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Content.

PATHOPHYSIOLOGY OF CARDIOVASCULAR SYSTEM

In a normal cardiovascular system provides optimal current needs of the organs and tissues in the blood supply. The level of activity of the heart is determined by the circulation, and blood vessels tone state (its overall weight and circulating, and rheological properties). Violation of cardiac function, vascular tone or blood system changes can lead to circulatory failure.

Under circulatory failure to understand a condition in which the cardiovascular system does not provide the needs of the tissues and organs in the blood supply - the delivery of oxygen to them with blood and substrate metabolism, as well as the transport of carbon dioxide from the tissues, and metabolites. The most common cause circulatory failure is a disorder of the cardiovascular system.

Although emerging in recent years the downward trend in mortality from cardiovascular diseases, they still occupy the first place among the causes of disability and death of modern man. The high level of morbidity and mortality from diseases of the cardiovascular system is largely determined by the prevalence of various forms of heart disease and especially coronary artery disease (CAD). In industrialized countries, 15 - 20% (ie, one in five) of the adult population suffer from coronary artery disease. The latter, in turn, is the cause of sudden death in 2/3 patients who died from cardiovascular disease. About half of sufferers of these diseases become disabled of working age. Constantly increasing morbidity and mortality from coronary heart disease among young people (under 35 years), as well as in rural areas.

The main risk factors that determine the high levels of morbidity and mortality from cardiovascular disease, include frequent, repeated stressful episodes with severe emotional negative "colored", "chronic" physical inactivity, alcohol intoxication, smoking, consumption of large quantities of tea, coffee and other "domestic doping", poor diet and overeating to the development of overweight and many others. Total to date is called more than 50 risk factors, the essential role of which in the event of heart disease and blood vessels clearly established. These facts indicate that the fight against diseases of the cardiovascular system is one of the most important not only biomedical, but also the social problems of mankind.

Most of the various diseases and pathological processes that affect the heart can be attributed to the three groups of typical forms of disease: coronary insufficiency, cardiac arrhythmias, heart failure.

Heart failure

Heart failure - one of the most frequent causes of incapacity, disability and death of patients suffering from cardiovascular diseases. Heart failure - not nosological form, not a disease. It is a syndrome that develops in many diseases, including those affecting the organs and tissues that do not belong to the CVS.

Heart failure - a typical form of disease in which the heart does not provide the needs of the organs and tissues in adequate (their function and level of plastic processes in them) blood supply. It shows less (in comparison with the needs of) the value of cardiac output and circulatory hypoxia.

Summary heart failure is heart (at a given TPR) can not move in the arterial tree whole blood entering the veins thereto.

Causes of heart failure

The two main groups of reasons lead to the development of heart failure: with a direct damaging effects on the heart and cause heart function overload.

Damage to heart

Factors that directly damage the heart, may have a physical, chemical or biological nature.

1. Physical factors: compression of the heart (exudate, blood, emphysematous lungs, tumor), the effect of an electric current (electrical accident when, holding heart defibrillation), mechanical trauma (contusions of the chest, penetrating wounds, surgical procedures).

2. Chemical factors: non-drug chemicals (eg, uncouplers oxidative phosphorylation, calcium salts and heavy metals, enzyme inhibitors, lipid hydroperoxide), in inadequate drug dosage (eg,

calcium channel blockers, cardiac glycosides, blockers), oxygen deficiency, lack of chemical compounds necessary for metabolism (such as salts of different metals).

3. Biological factors.

- High levels of biologically active substances (eg, catecholamines, T4).

- The absence or deficiency of bioactive substances required for the metabolism (e.g., enzymes, vitamins and others.).
- Prolonged ischemia or myocardial infarction. It is the cessation of myocardial contractions in the damaged area. This is followed by the functional area is overloaded myocardium or myocardial ischemia.

- Cardiomyopathy - myocardial damage, mostly non-inflammatory nature. They are characterized by significant structural and functional changes in the heart.

Overload heart

Causes of cardiac overload is divided into two subgroups: increase preload and afterload increase.

Preload. Increasing the preload (the amount of blood flowing to the heart and increases the pressure ventricular filling) occurs when fluid overload, polycythemia, hemoconcentration, valvular (accompanied by an increase in the residual volume of blood in the ventricles).

