplasmin.

In subhepatic jaundice - increased of total bilirubin mainly due to the bound bilirubin; dysproteinemia, negative thymol test; elevation of prothrombin index, significant increase of total cholesterol and β-lipoproteins, moderate (non-obligatory) increase of alanine aminotransferases, aspartate aminotransferases, alkaline phosphatase and ceruloplasmin.

CHRONIC HEPATITIS

Chronic hepatitis represents a series of liver disorders of varying causes and severity in which hepatic inflammation and necrosis continue for at least 6 months.

Classification

I. *According to causes*:

- chronic hepatitis B;
- cronic hepatitis C;
- cronic hepatitis D;
- cronic hepatitis other viral;
- atoimmune hepatitis;
- dug-associated chronic hepatitis;
- cyptogenic chronic hepatitis.

In 40-70 per cent of cases chronic hepatitis develops as an outcome of on acute epidemic or serum hepatitis.

II. *Classification by grade or by stage*:

0 - no fibrosis;
1 – mild fibrosis;
2 – moderate fibrosis;
3 – severe fibrosis, including bridging fibrosis;
4 – cirrhosis.

III. *Classification by according to the index of histologic activity on Knodell in points*:

a) periportal hepatocytis necrosis, including the bridge-like - 0-10 points;

b) intrasegmental focal necrosis and hepatocytis dystrophy - 0-4 points;
c) inflammatory infiltrate in portal tracts - 0-4 points;
d) fibrosis - 0-4 points.

The index of histologic activity from 1 up to 6 points testifies to presence of the "minimal" chronic hepatitis, 7-12 points - the "moderate", 13-18 points - a "grave" chronic hepatitis.

IV. *Classification by function of the liver on Child-Pugh*:

Class A (stage compensation);
Class B (stage subcompensation);
Class C (stage decompensation).

Pathological anatomy

Among diffuse inflammatory affections of the liver benign (non-active, persisting), active and cholestatic chronic hepatitis are distinguished. Non-active hepatitis is characterized by inflammation in the periportal zones, preservation of the lobular structure, and sometimes by moderate dystrophic changes in the hepatocytes. The inflammatory and cicatricial processes are more distinct in the liver affected by active hepatitis. Inflammatory infiltration extends from the periportal zones inside the liver. Hepatocytes are extensively necrotized and have dystrophic changes; fibrosis is found in the liver.

Clinical features

Chronic hepatitis are characterized by dyspeptic symptoms; jaundice; moderate enlargement and induration of the liver; enlargement of the spleen; dysfunction of the liver as determined by laboratory tests and radiohepatography.

But the clinical picture and also the course of each clinico-morphological form of hepatitis have their special features. Chronic benign hepatitis is characterized by obliterated clinical picture. The patients complain of heaviness or dull pain in the right hypochondrium, decreased appetite, bitter taste in the mouth, nausea and eructation. Jaundice is usually absent or it is moderate. Objective studies reveal a mildly enlarged liver with a smooth surface and a moderately firm edge, which is slightly tender to palpation. Enlargement of the spleen is not marked. Laboratory studies: the blood bilirubin content is usually normal; in the presence of jaundice it increases to about 17-50; the blood globulin content is mildly increased, activity of the enzymes is either normal or only slightly changed; the prothrombin content is normal or slightly decreased.

Chronic active hepatitis is characterized by complaints and objective symptoms: weakness, loss of weight, fever, pain in the right hypochondrium, loss of appetite, nausea, regurgitation, meteorism, skin itching, jaundice, and frequent nasal bleeding. The liver is enlarged, firm, with a sharp edge. The spleen is enlarged.

Additional methods of examination

Clinical blood analyses. Laboratory tests often reveal anaemia, leucopenia, thrombocytopenia (a sign of hypersplenism), and increased erythrocyte sedimentation rate.

Biochemical blood analysis: they show hyperbilirubinaemia, hyperproteinaemia, hypergammaglobulinaemia, positive protein-sedimentation tests, increased activity of transaminase and alkaline phosphotase; decreased activity of cholinesterase; the prothrombin index is sharply decreased; excretion of bromsulphthalein is delayed.

Puncture biopsy of the liver and (for special indications) laparoscopy establish the special histological and macroscopic changes in the liver characteristic of these forms. Chronic cholestatic hepatitis is mainly characterized by the cholestatic increased activity of alkaline phosphatase in the blood, and high cholesterol of blood. Persistent subfebrile temperature and regular increase erythrocyte sedimentation rate are also not infrequent.

CIRRHOSIS OF THE LIVER

Cirrhosis of the liver is a chronic progressive disease characterized by diffuse affection of liver's parenchyma and stroma with quantity reduction of functioning cells, their nodular

regeneration and excessive development of connective tissue that leads to cytoarchitectonic reorganization of the liver and development of hepatic insufficiency.

Etiology

Cirrhosis of the liver is a polyetiological disease. It may develop due to postviral hepatitis: hepatitis B, C and D; alcohol; drugs (isoniazid, methotrexate and other); toxic factor; biliary obstruction: primary and secondary biliary cirrhosis; genetically caused disorders of a metabolism: deficiency of alpha-1-antitripsini; Konovalov-Wilson's disease; cardiac failure; cryptogenic.

Clinical features

They are defined by a stage of process and presence of complications - from full absence of symptoms up to common clinical picture of hepatic coma. The sharp painful syndrome is not specific. More often, the patients have complaints on the feeling of weight and dull pains in right hypochondria and epigastria, that amplifying after taking food and physical activity. The patients also suffering from the dyspeptic symptoms that connected with disorders of digestion, general intoxication and accompanying pathologies of a gastro-intestinal tract: the swelling of a stomach, less often - a nausea, vomiting, a heartburn, bitterness in a mouth, infringements of a stool. Also can be present the general complaints - weakness, fatigue, decrease in working capacity, weight reduction, rise in temperature (asteno-vegetative syndrome); yellowness of the skin and visible mucosa, skin itch, hemorrhages, nasal and uteri bleedings (coagulopathy syndrome).

The liver cirrhosis allocates the following clinical syndromes:

- the syndrome of portal hypertension (includes edematous-ascitic syndrome);
- the syndrome of hepato-cellular insufficiency;
- hepatic encephalopathy;
- hepatolienal syndrome.

***Objective examination*:** *General patient's condition* is from satisfactory to extremely grave. May observed deranged consciousness with hepatic coma develops at final stage of diseases.

In general inspection may detect jaundice, expansion of the veins on the forward abdomen wall, palmary erythema, red lustrous lips, scarlet (lacquered) tongue, spider nevi or telangiectasia, Dupuitrens' contracture, hynecomastia at men, traces of scratches on all body, xanthomatous plaques on the skin (observed in patients with biliary cirrhosis of the liver. Inspection of the abdominal skin can relation or the veins that can be seen through the thinned skin of the abdominal wall (caput medusae). Collateral venous system can be seen on the chest as well. There can be an expressed loss of weight of a body down to cachexia, enlargement of abdomen in sizes, edematous ascitic syndrome even anasarca.

In superficial tentative oriental palpation of the abdomen may be detect moderate pain in right and left hypochondrias, muscular resistance and positive fluctuation symptoms.

In percussion of the liver according M. G. Kurlov and palpation of the liver and spleen may be detecting enlargement of the liver and spleen sizes with increase of their density and rough surface. However, in patients with significant amount of the fluid in abdominal cavity the enlarged lower liver border and spleen are not accessible for palpation.

Complications: encephalopathy, hepatic insufficiency, portal hypertension, hepatorenal syndrome, bacterial peritonitis, bleeding from varicous expanded veins.

Additional methods of examination

Clinical blood analyses. An active cirrhotic process is characterized by anaemia, leucopenia, thrombocytopenia, and increased ESR. Anaemia can be due to hypersplenism and gastro-intestinal haemorrhage, and often increased haemolysis, which is accompanied by reticulocytosis of the peripheral blood.

Biochemical blood analysis. The blood serum bilirubin content considerable only in the final stage of the disease. At the same time, the affection of the excretory motion of the cirrhotic liver can be

assessed by the presence of the conjugated fraction of bilirubin (bound bilirubin). Its content increases in normal and increased total bilirubin. The blood serum bilirubin content varies in biliary cirrhosis of the liver, mostly at the expense of bound bilirubin.