Afterload. Increased afterload (resistance to blood expelled from the ventricle into the aorta and the pulmonary artery, the main factor is the afterload PR) occurs when the arterial hypertension of any origin, stenosis of the valve opening of the heart, narrowing of the large arterial trunks (aorta, pulmonary artery).

Types of heart failure

Classification of heart failure based on the criteria of origin (myocardial and overload), the rate of development (acute and chronic), a primary lesion of the heart (left ventricle and right ventricle), the predominant failure of the cardiac cycle phase (systolic and diastolic) and the primary lesion (cardiogenic and non-cardiogenic).

Originally

According to this criterion are marked myocardial, overload and mixed forms of heart failure.

Myocardial form develops mainly as a result of direct damage to the myocardium.

Overload form of heart failure occurs mainly as a result of overloading of the heart (increase in pre - and afterload).

The mixed form of heart failure - the result of a combination of direct myocardial damage and overload.

As the rate of development

According to the speed of development of heart failure symptoms are marked acute and chronic forms.

1. **Acute** (developed for a few minutes and hours). It is the result of myocardial infarction, acute insufficiency mitral and aortic valves, rupture of the left ventricular wall.
2. **Chronic** (formed gradually, over weeks, months, years). It is a consequence of hypertension, chronic respiratory failure, prolonged anemia, heart disease. The course of chronic heart failure can worsen congestive heart failure.

On primary mechanism

To decrease myocardial contractility or decrease in venous blood flow to the heart isolated primary (cardiogenic) and secondary (non-cardiogenic) forms of heart failure.

Primary (cardiogenic). Developed as a result of the decrease of the contractile function of the heart at close to the normal value of the venous blood flow to it. The most frequently observed in ischemic heart disease (myocardial infarction may be accompanied, cardiosclerosis, myocardial

dystrophy), myocarditis (eg, inflammatory lesions of the heart muscle or the severity and duration of endotoxemia), cardiomyopathies.

Secondary (non-cardiogenic). There is due to the primary preferential reduction of venous flow to the heart at close to the normal value of the contractile function of the myocardium. The most common in acute massive blood loss, abuse diastolic relaxation and filling its chambers with blood (for example, by compression of the liquid heart, accumulating in the pericardial cavity blood, exudate), episodes of

paroxysmal tachycardia (which leads to a decrease in cardiac output and venous blood return to the heart), collapse (eg, hypovolemic or vasodilatory).

According mostly struck by parts of the heart

Depending on the primary lesion of the left or right heart distinguish left ventricular and right ventricular heart failure.

Left ventricular heart failure. Overload may be caused by the left ventricle (e.g., aortic stenosis), or decrease of its contractile function (e.g., myocardial infarction), i.e. states, leading to a decrease in ejection of blood into the systemic circulation, hyperinflation of the left atrium and the stagnation of blood in the pulmonary circulation.

Right ventricular heart failure. Occurs when a mechanical overload of the right ventricle (eg, narrowing of the valve opening of the pulmonary artery) or high pressure in the pulmonary artery (if pulmonary hypertension), ie states, accompanied by a decrease in blood output in the pulmonary circulation, overstretching of the right atrium and the stagnation of blood in the systemic circulation.

Total. When this form is expressed and left ventricular and right ventricular heart failure.

According to the predominant failure of the cardiac cycle phase

Depending on the kind of disturbance left ventricular myocardial function (reduction of the strength and the rate of its reduction rate of relaxation or disturbance) left ventricular heart failure is divided into systolic and diastolic.

Diastolic heart failure - a violation of relaxation and left ventricular filling. Due to its hypertrophy, fibrosis or infiltration and results in an increase in end diastolic pressure and heart failure.

Systolic heart failure (chronic) complicates the course of a number of diseases. When it is broken pump (The intake) heart function, leading to reduced cardiac output.

General mechanisms of heart failure

Myocardial form of heart failure is characterized by a decrease in the voltage developed by the heart. This is manifested fall force and speed of contraction and relaxation.

Overload form of heart failure, is formed on the background of a more or less long period of its hyperfunction. The latter eventually leads to a decrease in the strength and speed of contraction and relaxation of the heart.

In both cases (and in case of overload, and heart damage), decrease of its contractile function is accompanied by the inclusion of extra- and intracardiac compensate for this shift mechanisms. All of them, despite the known identity, in a whole organism are interrelated in such a way that the activation of one of them significantly affects the realization of the other.