- Affection of liver cells is manifested by characteristic changes in the protein indices: decreased concentration of serum albumins and hypergammaglobulinaemia which in turn decreases the albumin-globulin coefficient.

- The blood level of lipids and cholesterol also increases considerably in the presence of biliary cirrhosis. A sensitive index of liver dysfunction is the decreased activity of cholinesterase.

- Transaminase activity increases in exacerbation of liver cirrhosis. Activity of alkaline phosphatase also increases in biliary cirrhosis.

- The decreased prothrombin content (which is synthesized by the liver cells), increased antithrombin coagulative activity and decreased total coagulative activity of plasma are important in the aetiology of haemorrhagic diathesis in liver cirrhosis.

- Detection of α-phetoprotein is required for screening on malignant transformation of cirrhosis. Research of the ceruloplasmin maintenance - etiologic factor establishment (Konovalov-Wilson's disease).

Ultrasound examination (ultrasonography) - revealing of hepatomegalia, spleenomegalia and infringement of hepatic structure.

Varicose veins of the esophagus are revealed by X-rays or by upper *gastrointestinal endoscopy*. *Rectoromanoscopia* – detection of varicous dilated veins of rectal textures.

Instrumental non-obligatory methods (under indications): hepatoscyntigraphia; computed tomography and magnetic resonance imaging.

SYNDROME OF PORTAL HYPERTENSION

Portal hypertension results from destruction and distortion of the hepatic vasculature leading to obstruction of blood flow and increasing backward pressure, resulting in hypertension in portal circulation. Normal pressure is 2-5 mmHg. Patients developing complications usually have portal pressure above 12 mmHg. On ultrasound maximum normal diameter of portal vein is 1 cm, it becomes dilated in portal hypertension.

Classification

Depending on the etiology and mechanism of developing there are the next forms of the portal hypertension syndrome:

I. Suprahepatic block:

- hepatic veins thrombosis;
- hepatic veins compression;
- vena cava inferior compression and/or thrombosis.

II. Intrahepatic block:

- chronic hepatitis;
- liver cirrhosis;
- tumor of the liver;
- metastatic liver damage.

III. Subhepatic block:

- congenital anomaly of vena porta;
- compression of a portal collector by a tumor;
- spasms.

The features of portal hypertension are as follows: splenomegaly, hypersplenism, collateral circulation and ascites.

Splenomegaly. Splenomegaly is a cardinal finding, and a diagnosis of portal hypertension is unlikely when splenomegaly can not be detected clinically or by ultrasonography. Clinical splenomegaly is present in 35-50% of cases.

Hypersplenism. When spleen becomes enlarged its function of removing cells from circulation also increases, this is called hypersplenism. Moderate thrombocytopenia frequently occurs (platelet count around $l00x10^9$/lit). Leukopenia occurs occasionally and anemia rarely.

By definition hypersplenism is characterized by: splenomegaly; cytopenia (thrombocytopenia, granulocytopenia or pancytopenia); normal bone marrow.

Collateral circulation. Increased portal vascular resistance leads to gradual reduction in the flow of portal blood to the liver and simultaneously to the development of collateral vessels, allowing the portal blood to bypass the liver and enter the systemic circulation directly. Collateral vessel formation is more prominent in the following areas:

• in the distal esophagus and proximal stomach (esophagogastric varices);

• in the distal rectum and anus(causing hemorrhoids);

• on the anterior abdominal wall which radiate prominently from the umbilicus forming "caput Medusae";

• renal , lumber, ovarian and testicular vessels (rare).

The most important collateral vessels are the esophagogastric varices as they can cause bleeding which is usually severe and acute. Bleeding from rectum and anus is rare.

Ascites. Accumulation of fluid in peritoneal cavity (ascites) in cirrhosis occurs, owing to two factors: portal hypertension and hepatic dysfunction. Portal hypertension causes transudation of fluid in peritoneal cavity from the portal circulation (due to increased hydrostatic pressure), while the hepatic dysfunction causes ascites by three mechanisms:

• salt and water retention occurs as a result of peripheral arterial vasodilatation and consequent reduction in effective blood volume. Nitric oxide is probably the vasodilator although prostaglandins and atrial natriuretic peptide may also be involved. The reduction in effective blood volume due to vasodilatation stimulates reninangiotensin system that promotes salt and water retention through stimulation of aldosterone. Failure of liver to metabolize aldosterone causes salt and water retention;

• liver is not able to synthesize sufficient proteins thus causing hypoalbuminemia, which results in decreased colloid osmotic pressure of the plasma resulting in leakage of fluid and development of edema and ascites;

• normally liver causes aldosterone metabolism, in case of hepatic dysfunction liver is unable to metabolize it, resulting in secondary hyperaldosteronism, and retention of sodium and water.

HEPATIC INSUFFICIENCY

Following are the features of hepatic insufficiency:

1. Jaundice: it is usually mild or absent. If occurs, it is mainly due to failure of bilirubin metabolism.

2. Circulatory changes: these changes result from increased peripheral circulation (hyperdynamic circulation) causing the following manifestations: *palmar erythema: i*t is mottled redness of the thenar and hypothenar eminences due to increased peripheral blood flow. Palmar erythema may also be present in normal old person, rheumatoid arthritis, pregnancy, thyrotoxicosis. *Spider nevi:* these are telangiectasia that result from arteriolar changes and comprise a central arteriole from which small vessels radiate. Spider nevi are confined to the area above the nipple and occurs on the face, necklace area, forearms and dorsum of hands.

3. Endocrine abnormalities:

• gynecomastia (because liver is unable to metabolize estogen, it may also develop as a side effect of diuretic spironolactone that is commonly used in cirrhosis;

• loss of libido;

• impotence and testicular atrophy in man;

• breast atrophy and amenorrhea.

4. Hemorrhagic tendency: it occurs in advanced liver failure and is due to underproduction of coagulation factors. The manifestations of hemorrhagic tendency may be:

• bruising, purpura;

• epistaxis;
• menorrhagia;
• GIT bleeding.

5. Skin changes:

• pigmentation occurs in cirrhosis (especially caused by hemochromatosis) and cirrhosis due to any reason as a result of cholestasis;

• clubbing of fingers and toes may also present.

6. Dupuytren's contracture associated with alcoholic cirrhosis and is very rare.

7. Hepatic encephalopathy. The cerebral disturbance or encephalopathy develops due to the following two factors:

• collateral venous circulation in cirrhosis bypasses the liver and allows nitrogenous substances from the gut to reach the systemic circulation through which they reach to the brain directly and produce cerebral disturbance;

• liver is responsible for detoxification of substances. When there is severe loss of liver function the un-detoxified substances such as ammonia reach to the brain, and produce cerebral dysfunction.

8. Renal failure (hepatorenal syndrome). It presents as low urine output, raised urea and creatinine, hyponatremia, low urinary sodium and hypotension. Kidneys are histologically normal and can work normally if transplanted to non-cirrhotic person. It occurs in advanced cirrhosis mostly with ascites is caused by decreased effective blood volume and hypotension as a result of vasodilatation due to release of nitric oxide from the liver. Details are given in the section of complications of ascites.

9. Hepatopulmonary syndrome. In cirrhosis pulmonary arteriovenous shunts also develop, leading to hypoxia and eventually central cyanosis, this is called hepatopulmonary syndrome.

Topic 8. The Main Symptoms and Syndromes in Renal Disease - Acute and Chronic Glomerulonephritis and Pyelonephritis.

The definition and modern classification of glomerulonephritis and pyelonephritis. The main mechanisms of developing glomerulonephritis and pyelonephritis. Patient’s complaints in kidneys disorders and physical examination data in patients with glomerulonephritis and pyelonephritis. Edematous syndrome and syndrome of arterial hypertension in kidneys disease. The possibilities of instrumental diagnostics of kidneys pathology. Laboratory examination of urine, the analysis and the interpretation of the results of general clinical analysis of urine. The examination of urine by Nechiporenko, Ambjurrhe, Adiskakovsky, Zymnitskyj methods. Urinary, nephritic syndromes in renal diseases. The results of biochemical blood examination in kidneys pathology. The syndromes of renal insufficiency and renal colic.

GLOMERULONEPHRITIS

Glomerulonephritis is immune-inflammatory renal disease with obligatory glomerulus's injury and including to the pathological process of all renal structures.

In more cases glomerulonephritis is an independent nozological form but may be a result of systemic pathology or pathological states.

Classification

I. Acute glomerulonephritis

1. According to the variant:
   - with urinary syndrome;
   - with nephritic syndrome;
   - with hypertension syndrome;
   - mixed.
2. According to the duration:
   - recidivated;

- lingering.

II. Subacute glomerulonephritis
III. Fast advance glomerulonephritis
IV. Chronic glomerulonephritis
1. According to the variant:
- with urinary syndrome;
- with nephritic syndrome;
- with hypertension syndrome;
- mixed;
- latent.
2. According to the stage:
- anhypertensive;
- hypertensive;
- renal failure:
• the period of anuria/oliguria;
• the period of diuresis reparation;
• the period of complete renal function reimbursement.
3. According to the duration:
- stable;
- progressive.
4. According to the phase:
- remission;
- aggravation.

Etiology

1. Influence of infection agent (primary streptococcus);
2. Endogenous antigens:
- systemic connective tissue diseases;
- systemic vasculitis;
- diabetes mellitus I or II type;
- viral hepatitis B or C type;
- the syndrome of arterial hypertension;
- later hystosis;
- other reasons.
3. Exogenous antigens:
- alcohol;
- toxic substances;
- poisons;
- bite of animals and insect;
- drugs.
4. Hereditary origin.

ACUTE GLOMERULONEPHRITIS

Acute glomerulonephritis is acute immuno-inflammatory renal disease with obligatory glomerulus's injury and afterward including to the pathological process of all renal structures.

Acute nephritis typically arises not during an infectious disease but only following a period of time, usually 2-3 weeks later. Attempts to isolate the streptococcus from the kidney tissue end in failure. Thus, the onset of acute nephritis usually coincides with the period when antibodies to streptococcus are produced.

Clinical features

The main complaint in patients with acute glomerulonephritis are weakness, thirst, pain in the back, dyspnea, palpitation, headache, nausea, vomiting, edema and lost of vision.

Objective examination: *General patient's condition* is from moderate grave to extremely grave. In general inspection detect "faces nephritica" - the face is edematous and often pale. Swelling usually appears first around the eyes in the morning and eyes may become slit like when edema is pronounced.

The color of the skin characterized by pathological pale, observed decreased turgor and elasticity of the skin, scars on the abdomen and hips due to the over stretching of the skin.

Edema in patients with nephritic syndrome (edema renalis) characterized by symmetrical localization, in initial stages arises on the face in the morning, has descending character and spreads on extremities, loin region with next fluid accumulation in cavities (hydrothorax, hydropericardium and anasarca). The skin over edema is glossy.

The apex beat is somewhat shifted to the left. In heart percussion observed displacement of the left border of the heart to the left. In heart auscultation detects tachycardia and gallops rhythm. Arterial pressure is increased.

Complications: acute renal failure, acute heart failure, encephalopathy, stroke, eclampsia, transitory vision impair.

Outcomes of disease: complete recovery, transformation to the chronic form.

Additional methods of examination

Clinical blood analysis: leukocytosis and increase of accelerated ESR.
Clinical urine analysis: in macroscopic study - urine is "meat wastes" color, cloudiness, without odor, olyguria, low specific gravity and moderate or significant proteinuria: in microscopic study observed large amount of altered erythrocytes (hematuria), cylinders (hyaline, erythrocytes and waxy casts) and leucocytes (non-constant).
Zimnitsky's test: izostenuria.
Nechiporenko's method: prevalence of erythrocytes under leucocytes; casts more 250 in ml.
Biochemistry of the blood: hypoproteinemia (hypoalbuminemia) and dysproteinemia.
Electrocardiography reveals signs of hypertrophy and overload of the left-ventricular myocardium. The amplitude of ECG waves decreases.
Renal biopsy: use for differential diagnosis and determination of the glomerulonephritis cause.

CHRONIC GLOMERULONEPHRITIS (nephritic form)

Chronic glomerulonephritis (nephritic form) is the variant of glomerulus's injury that characterized by the prevalence in clinic of nephritic syndrome signs.

Clinical features

The clinical features more frequently develop gradually accordantly to the proteinuria level.

The main complaint in patients with nephritic syndrome is edema that initially arises on the face and in disease progression spreads from the face downward up t hydrothorax, hydropericardium and anasarca.

Objective examination: *General patient's condition* is from moderate grave 1 extremely grave. In general examination is detected "fades nephritica " - the face is edematous and often pale. Swelling usually appears first around the eyes in the morning and eyes may become slit like when edema is pronounced.

The color of the skin characterized by pathological pale, observed decreased turgor and elasticity of the skin, scars on the abdomen and hips due to the over stretching of the skin.

Edema in patients with nephritic syndrome (edema renalis) characterized by symmetrical localization, in initial stages arises on the face in the morning, has descending character and spreads on extremities, loin region with next fluid accumulation in cavities (hydrothorax, hydropericardium and anasarca). The skin over edema is glossy.

In heart auscultation detects decreased loudness of the heart sounds. The data of percussion and renal palpation aren't specific.

Complications: renal failure, heart failure, encephalopathy, stroke, eclampsia.

Outcomes of disease: fast progression with poor prognosis, renal failure and death.

Additional methods of examination

Clinical blood analysis: leukocytosis and increase of accelerated ESR, anemia.
Clinical urine analysis: in macroscopic study - urine is "meat wastes" color, cloudiness, without odor, olyguria, low specific gravity and significant proteinuria: in microscopic study observed large amount of altered erythrocytes (hematuria), cylinders (hyaline, erythrocytes and waxy casts) and leucocytes (non-constant).
Zimnitsky's test: olyguria, nocturia, izostenuria.
Nechiporenko's method: prevalence of erythrocytes under leucocytes; casts more 250 in ml.
Biochemical blood analysis: increase of creatinin, ammonium and urine acid levels, hypoproteinemia (hypoalbuminemia) and dysproteinemia, increased potassium, magnum, sulphatis and phosphates level with sodium, calcium, chloral and hydrocarbonatis concentration is decreased. Decrease of Glomerulus's filtration rate.
Renal biopsy: use for differential diagnosis and determination of the glomerulonephritis origin.
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CHRONIC GLOMERULONEPHRITIS (hypertensive form)

Chronic glomerulonephritis (hypertensive form) is the variant of glomerulus's injury that characterized by the stable blood pressure increase.

Clinical features

The clinical features more frequently develop gradually accordanly to the proteinuria level.

The main complaint in patients are headache, lost of vision, dizziness, lost of sleeping and edema that initially arises on the face and in disease progression spreads from the face downward up to hydrothorax, hydropericardium and anasarca.

Objective examination: *General patient's condition* is from moderate grave to extremely grave. In general examination detects "faces nephritica ", pale color of the skin and visible mucus, edema renalis.

In heart percussion detect displacement of the left heart border outward and downward.

In heart palpation - apex beat displaced outward and downward, diffuse, high and strong strength.

In heart auscultation detects decreased loudness of the heart sounds, accentuated II heart sound over aortic valve. Stable blood pressure increases (with high diastolic blood pressure level).

Complications: edema of the brain, edema of the retina, myocardial infarction, cardiac asthma, encephalopathy and chronic renal failure.

Additional methods of examination

Clinical blood analysis: without significant changes.
Clinical urine analysis: decrease of specific gravity, proteinuria; in microscopic study cylinderuria, microhematuria.
Zimnitsky's test: olyguria, nocturia, izostenuria.
Biochemical blood analysis: increase of creatinin, ammonium and urine acid levels, decrease of Glomerulus's filtration speed, non-constant - hypoproteinemia and dysproteinemia.
ECG: the signs of left ventricle hypertrophy and systolic overload.
In ophthalmoscope examination: the signs of renal retinopathy- edema of the retina, spasm of the arteries, dilation of the veins, hemorrhages.
Renal biopsy: use for differential diagnosis and determination of the chronic gromerulonephritis origin.

CHRONIC GLOMERULONEPHRITIS (mixed form).

Chronic glomerulonephritis (mixed form) is the variant of glomerulus's injury that characterized by the presence of hypertensive and nephritic syndromes.

Clinical features

The clinical features more frequently develop gradually accordantly to the proteinuria level. The main complaint in patients is edema that initially arises on the face and in disease progression spreads from the face downward up to hydrothorax, hydropericardium and anasarca.