MECHANISMS hypertrophic heart decompensation

Potential hypertrophied myocardium to increase the strength and speed of contraction are not unlimited. If the heart continues to operate an increased load or it is further damaged, the power and speed of its rate fall, and their energy "cost" increases: developing decompensation hypertrophied heart.

At the heart of decompensation long hypertrophied myocardium is a violation of a balanced growth of its various structures. These changes - along with lagging growth of microvessels from the increase of myocardial mass, behind the biogenesis of mitochondria by weight of the myofibrils, the backlog of activity ATPase myosin on the needs, the rate of synthesis backlog cardiomyocytes

structures from proper - in the long run, cause a decrease in strength of heart rate and contractile speed of the process, ie, .e. the development of heart failure.

Cellular molecular mechanisms of heart failure

The decline of the contractile function of the heart is the result of heart failure of diverse etiologies. Despite the different causes and known peculiarity of the initial pathogenesis of heart failure, its mechanisms at the cellular and molecular level one.

Violation of the energy supply of myocardial cells

Breakdown of energy supply of the basic processes occurring in myocardial cells (primarily its contraction and relaxation), develops due to damage to the re-synthesis of ATP mechanisms of transport of its energy to the effector structures of cardiomyocytes and energy utilization of high-energy phosphate compounds.

Reduced ATP resynthesis is mainly a consequence of the suppression of the process of aerobic oxidation of carbohydrates. This is because most of the action of pathogenic factors, and to the greatest extent particularly damaged mitochondria.

Normally, under aerobic conditions, the main energy source for the myocardium are higher fatty acids. Thus, the oxidation of 1 molecule of palmitic acid containing 16 carbon atoms forms 130 ATP molecules.

As a result of myocardial damage or excessive prolonged stress increase it higher fatty acids oxidation in mitochondria and ATP is broken "exit" is reduced.

The major source of ATP thus becomes glycolytic pathway cleavage of glucose, which is about 18 times less efficient than its mitochondrial oxidation, and can not adequately compensate for the deficiency of energy phosphates.

However, there are studies showing that heart failure may develop on the background of normal or slight decrease in ATP levels in the myocardium. This is due to the fact that the ATP itself is not a carrier of energy to the point of use. As a result, coupled with a high total content of ATP in the cell can develop its deficit energy-consumable effector structures, primarily in the myofibrils and the sarcoplasmic reticulum (SR). The reason for this is a disorder of energy transport system from the seats of its products to the effector organelles using creatine phosphate (CP) with the participation of enzymes: 1) ATP - ADP translocase (providing ATP energy transport from the matrix of the mitochondria through its inner membrane) and 2) mitochondrial creatine phosphokinase (CK), is localized on the outer side of the inner membrane of the mitochondria (providing transport-energy phosphate due to creatine to form phosphocreatine). Further HF enters the cytosol. The presence of CK in myofibrils and other effector structures for effective use of the HF to maintain the necessary concentration of ATP.

System energy transport in cardiomyocytes significantly damaged determinants of heart failure development. The action of the pathogenic agents that cause heart failure, and initially to a greater degree in myocardial creatine phosphate concentration of cells decreases, and then to a lesser extent - ATP. Furthermore, the development of heart failure is accompanied by a massive loss of CK myocardial cells, as evidenced by increased cardiac isoenzymes activity of this enzyme in serum. Given that the bulk of ATP (about 90% of the total) is consumed in reactions that provide contractile process (about 70% is used for the reduction of infarction, 15% - for the transport of calcium ions in the ATP and cation exchange in the mitochondria, 5% - for active transport sodium ions across the sarcolemma), damage to the ATP delivery mechanism to the effector apparatus of myocardial cells contributes to the rapid and substantial reduction in contractility.

Heart failure due to myocardial energy disorder can develop in conditions of sufficient production and transportation of ATP in cardiomyocytes. This may be due to enzyme damage energy recovery mechanisms myocardial cells mainly by reducing the ATPase activity. First of all it refers to the myosin ATPase, K + ATPase -Ca + -dependent sarcolemma, of Mg + -dependent ATPase "calcium pump" the PCA. As a result, the energy of ATP is not used effector apparatus of myocardial cells.

Thus, violation of energy for providing cardiomyocyte stages of its production, transportation and disposal may be either an initial torque reduction contractile function of the heart and a significant factor in the growth of its depression.