Also may be present general weakness, thirst, and loss of appetite, headache, vision changes and dizziness.

Objective examination: *General patient's condition* is from moderate grave to extremely grave. In general examination detects "faces nephritica" and edema renalis with next fluid accumulation in cavities.

The color of the skin characterized by pathological pale, observed decreased turgor and elasticity of the skin, scars on the abdomen and hips due to the over stretching of the skin. The skin over edema is glossy.

In objective examination detect displacement of the left border of the heart to the left, tachycardia, decrease loudness of the heart sounds and stable secondary arterial hypertension.

Complications: cardiac asthma, pulmonary edema, stroke, shock and chronic renal failure

Additional methods of examination

Clinical blood analysis: moderate leukocytosis and increase of accelerated ESR (in stage of aggravation), anemia.

Clinical urine analysis: in initial stage - poliuria, in late - olyguria with low specific gravity and significant proteinuria: in microscopic study observed non-constant hematuria, cylinders (hyaline) and leucocytes (non-constant).

Zimnitsky's test: olyguria, nocturia, hypo- or izostenuria.

Biochemical blood analysis: increase of creatinin, ammonium and urine acid levels, decrease of creatinin clireance, non-constant - hypoproteinemia and dyspro-teinemia.

ECG: the signs of left ventricle hypertrophy and impaired repolarization.

Renal biopsy: use for differential diagnosis and determination of the glomerulonephritis origin.

CHRONIC GLOMERULONEPHRITIS (latent form)

Chronic glomerulonephritis (latent form) is the variant of glomerulus's injury that characterized by the non-symptomatic duration or clinical manifestation with isolated urinary syndrome.

Clinical features

As usual the patients don't have any complaints.

Objective examination: *General patient's condition* is from satisfactory to moderate grave. During general examinations in the early stages of disease aren't detect any particularities. In later stages may appears clinic of nephritic and hypertensive syndromes.

Complications: development of chronic renal failure.

Additional methods of examination

Clinical blood analysis: anemia.

Clinical urine analysis: in initial stage - normal specific gravity and non-significant proteinuria: in microscopic study observed non-constant hematuria, cylinders (hyaline) and leucocytes (non-constant).

Nechiporenko's method: prevalence of erythrocytes under leucocytes; casts more 250 per ml.

Biochemical blood analysis: increase of creatinin, ammonium and urine acid levels and decrease of creatinin clireance detect in 25 % of patients, non-constant - hypoproteinemia and dysproteinemia.

Renal biopsy: use for differential diagnosis and determination of the glomerulonephritis origin.

PYELONEPHRITIS

Pyelonephritis - inflammatory renal disease with obligatory renal parenchyma and pelvis injury.

Classification

I. According to the duration:
- acute;
- chronic.

II. According to the complication development:
- complicated;
- non-complicated.

Etiology

I. Primary infection of renal structures (more frequently bacterial, protozoa, fungus).

II. Secondary to the:

1. Renal system pathology:
- urine tract infection and injury (cystitis, urethritis, strangulation of stones or foreign bodies in the urethra; phimosis);
- prostate gland diseases (prostatitis, prostate adenoma, prostate tumor);
- uterus and uteri cervical diseases.

2. Extra renal pathology:
- sepsis;
- diabetes;
- inflammatory process with different localization;
- immune deficiency states;
- post operative period.

Pathogenesis

Infectious agents may be transmitted by contact, hematogenous or lymphatic ways in obligatory presence of urodynamic abnormalities.

ACUTE PYELONEPHRITIS

Acute pyelonephritis - acute non-specific inflammatory process that characterized by primary affection of renal parenchyma, renal pelvis and tubules with futher involvement to the pathological process of glomerulus and vessels.

Clinical features

The main complaints in patients with acute pyelonephritis are fever, dull, constant and increasing in intensity pain in the back, perspiration, headache, nausea, vomiting and pain in the muscles, arthralgia and disorders of urination.

Objective examination: *General patient's condition* is from moderate grave to extremely grave. The temperature is constant increase to 38-39,5°C or has hectic type. May observed the clinic of bacterial shock. Pasternatsky's symptom is positive on one or bilateral, may detect tenderness of the muscles in loin region.

Complications: renal abscess, urosepsis, paranephritis.

Outcomes of disease: complete recovery, transformation to the chronic form.

Additional methods of examination

Clinical blood analysis: leukocytosis and accelerated ERS.

Clinical urine analysis: in macroscopic study - urine is yellow color, cloudiness, without odor, high specific gravity and non-significant proteinuria: in microscopic study observed large amount of leucocytes, pyuria, non-concstant microhematuria, cylindruna, in bacteriological study - bacteriuria.

Nechiporenko's method: prevalence of leucocytes under erythrocytes; casts more 250 in ml.

Biochemical blood analysis: without changes.

Additional instrumental methods: excretory urographia, ultrasound examination.

CHRONIC PYELONEPHRITIS

Chronic pyelonephritis - chronic non-specific inflammatory process that characterized by primary affection of renal parenchyma, renal pelvis and tubules with father involvement to the pathological process of glomerulus and vessels.

Clinical features

The main complaints in patients with chronic pyelonephritis are subfebrile fever, dull, constant loin pain, perspiration, headache, nausea, arthralgia and disorders of urination.

Objective examination*: General patient's condition* is from moderate grave to extremely grave. The temperature is periods of progression increase to 38-39,5° C or has hectic type. May observed lost of weight. Pasternatsky's symptom is positive on one side or bilateral, may detect tenderness of the muscles in loin region.

Additional methods of examination

Clinical blood analysis: leukocytosis and accelerated ERS, anemia, erythropenia.
Clinical urine analysis: in macroscopic study - urine is yellow color, cloudiness, without odor, high specific gravity; in microscopic study observed large amount of leucocytes, non-constant microhematuria, cylindruria, in bacteriological study - bacteriuria.
Zimnitsky's test: in normal limited.
Nechiporenko's method: prevalence of leucocytes under erythrocytes.
Biochemical blood analysis: may observed increase of creatinin level.
Additional instrumental methods: excretory urography, ultrasound examination, renography, computed tomography, magnetic resonance imaging.

SYNDROM OF CHRONIC RENAL FAILURE

Syndrome of chronic renal failure - clinical-laboratory symptomocomplex that occurs due to the significant decrease of nephrones quantity and quality that leads to the impaired secretory and excretory renal function, homeostasis disbalance, disturbances of all substances exchange, acid-alkaline disorder and abnormal all organs and systems work.

Etiology

The most frequent causes:

- glomerulonephritis (30 %);
- pyelonephritis (20 %);
- polycystic disease (10 %);
- systemic disease with renal injury (8 %);
- hereditary nephropathies (10 %);
- tumor of the kidney (5 %);
- other pathology (7 %);
- unknown etiology (10 %).

Pathogenesis

In chronic renal failure define not only decrease of nephrones quantity but also significant remodeling of the last one (hypertrophy and dilation). The process develops step by step - from latent functional incompetence to significant uremia. Accordantly to renal failure progression increase impossibility of kidney for metabolic products excretion that leads to their accumulation in organism.

Metabolic disorders complicated by uremia intoxication that leads to: nitrousemia, anemia, osteodystrophy, acid-alkaline disbalance, arterial hypertension, hemorrhagic syndrome and immune deficiency.

The clinic of chronic renal failure augments gradually with slowly changes of homeostasis: increase concentration of creatinin and uric acid in plasma, levels of guanidine acid, sulfates, phosphates and other metabolites. Metabolic acidosis develops. With oliguria advance patient's condition becomes worth: hurriedly increase nitrousemia and acidosis, decrease sodium, calcium

and chloral level with hyper concentration in plasma of magnum and potassium. Combination of those impairments lays in the basis of renal failure symptoms.

Classification of chronic renal diseases (NKF, USA)

Stage	Characteristic	Glomerular filtration rate (GFR, ml/min/1.73 m^2)	Recommendation
	Risk factors presence	More than 90	Observation, risk factors correction
I	Renal damage with normal or decreased GRF	More than 90	Lowering of risk progression of the main desease
II	Renal damage with insignificant decreased GRF	60-89	Lowering of risk progression of the main desease and cardiovascular complications
III	Moderate degree of GRF decreasing	30-59	Complications treatment
IV	Significant degree of GRF decreasing	15-29	Preparing to replacement therapy
V	Chronic renal failure	Less than 15 or dialysis	Replacement therapy

Clinical features

Intensity of chronic renal failure clinical sings, particularly in the initial stage, depends on the etiologic factor. Within disease progression, differences in clinical picture become smoothed and complaints explained by intoxication via abnormal nitrogen metabolism.

Depending on disease particularities the primary position obtains the next clinical symptoms and syndromes:

- affection of the cardiovascular system: arterial hypertension, pericarditis, uremic cardiomyopathy, arrhythmias and acute left ventricular failure;
- gastro-intestinal syndrome: mucosa injury - cheilitis, glossitis, stomatitis, esophagitis, gastritis, enteritis, colitis, gastric and intestinal ulcer; organic glands damage (parotisis, pancreatitis);
- neurological syndrome and central nervous system damage: uremic encephalopathy: symptoms of asthenia (fatigue, memory impairments, irritation, dreadful sleeping); symptoms of depression (bad mood, decreased mental activity, suicidal ideas); phobias, changes of character and conduct (emotional weakness, indifference, eccentric conduction); deranged consciousness (stupor, sopor, coma), vascular complications (hemorrhagic or ishematic stroke); uremic polyneuropathy: small paresis and paralysis, other changes of felling and moving function;
- endocrine syndrome: endocrine pathology (hyperparathyreoidism, loss of libido, impotencies, impairment of spermatogenesis, hynecomastia, olygo-and menorrhea, sterility); pain and muscular weakness, cramps, proximal myopathy, aseptic bones necrosis, arthritis, intra and subcutaneous calcina-tis, accumulation of urine crystals in the skin, ammonium smelling from the mouth and hyperlipidemia);
- anemic-hemorrhagic syndrome: anemia (normochromic, sometimes erythro-poetin deficient or iron deficient), lymphopenia, non-significant thrombocytopenia; clinical symptoms (pale color of the skin and visible mucosa with yellowish tint, eruption and dryness of the skin, hemorrhage lesions;
- affection of immune system: intercurrent infections, decrease of immunity.

There are such signs of chronic renal failure according to the periods:

/. *The early signs of chronic renal failure:*

1. Clinical: polyuria, nocturia, arterial hypertension, hypochromic anemia;

2. Laboratory: decrease of concentrated and filtrated function of kidneys.

//. *The late signs of chronic renal failure:*

1. Laboratory: nitrousemia (increased creatinin level, ammonium and urine acid concentration in plasma);

2. Instrumental: decrease of both renal size and cortex according to ultrasound examination and uroroentgenogram.

Additional methods of examination

Clinical blood analysis: anemia, erythropenia.

Biochemical blood analysis: increase of creatinin and ammonium levels, hyperuricemia (non-constant sign). Blood electrolytes detection: - decrease of sodium and calcium concentration, the level of chloral normal or decreased, the level of potassium normal or increased, concentration of magnum and phosphorus increased. Specific is development of metabolic acidosis.

Determination of the glomerulus's filtration rate:

- radiological method - with use of inulini iotalamatis, EDTA;

- classic method - according to plasma's creatinin level, its 24h urine excretion and diuresis per minute;

Decrease of glomerulus's filtration (GF) - is the earliest sign of renal failure.

Clinical urine analysis: at the initial stage observed polyuria, nocturia, isuria and hypostenuria, low specific gravity (less than 1.018), in late stages - oliguria till anuria, hypostenuria and isuria stay be present.

Additional instrumental methods of examination: plain radiography of the urinary tract, excretion urography (synonyms: intravenous pyelography; IVP; IVU), retrograde pyelography/ureterography, renal arteriography, renal venography, computed tomography (CT scanning), magnetic resonance imaging (MRI).

Nuclear renal imaging. The value of radiolabeled traces in the investigation of renal disease lies in the ability to obtain important information about organ function as opposed to the predominantly structural information obtained from the previously described imaging procedures. In particular, nuclear imaging of the kidneys provides the only non-invasive quantitative assessment of individual kidney function. Radionuclides (such as ^{l23}I, $^{99}Tc^{m}$) are linked to compounds that depend on either glomerular filtration alone, tubular excretion, or a combination of both for excretion from the body. These compounds can therefore provide quantitative information on these functions of the kidney, in addition to dynamic images.

Renal biopsy: use for differential diagnosis and determination of the chronic renal failure cause.

***Topic 9*. The Main Symptoms and Syndromes in Anemia. General Clinical Blood Tests.**

The definition and modern classification of anemia. The mechanism of developing iron insufficiency in the body and the occurring of iron deficiency anemia. The main clinical signs of syderopenic and general hypoxic syndromes in iron deficiency anemia. Laboratory criteria of iron deficiency anemia. The reasons and the pathogenesis of B_{12} - folia deficiency anemia. The manifestations of general anemia syndrome, the syndromes of affected digestive organ, funicular myelosis and affected peripheral blood in B_{12} – folic deficiency anemia. The main laboratory signs of B_{12} - folic deficiency anemia. Congenital and acquired hemolytic anemias. The signs of general anemia and icteric syndromes, splenomegaly and hemosiderosis of inner organs. The main laboratory criteria of hemolytic anemias and the peculiarities of bilirubin metabolism disorder. The complete blood count and the interpretation of general and clinical blood test.

SYNDROME OF ANEMIA

Decreases in numbers of RBCs or Hb content caused by blood loss, deficient erythropoiesis, excessive hemolysis, or a combination of these changes.

The term anemia has been used incorrectly as a diagnosis; more properly, it denotes a complex of signs and symptoms. The type of anemia defines its pathophysiologic mechanism and

its essential nature, allowing for appropriate therapy. Not investigating mild anemia is a serious error; its presence indicates an underlying disorder, and its severity reveals little about its genesis or true clinical significance.

The symptoms and signs of anemia represent cardiovascular-pulmonary compensatory responses to the severity and duration of tissue hypoxia. Severe anemia (eg, Hb <7 g/dL) can be associated with weakness, vertigo, headache, tinnitus, spots before the eyes, fatigability, drowsiness, irritability.

Anemia results from one or more of three basic mechanisms: **blood loss, deficient erythropoiesis** (RBC; production), and **excessive hemolysis** (RBC destruction). Blood loss should be the first consideration. Once it is ruled out, only the other two mechanisms need to be considered. Because RBC survival is 120 days, maintenance of a steady RBC population requires daily renewal of 1/120 of the cells. Complete cessation of erythropoiesis results in a decline of about 10%/wk (1%/day) of RBCs. Deficient erythropoiesis results in relative or absolute reticulocytopenia. When RBC values fall > 10%/wk (500,000 RBCs/uL) without blood loss, hemolysis is a causative factor.

CLASSIFICATION

There are two classifications:

Classification according to the cause

I. Blood loss:

- acute post-hemorrhagic anemia;
- chronic post-hemorrhagic anemia.

II. Impaired red cell formation:

Disturbance of bone marrow function due to deficiency of substances essential for erythropoiesis:

- iron deficiency anemia;
- megalobastic macrocytic anemias due to deficiency of vitamin B_{12} or folic acid;
- aplastic anemia.

III. Increased red cell destruction (hemolytic anemias):

- hemolytic anemias due to corpuscular defect (intracorpuscular or intrinsic abnormality). The basic defect may in any of three main components of the cell: the membrane, the hemoglobin molecule and the enzymes related to cell metabolism;
- hemolytic anemias due to an abnormal hemolytic mechanism (extracorpuscular or extrinsic abnormality). These are acquired and result from either an immune or non-immune mechanism.

Classification according to the morphology

1. Microcytic (MCV<80fl)

- Iron deficiency anemia;
- Thalassemia minor;
- Sideroblastic anemia;
- Lead poisoning.

2. Macrocytic (MCV>100fl)

- Megaloblastic: due to Vit. B_{12} and folic acid deficiency. Severely macrocytic anemia (MCV>125) is almost always due to megaloblastic anemia);
- Macrocytic without megaloblastic: due to alcohol excess, cirrhosis of liver, hypothyroidism and reticulocytosis, marrow infiltration and myelodysplasia syndrome.

3. Normocytic (80-100 fl)

- Aplastic anemia (bone marrow failure);
- Myelodysplastic syndrome.