Damage to the membrane device and enzyme systems cardiomyocytes

The main mechanisms damaged membranes and enzymes of myocardial cells in heart failure are as follows.

1. Excessive intensification of free radical lipid peroxidation (FRPOL) and cardiotoxic effects of the products of this process. The main factors in the intensification of reactions lipoperoksidnyh increase myocardium are contained prooxidant factors (ATP hydrolysis products catecholamine metabolites and reduced forms of coenzymes, a variable valence metals, particularly iron myoglobin); decreased activity and (or) the content of the antioxidant defense factors myocardial cells and non-enzymatic nature of an enzyme (catalase, glutathione peroxidase, superoxide dismutase, tocopherol, selenium compounds, ubiquinone, ascorbic acid, etc.); excess substrates POL (higher fatty acids, phospholipids, amino acids, proteins).

2. Excessive activation of hydrolytic enzymes of myocardial cells due to the accumulation of hydrogen ions therein (promote the release and activation of lysosomal hydrolases); Calcium ions (activating free and membrane-bound lipases, phospholipases, proteases); excess catecholamines, higher fatty acids, foods spol activating phospholipase.

Detergent effects on membranes products FRPOL and hydrolysis of lipids, consisting in the inclusion of these agents in the membrane with violation of their conformation, "displacement" of the membrane integral and peripheral proteins ("deproteinization" membranes), lipids ("delipidization"), and - in the formation of through "simple" constant channel clusters.

Braking process resynthesis denatured protein and lipid membrane molecules, as well as their re-synthesis.

Modification of the conformation of the protein and lipoprotein molecules in connection with the "deenergization" (dephosphorylation) of these molecules in a process of impaired energy cardiomyocytes.

Hyperextension and microfractures sarcolemmal membranes and organelles of myocardial cells. The reason for this is to increase the intracellular osmotic and oncotic pressure due to an excess of hydrophilic cations (sodium and calcium) and organic compounds (lactate, pyruvate, glucose, adenine nucleotide et al.).

Together, damage to membranes and enzymes these factors is most important, and often - initial link of pathogenesis of HF. Changes in the physicochemical properties and the conformation of the protein molecules (structural and enzymes), lipids, phospholipids and lipoproteins causes significant reversible and often - the irreversible modification of the structures and functions of the membranes and enzymes, including mitochondrial ATP myofibrils sarcolemma and other structures and factors that ensure the implementation of the contractile function of the heart.

The imbalance in ion and fluid cardiomyocytes

Ion imbalance characterized by impaired individual ions relationship between, on the one hand, and hyaloplasm cellular organelles (mitochondria, ATP myofibrils), on the other - in the most hyaloplasm in the third - on opposite sides of the sarcolemma of cardiomyocytes.

Various factors that cause heart failure, disrupt the processes of energy supply and damage the membranes of cardiomyocytes. As a consequence of recent changes significantly the permeability for ions and the activity of the cationic transport enzymes. As a result, violated the balance and concentration of ions. To the greatest extent it relates to ions of potassium, sodium, calcium, magnesium, i.e. ions, is mainly determined by the implementation of processes such as excitation, electro-mate, contraction and relaxation of the myocardium.

CH is characterized by a decrease in the activity of K + -Na + - dependent ATPase and as a consequence - the accumulation in cardiomyocytes of sodium and potassium loss by them. The increase of intracellular Na + concentration causes a delay in mioplazme calcium ions. The latter is

a consequence of dysfunction of sodium-calcium ion exchange mechanism which enables the exchange of two sodium ions contained in one cell to a

calcium ion exiting therefrom. This process is realized thanks to the total for the Na + and Ca2 + transmembrane transporter. The increase in intracellular sodium that competes with calcium for the overall vehicle, prevent the emergence of Ca2 + and thus contributes to its accumulation in the cell. Also, when main variants CH increase of calcium intracellular determined by several other factors: increased permeability of the sarcolemma, which normally prevents intracellular current Ca2 + concentration gradient (the content of Ca2 + in the sarcoplasm is 10 ~ 7 mol during diastole and 10 mol during systole whereas in the plasma it 3 - 5 orders of magnitude higher and is 10 3 1 (T2 mol) decreased activity of the calcium pump sarcoplasmic reticulum, Ca2 + accumulates; derating volatile mechanisms responsible for the removal of Ca2 + from the sarcoplasmic.

Excessive accumulation of intracellular calcium has several important consequences. Firstly, it is a violation of relaxation of myofibrils, which is manifested by increased end diastolic pressure or even cardiac arrest in systole (irreversible myocardial contracture). Secondly, an increase in the capture of Ca2 + in mitochondria, leading to dissociation of oxidation and phosphorylation, and depending on the extent to more or less pronounced decrease in ATP content and increase damage caused by energy deficiency. One of the most important among them - the intensification of glycolysis and the accumulation of hydrogen ions. The excess protons are not only displaces Ca2 + from the SR and the sarcolemma, and can compete with them for binding to troponin points. All this leads to a significant decrease in contractile function of the heart. Third, activation of Ca2 + - dependent proteases and lipases, which, as mentioned above, the membrane device exacerbate damage of cardiomyocytes and enzyme systems.

Excess Ca 2+ causes and regulatory changes, which to some extent prevent the further flow of ions into cells. One such effect - reduced cardiac adrenergic properties. This is because the calcium ions inhibit adenylate cyclase and phosphodiesterase activated. This reduces the catecholamine-stimulated calcium entry into the myocardial cells. The second effect - calcium activation of glycolysis delivering ATP for the ATP, "pumpout" calcium from mioplazmy. Both of these effects are only to some extent counteract, but do not prevent the alteration of myocardial calcium in heart failure.

Accumulation of cells in the myocardium of sodium and calcium, in addition to the above effects, also causes overhydration hyaloplasm cardiomyocytes and organelles. The latter, in turn, aggravates the rupture of membranes (in particular, as a result of hyperextension), and - the processes of power supply cells (due to the swelling of mitochondria, rupture of membranes, spatial dissociation of enzymes, additional damage to transport and utilization of ATP energy mechanisms).

Myocardial damage cells causal factors HF is also accompanied by dysregulation of the mechanisms of their volume. The latter is a result of increasing the cardiomyocyte membrane permeability for ions and hydrophilic organic molecules, resulting in an increase in intracellular osmotic pressure; reduce the "mechanical strength" damaged biological membranes, and hyperextension of their education in these "pinholes"; hydration and swelling of the cells and organelles with increasing volume.

The disorder neurohumoral regulation of heart function

Nervous and humoral regulatory effect on the heart is to a large extent influence the processes occurring in the cells of the myocardium. Normally, they ensure the implementation of adaptive responses, emergency and long-term changes in heart function in accordance with the body's needs.

When HF greatest role in shaping adaptive and pathogenic mechanisms of reactions play a nerve (sympathetic and parasympathetic) effects on the heart.

The development of heart failure is characterized by a decrease in the concentration of neurotransmitters of the sympathetic nervous system (noradrenaline) in the heart tissue. This is due mainly to two factors: firstly, the decrease of noradrenaline synthesis in neurons of the sympathetic

nervous system (which normally is formed in about 80% of the mediator contained in the myocardium), and secondly, a violation norepinephrine from nerve endings synaptic cleft.

One of the most important reasons for the suppression of the biosynthesis of neurotransmitter is to reduce the activity of tyrosine hydroxylase limiting enzyme for this process. Reduction of neurotransmitter reuptake axon terminals of the sympathetic nervous system is largely due to the deficit of ATP (this process energy-dependent), biochemical changes in the heart (acidosis, increased extracellular potassium), and resulting damage to the nerve endings of the sympathetic neuronal membranes. Significantly, also accompanied by a decrease in HF cardiac effects caused by norepinephrine. This suggests decreasing cardiac adrenergic properties.

The content in the myocardium of the neurotransmitter of the parasympathetic nervous system

- acetylcholine, as well as heart cholinergic properties at various stages of development of heart failure or do not differ significantly from the norm or slightly increased.

One of the main consequences of reducing the effectiveness of sympatergic effects on the myocardium in heart failure is a decrease in the degree of control and reliability of the regulation of the heart. This is manifested primarily reduction in the rate and magnitude of mobilization of its contractile function in different adaptive reactions of the organism, especially in emergency situations.

The above-mentioned violations of the processes of energy supply myocardial cells, damage to their membrane apparatus and enzyme systems, the imbalance of ions and fluid disorder neuroeffector regulation of heart function eventually cause a significant reduction in the strength and speed of its reduction and relaxation.