IRON DEFICIENCY ANEMIA

(Anemia of Chronic Blood Loss; Hypochromic-Microcytic Anemia; Chlorosis; Hypochromic Anemia of Pregnancy, Infancy and Childhood)

Chronic anemia characterized by small, pale RBCs and Fe depletion.

Etiology

Blood loss:

Uterine (menorrhagia, metrorrhagia).

Chronic gastrointestinal blood loss:

- esophageal varices;
- hiatus hernia;
- peptic ulcer;
- chronic aspirin ingestion;
- carcinoma of stomach, colon, caecum, rectum;
- ulcerative colitis;
- hemorrhoids;
- diverticulosis;
- hookworm infestation (anemia with eosinophilia).

Urine bladder and kidney:

- glomerulonephritis;
- carcinoma of kidney and urine bladder.

Increased requirements:

- prematurity (diminished iron stores);
- growth (infants and young children);
- females in reproductive age group: menstruation, pregnancy, lactation.

Impaired absorption:

- achlorhydria (especially in middle aged females);
- atrophic gastritis;
- gastrectomy;
- gastroenterostomy;
- tropical sprue or coeliac disease.

Inadequate intake:

- improper feeding in infants and young children;
- poverty;
- dietary fads;
- anorexia (nervosa, of pregnancy or malignancies).

Pathophysiology: The amounts of iron in organism are distributed between active iron pools (hemoglobin and tissue enzymes) and iron stores (ferritin and hemociderin). Iron deficiency develops when iron loss more than iron intake with food or when increased natural iron requirements or impaired iron absorption appears negative iron balance between iron intake and iron stores that causes decreased iron supply to the bone marrow and iron-deficient erythropoiesis. The several stages of iron deficiency are distinguished: iron-store depletion, iron-deficiency erythropoiesis, iron-deficiency anemia.

The pathogenesis of clinical features may be explained by decreased amount of iron resulted by insufficient tissue supply with oxygen. Reduction in oxygen carrying capacity leads to tissue hypoxia symptoms referable to systems with high oxygen requirements, such as skeletal musculature, cardiovascular system and central nervous system are particularly prominent. Specific action of iron deficiency on the activity of hem content enzymes leads to the trophic disturbance of tissue.

Clinical features

The clinical features include two syndromes: general anemic and specific one due to the iron lack.

Anemic syndrome. The patients complaint on fatigue, tiredness, faintness, easy fatigability, dyspnea, palpitation, heart pain, headache, giddiness, spots before the eyes, lack of concentration,

drowsiness, numbness, coldness, tingling of hands and feets. Mild fever 37,2-38,2 °C is observed. Physical examination of the cardiovascular system reveals the displacement of the left relative cardiac border outside, diminished first sound, functional systolic murmurs over sound points with maximal intensity over pulmonary artery, systolic bruits over carotic arteries. ECG changes occur-ST-segment depression and flattening or inversion of T-wave. Amenorrhoea, menorrhagia in females and loss of libido in the males appear.

Cideropenic syndrome was first described by Basenstrom in 1930. The patient complains on the generalized muscular weakness, disorders of muscular sphincters and disorders of urination.

The colour of the skin is pallor with greenish tint. Pallor of the nail beds, mucous membranes of the mouth, conjunctivae, sclerae are revealed. The skin is dry with creak (chirp rattle) on the legs and hands leukoplakia. The nail beds became dry, fragile, with sketch, spoon-shaped named koilonychias. The hair became thin, fragile, and grey.

The gastrointestinal disorders are the specific symptoms and signs of iron deficiency anemia. The patients complain on the difficulties during swallowing solid food - Plummer-Vinson syndrome according to the atrophy of the postcricoid esophageal web. In chronic, severe iron deficiency the patients have specific features - pica chlorotica, which characterized by the eating of unusual items such as coal, earth, chalk, clay, starch, ice (pagophagia) and smell acetone, petroleum.

Nausea, regurgitation, pain and dulling at the epigastric region after meal, diarrhea, anorexia are the specific symptoms of the patients with iron deficiency anemia. The clinical signs of anemia-glossitis with redness and papillae atrophy, angular stomatitis, inflammation of the gum, cheilosis.

During the endoscopic investigations and biopsy the atrophy esophagitis and gastritis are detected. Sometimes may be splenomegaly.

Additional methods of examination

Clinical blood analysis:

- hemoglobin concentration is decreased;
- red blood cells count decreased normal or slightly decreased;
- mean cell volume (MCV) < 76 fl;
- mean cell hemoglobin (MCH) < 27 pg;
- mean cell hemoglobin concentration (MCHC) < 30 gm%;
- color index < 0,8;
- anisocytosis, microcytic red cells;
- poikilocytosis, pencil shaped cells and target cells;
- hypoehromia, ring or pessary cells;
- few polychromatophils;
- reticulocyte count is variable;
- red blood cells osmotic fragility is slightly decreased;
- hematocrit low.

Bone marrow:

- micronormoblaslic erythroid hyperplasia;
- predominantly intermediate normoblasts;
- cytoplasm decreased and shows differential staining;
- bone marrow iron is reduced or absent.

Biochemical blood analysis:

- serum iron level is reduced;
- total iron binding capacity is increased;
- unsaturated iron binding capacity is also raised; percentage saturation reduced.

VITAMIN B_{12} DEFICIENCY ANEMIA

Anemia caused by vitamin B_{12} deficiency anemia is blood disorder, which characterized by abnormalities in the DNA synthesis of the blast cells due to the deficiency of vitamin B_{12} and/or folic acid.

The vitamin B_{12} molecule consists of the nucleotide 5,6-dimethylbenzimidazole linked at right angles to a four-pyrrole ring with a cobalt atom (the corrin nucleus). Several cobalamins (vitamin B_{12} compounds), which vary only in the ligand attached to the cobalt atom, occur in nature.

Methylcobalamin (MeCbl) and **adeno-sylcobalamin** (AdoCbl), physiologic cobalamin coenzymes, perform the biochemical roles of B_{12}. MeCbl functions in nucleic acid metabolism and is the cofactor involved in defective DNA synthesis. AdoCbl serves as a scavenger system for catabolism of aliphatic amino acids, lipid membranes, and precursors of propionate; it may be the cofactor involved in altered myelin synthesis and repair.

Vitamin B_{12} is available in meat and animal protein foods. Its absorption is complex; it occurs in the terminal ileum and requires intrinsic factor**,** a secretion of parietal cells of the gastric mucosa, for transport across the intestinal mucosa. Vitamin B_{12} in food binds to binding proteins (R binders) in saliva that protect B_{12} in the acid milieu of the stomach. When this B_{12} complex (B_{12}-R binders) enters the small intestine, pancreatic enzymes cleave it, and the vitamin B_{12} binds to the intrinsic factor.

Etiology of vitamin B_{12}-deficiency anemia

1. Reduced intake: nutritional deficiency.
2. Strict veganism.
3. Impaired absorption:
   - gastric cause: total or partial gastrectomy;
   - intestinal cause: chronic tropical sprue, intestinal stagnant loop syndrome (e.g. jejunal diverticulosis, blind loop, strictures), scleroderma, Crohn's disease and ileal resection, congenital selective malabsorption with proteinuria, Zollinger Ellison syndrome, severe pancreatitis, coeliac disease;
   - hemodialysis;
   - transport protein defects: hereditary lack of transcobalamin II, abnormal transcobalamin II, abnormal B_{12} binding protein.
4. Competition for cobalamin:
   - bacterial colonization of the small intenstine;
   - fish tapeworm infection;
   - bacteria "blind loop" syndrome.
5. Impaired metabolism:
   - inhibitors of dihydrofolate reductase;
   - purine antagonists;
   - pyrimidine antagonists;
   - alcohol.

Pathogenesis: Methylcolabamin is an essential cofactor in the conversion folic acid to its active form. When this reaction is impaired folate metabolism is deranged and occurs defects in DNA synthesis with megaloblastic maturation patterns in patients who are deficient to cobalamin.

The lack of vitamin B_{12} lead to the biochemical disorder such as conversion of homocysteine to methionine which takes part in production of phospholipids required for myelin formation. This biochemical abnormality may contribute to the neurological complication of cobalamine deficiency.