Manifestations of heart failure

Depression forces and reduce speed, as well as relaxation of the myocardium in heart failure manifests abnormalities indices of cardiac function, and central hemodynamics organotissues.

1. Reduction of the stroke and minute heart ejection. Developed as a result of depressed myocardial contractility.

- The vast majority of cardiac output below the normal (usually less than 3 l / min).

- Under certain conditions, cardiac output, prior to the development of heart failure is higher than normal. This is observed, for example, in patients with thyrotoxicosis, chronic anemia, arteriovenous shunts, after the infusion excess fluid in the bloodstream. In these patients the development of heart

failure, cardiac output value remains above the normal range (for example, a 7.8 L / min). However, even in these conditions, insufficiency of blood supply to organs and tissues as cardiac output is lower than the required value. Such conditions are known as heart failure, high blood ejection.

2. Increasing the residual systolic blood volume in the cavities of the heart ventricles. It is a consequence of the so-called part-systole.

Incomplete emptying of the ventricles of the heart is the result of excess blood flow to it (for example, valvular insufficiency), excessively high PR (for example, hypertension, aortic stenosis), direct myocardial damage.

3. Increased end-diastolic pressure in the cardiac ventricles. Due to an increase in the amount of blood that accumulates in their cavity, myocardial relaxation disorder, dilatation of the heart chambers due to an increase in their blood volume and myocardial stretch.

4. Increased blood pressure in the venous blood vessels and heart cavities where blood enters the heart mainly the affected departments. Thus, with increased left ventricular heart failure, left atrial pressure, pulmonary circulation and the right ventricle. When right ventricular heart failure increases the pressure in the right atrium and in the veins of the systemic circulation.

5. Reducing the speed of systolic contraction and diastolic relaxation of the myocardium. It manifested mainly of extended periods of isometric tension and systole of the heart as a whole.

Clinical forms of heart failure

Acute heart failure

Acute heart failure - a sudden breach of the pumping function of the heart, leading to the inability to ensure adequate circulation, despite the inclusion of compensatory mechanisms.

Etiology

Acute heart failure often develops as a result of diseases, leading to a rapid and significant decrease in cardiac output (most frequently myocardial infarction). However, possible congestive heart failure and high cardiac output.

The main causes of acute heart failure

Low cardiac output

1. Myocardial infarction - a large amount of damaged myocardium, heart wall rupture, acute mitral insufficiency

2. decompensation of chronic heart failure - inadequate treatment, arrhythmia, heavy concomitant disease

3. arrhythmias (supraventricular and ventricular tachycardia, bradycardia, arrhythmia, conduction block excitation)
4. The obstacle in the path of blood flow - aortic stenosis and mitral orifice, hypertrophic cardiomyopathy, tumors, blood clots
5. Insufficiency of the mitral or aortic valve

6. Myocarditis

7. Massive pulmonary embolism

8. "pulmonary heart disease"

9. Hypertension

10. Cardiac tamponade

11. Heart Injury

With relatively high cardiac output

1. Anemia
2. Hyperthyroidism

3. Acute glomerulonephritis with hypertension

4. arteriovenous shunting

Acute heart failure has three clinical manifestations: cardiac asthma, pulmonary edema, and cardiogenic shock. In each case, it is recommended to specify the form of acute heart failure (cardiac asthma, cardiogenic shock or pulmonary edema), not the generic term "acute heart failure".

Mechanisms of compensation of hemodynamic disturbances in acute heart failure

At the initial stage of systolic dysfunction ventricular intracardiac factors include the compensation of heart failure, the most important of which is the mechanism of the Frank - Starling. The implementation can be summarized as follows. Violation of the contractile function of the heart leads to a decrease in stroke volume and renal hypoperfusion. This contributes to the activation of the renin-angiotensin-aldosterone system, causing delay in the body of water and an increase in blood volume. Under the conditions arising hypovolemia occurs enhanced inflow of venous blood to the heart, increasing the blood supply in diastolic ventricular myocardium myofibrils stretching and compensatory increase in force of contraction of the heart muscle, which provides increase in stroke volume. However, if the end-diastolic pressure rises more than 18-22 mm Hg. Art., there is an excessive hyperextension of myofibrils. In this case, compensatory mechanism Frank - Starling is no longer valid, and a further increase in end-diastolic volume or pressure is no longer the rise and decline in vivo.

Along with intracardiac compensation mechanisms in acute left ventricular failure started unloading extracardiac reflexes that contribute to the tachycardia and increased cardiac output (CO). One of the most important cardiovascular reflexes, providing an increase in the CO, is the Bainbridge reflex - increase in heart rate in response to an increase in blood volume. This reflex is

realized during stimulation of mechanoreceptors, which are localized in the mouth of the hollow and the pulmonary veins. These mechanoreceptors are afferent vagal endings and their stimulation is transmitted to the central sympathetic nucleus of the medulla oblongata, thereby increasing the tonic activity of the sympathetic component of the autonomic nervous system and develops reflex tachycardia. Bainbridge Reflex aims to increase cardiac output.

Reflex Bezold—Jarich- a reflex expansion of arterioles systemic circulation in response to stimulation of mechano-and chemoreceptors, localized in the ventricles and atria. As a result, there is hypotension, bradycardia, and which is accompanied by a temporary cessation of breathing. In the implementation of this reflex participate afferent and efferent fibers n. vagus. This reflex is directed to left ventricular unloading.

Among the compensatory mechanisms in acute heart failure and increased activity relates sympathoadrenal system, one link of which is the release of noradrenaline from the endings of the sympathetic nerves that innervate the heart and kidneys. The observed with excitement β-adrenergic myocardial leads to the development of tachycardia, and stimulation of these receptors in the cells of the juxtaglomerular apparatus is enhanced renin secretion. Another incentive is the reduction of renin secretion in renal blood flow caused by catecholamines resulting constriction of arterioles glomeruli. Compensatory inherently increased adrenergic effects on the myocardium in acute heart failure is directed to an increase in stroke volume and minute blood. Positive inotropic effect also provides angiotensin-II. However, these compensatory mechanisms can exacerbate heart failure, if the increased activity of the adrenergic and renin-angiotensin system is maintained for quite a long time (over 24 hours).

Everything said about the heart activity compensation mechanisms applies equally to both the left - and to right ventricular failure. The exception is the reflex Parin, the effect of which is realized only when the right ventricular overload observed in pulmonary embolism.

Reflex Parin - a drop in blood pressure caused by the expansion of the arteries of the systemic circulation, reduced cardiac output as a result of the emerging bradycardia and a decrease in the bcc of blood deposition in the liver and spleen. In addition, the characteristic of reflex Parin appearance of shortness of breath associated with advancing hypoxia of the brain. It is believed that Parin reflex is realized by strengthening tonic n.vagus influence on the cardiovascular system with pulmonary embolism.

Mechanisms of damage in acute heart failure

Cause

↓

↑↑↑the load on the heart

↓

compensatory mechanisms

↓

↑↑↑Overall cardiac function in 2-fold

↓

↑↑↑the number per unit mass of myocardial function in 2 times (IFS↑↑↑)

↓

CHANGE OF HEART BIOENERGY:

↓

ATP is the decay

+

↑ O2 demand (Frank-Starling mechanism
by 25% Anrep - 100%; tachycardia →
Shortening of diastole →

↓ blood supply to the heart).

↓

Hypoxia

↓

hypoxia → anaerobic glycolysis

↓

little formed ATP

↓

energy deficiency heart in general and myocardial mass units

↓

IFS ↓ (IFS = 2 functions

IFS = 1.5; IFS = 1, FIS = 0.5; IFS = 0.3, IFS-0)

↓

Acute heart failure

(Breakdown of term compensation mechanisms)

↓

↓↓ SV

Chronic systolic heart failure

Chronic systolic heart failure - clinical syndrome, complicating the course of a number of diseases. It characterized by the presence of dyspnea on exertion in the beginning and then at rest, fatigue, peripheral edema and objective evidence of cardiac dysfunction at rest (eg, auscultation or echocardiography).