The jaundice may be explained by the excess breakdown of hemoglobin from immature crythroid bone marrow which easily damaged than normal erythrocytes and hence have a shortened life span.

Clinical features

There are three clinical syndromes: anemic, affection of the digestive system and neurological syndrome.

Anemic syndrome includes such complaints: fatigue, tiredness, palpitation, dyspnea, giddiness. The skin is pallor with lemon yellow tint, slightly icteric skin and sclerae, swallowing face, slight pedal edema. Physical examination of the cardiovascular system reveals tachycardia,

systolic murmur at the apex and pulmonary artery, systolic bruits over carotid arteries, ischemic changes on ECG, heart failure. The symptoms and signs of *gastrointestinal affection*: anorexia, Hunter's glossitis (sore, smooth red tongue, with ulcer over the edge), atrophic gastritis, bladder and bowel dysfunction, diarrhea, enlarged liver and sometimes spleen.

Neurological syndrome includes peripheral neuropathy and combined degeneration of the spinal cord where the posterior and lateral columns undergo demyelization. The symptoms and signs are next: numbness, tingling, paresthesia in the extremities, difficulty in walking, ataxia, position and vibration senses are diminished, dumbness. There may be sphincter disturbance. Reflexes may be diminished or increased. The Romberg and Babinski signs may be positive. Affections of the mental state reflect irritability, diminished memory, even severe dementia or psychosis. In young females there may be infertility.

Additional methods of examination

Clinical blood analysis:

- hemoglobin concentration decreased moderately; red blood cell count decreased pronouncly;
- mean cell volume ranging from 100 to 140 fl;
- color index > 1,2;
- moderate leucopenia;
- mild, usually asymptomatic thrombocytopenia;
- anisocytosis - macrocytosis;
- poikilocytosis - ovalocytosis;
- hyperchromia, ring or pessary cells;
- red blood cells may show: Howel-Jolly bodies, Cabot rings;
- hypersegmentes neutrophils;
- macropolycytes (large neutrophils).

Bone marrow:

- hyperplasia of erythroid elements;
- megaloblasts - gigantic cells with large nucleus oval shape and basophilic cytoplasm;
- gigantic metamyelocytes;
- megakaryocytes.

Biochemical blood analysis:

- increased level of unconjugated bilirubin;
- increased level faeces stercobilin;
- increased level of lactatdehydrogenasa.

Special tests for diagnosing vitamin B_{12} deficiency:

- low serum vitamin B_{12} assay;
- increased urinary excretion of methylmalonic acid;
- low radioactive vitamin B_{12} absorption test (Schilling's test);
- reticulocyte response to vitamin B_{12} administration.

HEMOLYTIC ANEMIA

Hemolytic anemias are the geterogenous group of anemias, which characterized by shortened life span of erythrocytes in the circulation resulting from their accelerated destruction.

At the end of their normal life span (about 120 days), RBCs are removed by components of the mononuclear phagocyte system, principally in the spleen, where Hb catabolism takes place. The essential feature of hemolysis is a shortened RBC life span; hemolytic anemia results when bone marrow production can no longer compensate for the shortened RBC survival.

Classification of hemolytic anemias

Hereditary hemolytic anemias

Defects of the cell membrane:

- hereditary spherocytic anemia;
- hereditary elliptocytic anemia.

Defects of erythrocytic metabolism:

- glucose-6-phosphate dehydrogenase (G-6-PD) deficiency anemia.

Abnormal hemoglobins:

- sickle cell anemia;
- -thalassemia.

Acquired hemolytic anemia

Immunological destruction of red blood cells:

- transfusion with incompatible blood;
- hemolytic disease of the newborn;
- autoimmune hemolytic anemia (AIHA) (warm-active AIHA and cold-active AIHA).

Physical destruction of red blood cells:

-march hemoglobinuria;

- traumatic cardiac hemolytic anemia.

Hemolytic anemia induced by chemical agents.

Hemolytic anemia caused by microorganism:

- anemia of malaria;
- anemia of Clostridia.

Hemolytic anemia secondary to other disease.

Paroxysmal nocturnal hemoglobinuria.

Etiology

The causes of hemolytic anemias may be hereditary or acquired. The causes of hereditary hemolytic anemia are grouped into three categories: 1) defect of the cell membrane; 2) defects of erythrocyte metabolism; 3) abnormal hemoglobins.

Pathogenesis. Acquired hemolytic anemias have numerous causes hence corresponds with different pathogenesis. Destruction of red blood cells refers to inappropriate activation of the body's immune system and appearance either alloantibodies or autoantibodies. A number ingestion of drugs and chemicals may result to shortened life span of erythrocytes. Inflammation of blood vessels or presence of blood clots may interfere the structure and function of red blood cells and lead to early destruction. Such physical factors as vascular protheses, heart valves protheses cause accelerated hemolysis of red blood cells. Some infectious agents for example malaria parasite (Plasmodium falciparum, Clostridiax) use red blood cells for their propagation and this process destroy them. Hemolytic anemia could develop as a secondary effect of certain clinical condition such vitamin B_{12} -deficiency anemia, splenomegalia, liver disease and renal failure.

Hemolysis may occur intravascularly or extravascularly. Hemoglobin liberated into the plasma is bound mainly by the alpha-2 globin, haptoglobin, to form a complex too large to be lost in the urine. It is taken up by the liver and degraded. Some hemoglobin is partially degraded and bound to albumin to form methemoglobin. If all the haptoglobin has been consumed, free hemoglobin may be lost in the urine. In small amounts this is reabsorbed by the renal tubules where the hemoglobin is degraded and the iron stored as hemosiderin. Sloughing of the renal tubular cells gives rise to hemosiderinuria which, if found, always indicates intravascular hemolysis. Hemoglobinuria occurs when greater amounts of hemoglobin are lost, giving the urine a black appearance (black water).

Extravascular hemolysis occurs in the phagocytic cells of the spleen, liver, bone marrow and other organs and there may be little or no depletion of haptoglobin.

Clinical features

Clinical features include three indications: anemia, jaundice and splenomegalia. The symptoms of anemia are common as most other one: weakness, fatigue, dyspnea, palpation, headache, dizziness, inability to concentrate. The most important sign of hemolytic anemia is jaundice, which differ from slightly yellow tint to intense lemon color of mucosa membrane, sclera and skin. Splenomegaly is specific sign, explained by hyperplasia of cells, which take part in phagocytosis. Commonly spleen is enlarged moderately.

Latent compensated hemolytic anemia explained by capacity of bone marrow to produce increased number of reticulocytes and in the peripheral circulation red blood cell counts may be fairly normal.

However the bone marrow will no longer be able to compensate and breakdown rate of erythrocytes becomes greater than the production rate of new erythrocytes. In acute cases is developed the hemolytic crisis with abrupt onset, high temperature, severe fatigue, nausea, vomiting pain in the abdomen, pronounced pallor with yellow color of mucosa and skin, hemorrhage lesions. Patient has grave condition, may be occur hemolytic coma. Tachycardia, systolic murmur, hypotension are observed. During palpation of abdomen the hepatosplenomegalia is detected.

Hemolysis may be acute, chronic, or episodic. *Hemolytic crisis* (acute, severe hemolysis) is uncommon; it may be accompanied by chills, fever, pain in the back and abdomen, prostration, and shock. In severe cases, hemolysis increases (jaundice, splenomegaly, and, in certain types of hemolysis, hemoglobinuria and hemosiderinuria), and erythropoiesis increases (reticulocytosis, hyperactive bone marrow). In chronic hemolysis, anemia may be exacerbated by aplastic crisis (temporary failure of erythropoiesis); this is usually related to an infection, often parvovirus.

Additional methods of examination

Clinical blood analysis:

- hemoglobin concentration decreased;
- red blood cells count decreased;
- reticulocytes increased;
- macrocytosis;
- polychromasia;
- polymorphonuclear.

Bone marrow:

- compensatory erythroid hyperplasia.

Biochemical blood analysis:

- increased plasma unconjugated bilirubin;
- increased urinary urobilinogen; increased faecal urobilinogen;
- increased plasma lactatdehydrogenasa.

Findings of intravascular hemolysis:

- reduced or absence of haptoglobin in the blood;
- presence of free hemoglobin in the blood;
- presence of free hemoglobin in the urine;
- presence of methemalbumemia.

Special test for determining RBC life span using the ^{51}Cr.

Complete Blood Count (CBC)

In a complete blood count (CBC) a routine hematology screening includes the following determinations: white blood cell count (WBC), red blood cell count (RBC), hematocrit (Hct), hemoglobin (Hgb), and differential white cell count (Diff). The differential states the neutrophils, lymphocytes, monocytes, eosinophils, basophils, and any abnormal cells as a percent of the total WBC count.

A complete hematologic examination also includes the indices, which are mean cell volume (MCV), mean cell hemoglobin (MCH), and mean cell hemoglobin concentration (MCHC). In addition, a careful inspection of the peripheral blood smear is important, as is a sedimentation rate (Sed rate or ESR).

Clinical blood analysis

- RBC: Red Blood Cells 4.2- 5.9 million/mm^3
- Hemoglobin (Hgb):

Males: 14- 18g/dL

Females: 12- 16g/dL

- Hematocrit (Hct)

Males 40 - 54%

Females: 37- 47%

- MCV: Mean Cell Volume: 86 - 98 fl
- MCH: Mean Cell Hemoglobin: 27 - 32 pg
- MCHC: Mean Cell Hemoglobin Concentration: 31 – 35g/dl
- Platelet Count: 150,000 - 400,000 / mm^3
- WBC: White Blood Cells: 4,000-10,000/mm^3

Differential:

Neutrophils	40-75%
Lymphocytes	15-45%
Monocytes	1-10%
Eosinophils	1-6%
Basophils	0-2%

- ESR

Red cell absolute values

These can be calculated from:

a) hematocrit;

b) hemoglobin estimation;

c) red cell count.

The International Committee for Standardization in Hematology has recommended that the following units be used (SI units): mean cell volume as "fl" (femtoliters), mean cell hemoglobin as "pg" (picograms) and mean cell hemoglobin concentration as "g/dl".

Red cell absolute values are analyzed using the formulas:

hematocrit (Hct) is the volume of packed red blood cells found in 100ml of blood. For example, a value of 46% implies that there are 46 ml of red blood cells in 100 ml of blood.

mean cell volume (MCV) describes the red cells in terms of individual cell size. It is given usually as a direct whiteout from the automated system. However, it can also be calculated by dividing the volume of packed cells (hematocrit) by the number of RBCs.

$$MCV = \frac{Hct * 10^{15}}{\text{Red cell count per litre}} \text{ fl}$$

mean cell hemoglobin concentration (MCHC) measures the concentration of hemoglobin in grams per 100ml of RBCs.

$$MCHC = \frac{\text{Hemoglobin in g\% gm \%}}{Hct}$$

mean cell hemoglobin (MCH) is the hemoglobin content of each individual red blood cell and is calculated by dividing the hemoglobin by the red blood cell count.

$$MCH = \frac{\text{Hemoglobin in gm\%} * 10^{13}}{\text{Red cell count per litre}} \text{ pg}$$

Colour index. Once the quantity of erythrocytes and hemoglobin in a given blood specimen is known, it is possible to calculate the hemoglobin content of each erythrocyte. There are many methods by which hemoglobin saturation can be determined. One of them is the calculation of the *colour index.* This is a conventional value derived from the ratio of hemoglobin to the number of erythrocytes. This value is found by dividing a triplet quantity of hemoglobin in grams by the first three figures expressing the quantity of erythrocytes. Normally this value approaches 0,85-1.1. If it is less than 0,8, the erythrocyte saturation of hemoglobin is insufficient; it the value exceeds 1,1 the volume of erythrocytes is higher than normal.

Red blood cell morphology can be determined from a thin blood film stained with Romanowsky dyes. The three basic features of a red blood cell are its size, its shape and its inclusions.

Size of erythrocytes. Normal erythrocyte is nearly uniform in size with diameter of 7,2 to 7,9 nm. An increasing and decreasing in the size of a red blood cell is known as anisocytosis.

Shape of normal erythrocytes is a biconcave disc, which is thickest at its edges. The presence of many abnormal shapes on a blood smear is known as poikilocytosis.

Inclusions in erythrocytes. The normal red blood cell filled mainly with hemoglobin. In pathological states blood films will show red blood cells with colored spots or rings inside their cytoplasm.

Howell-Jolly bodies. These are small, well-defined, round, densely staining basophilic inclusion bodies about 1 urn in diameter, which usually occur singly but sometimes in multiples. They appear after splenectomy and are also seen in cases of severe anemia from a variety of causes. They contain DNA and may be chromosomal remnants or nuclear fragments.

Cabot rings. These are blue-staining, threadlike inclusions in the red cells in severe anemia. They may appear as rings, or twisted and convoluted in a variety of shapes. They may occupy the entire periphery of the cell but frequently are much smaller. They are not often seen. It has been postulated that they are remnants of the mitotic spindle, but others have found that they contain histone and iron.

Heinz bodies can be seen with special supravital stains such as methylviolet Heinz bodies are granules of precipitated hemoglobin.

Normal WBC count

The **normal** WBC count is usually between 4500 and 11,000/mm^3 and may vary in a particular individual at different times of the day. A minor variation outside the normal range is not significant as long as the differential count and the peripheral blood smear are both normal. However, some early disorder, whether infectious or myeloproliferative, is not necessarily ruled out.

*Mild to moderate leukocytosis (11,000-17,000/mm^3)***:** mild to moderate elevation of the WBC count usually indicates infectious disease, mainly of bacterial etiology. Usually, the leukocytosis increases with the severity of the infection. However, there are exceptions to this rule, particularly in elderly patients in whom severe sepsis can coexist with only a modest leukocytosis. As mentioned previously, the differential WBC count is of additional help.

Leukemoid reaction: occasionally such massive leukocytosis accompanies a systemic disease that the blood picture of leukemia is simulated. When a blood picture looks like leukemia but is not, the term "leukemoid reaction" is used. Severe sepsis, miliary tuberculosis, and other nonmalignant infectious conditions are among the more common causes.

In the differentiation of myelogenous leukemia versus leukemoid reaction determination of the leukocyte alkaline phosphatase is helpful. This enzyme is high in leukemoid reaction and is decreased in myelogenous leukemia. Also, the presence of Philadelphia antigen is specific for the majority of cases of chronic myeloid leukemia.

Leukopenia: a decreased absolute WBC count (leukopenia) can be mild (3000-5000/mm^3), moderate (1500-3000/mm^3), or extremely severe (<1500/mm^3), and may be associated with diminution of the WBC count as a whole, decreases in neutrophils, or diminution of all the blood particles (pancytopenia).

Complete Blood Count (CBC)

Test	Name	Increased/Decreased
WBC	White Blood Cell	May be increased with infections, inflammation, cancer, leukemia; decreased with some medications (such as methotrexate), some autoimmune conditions, some severe infections, bone marrow failure, and congenital marrow aplasia (marrow doesn't

		develop normally)
% Neutrophil	Neutrophil/Band/Seg/Gran	This is a dynamic population that varies somewhat from day to day depending on what is going on in the body. Significant increases in particular types are associated with different temporary/acute and/or chronic conditions. An example of this is the increased number of lymphocytes seen with lymphocytic leukemia
% Lymphs	Lymphocyte	
% Mono	Monocyte	
% Eos	Eosinophil	
% Baso	Basophil	
RBC	Red Blood Cell	Decreased with anemia; increased when too many made and with fluid loss due to diarrhea, dehydration, burns
Hgb	Hemoglobin	Mirrors RBC results
Hct	Hematocrit	Mirrors RBC results
MCV	Mean Cell Volume	Increased with B_{12} and Folate deficiency; decreased with iron deficiency and thalassemia
MCH	Mean Cell Hemoglobin	Mirrors MCV results
MCHC	Mean Cell Hemoglobin Concentration	May be decreased when MCV is decreased; increases limited to amount of Hgb that will fit inside a RBC
Platelet	Platelet	Decreased or increased with conditions that affect platelet production; decreased when greater numbers used, as with bleeding; decreased with some inherited disorders (such as Wiskott-Aldrich, Bernard-Soulier), with Systemic lupus erythematosus, pernicious anemia, hypersplenism (spleen takes too many out of circulation), leukemia, and chemotherapy
MPV	Mean Platelet Volume	Vary with platelet production; younger platelets are larger than older ones

***Topic 10*. Final module control**

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