The main causes of acute heart failure

Low cardiac output

1. Defeat infarction
2. IHD (myocardial infarction, chronic myocardial ischemia), cardiomyopathy, myocarditis, toxic exposure (eg, alcohol, doxorubicin), infiltrative disease (sarcoidosis, amyloidosis), endocrine disorders, eating disorders (deficiency of vitamin B1)
3. Overload infarction
4. Hypertension, heart disease
5. Arrhythmias
6. supraventricular and ventricular tachycardia, atrial fibrillation

With relatively high cardiac output

1. Anemia
2. Hyperthyroidism,
3. arteriovenous shunting

Under the influence of these causes impaired pumping function of the heart. This leads to a decrease in cardiac output. As a result, developing hypoperfusion of organs and tissues. Most importantly, the reduction in the perfusion of the heart, kidneys and peripheral muscles. The reduction of blood supply to the heart, and the development of its failure leads to activation of the sympathetic-adrenal system and rapid heart rate. Reduced renal perfusion causes stimulation of the renin-angiotensin system. Increased renin production, which triggers the excess production of angiotensin II. Last causes vasoconstriction, water retention (edema, increased VCB), and the subsequent increase in preload on the heart. Reduced perfusion of the peripheral muscles (and as a consequence - the development of hypoxia) causes accumulation of these oxidized products of metabolism, and as a result - expressed fatigue.

Classification

Phase I (initial) - latent heart failure, occurs only on exertion (shortness of breath, palpitations, fatigue)

Stage II (severe) - long-term circulatory insufficiency, hemodynamic instability (the stagnation in the systemic and pulmonary circulation), dysfunction of organs and metabolism and expressed alone

A period - the beginning of a long stage, characterized by mild cerebral blood flow, cardiac function, or just parts of them

Period B - the end of a long stage, characterized by profound disturbances of hemodynamics in the process involves the entire cardiovascular system

Phase III (final, dystrophic) - severe hemodynamic instability, persistent changes in the metabolism and function of all organs, irreversible changes in the structure of tissues and organs.

Manifestations

The clinical manifestations of heart failure significantly depend on its stage.

Stage I. The symptoms (fatigue, shortness of breath and palpitations) occur during normal exertion, alone manifestations of heart failure is not present.

Stage IIA. Mild hemodynamic disturbances. Clinical manifestations depend on the mostly affected parts of the heart (right or left).

- Left ventricular failure is characterized by stagnation in the pulmonary circulation. Manifested dyspnea at moderate exertion, paroxysmal nocturnal dyspnea, fatigue.
- Right ventricular failure is characterized by the formation of stagnation in the systemic circulation. Patients concerned about pain and heaviness in the right upper quadrant, a decrease in urine output. Characteristic enlargement of the liver. A distinctive feature of heart failure stage IIA is considered full compensation of the state during the treatment, ie, reversibility of heart failure as a result of an adequate therapy.

Stage IIB. Develop deep hemodynamic disturbances. The process involved the entire circulatory system. Shortness of breath occurs at the slightest exertion. Patients are disturbed by a feeling of heaviness in the right hypochondrium, general weakness, sleep disturbance. Characterized orthopnea, edema, ascites (due to increased pressure in the hepatic veins and enhanced extravasation excess fluid accumulated in the abdominal cavity), hydrothorax, hydropericardium.

Stage III. End (dystrophic) stage with deep irreversible metabolic disorders. Generally, the condition of patients in this stage heavy. Shortness of breath is expressed even at rest. Characterized by massive edema, accumulation of fluid in body cavities (ascites, hydrothorax, hydropericardium, swelling of the genitals). At this stage, cachexia occurs due to the following reasons.

- Increased secretion of tumor necrosis factor.

- Strengthening of metabolism due to the increased work of the respiratory muscles, increasing needs of the hypertrophied heart of oxygen.
- Loss of appetite, nausea, vomiting, central origin as well as due to toxic glycosides, stagnation in the abdominal cavity.

- Deterioration of the suction in the intestine due to stagnation in the portal vein system.

Pathogenesis of chronic heart failure

1 stage. Emergency compensatory hyperfunction stage of developing heart and hypertrophy.

Cause

↓

Improving heart function as a whole, the IFS↑↑↑

↓

breakup ATP (ADP + NF)

+

↑O2 demand hypoxia

Anaerobic glycolysis

ATP production (energy deficiency), SOS!

+

↓ PH + ↑Ca (comes from the blood under stress)

+

↑ Catecholamines

↓

activation of the genetic apparatus of cells of the heart

↑The synthesis of DNA, RNA, protein (base of long-term adaptation, hypertrophy

Infarction, cardiac hypertrophy)

↓

There is synthesis of 3 groups of proteins:

Proteins are long-term adaptation of the heart

Group 1 - protein energy supply increased heart function: structural proteins capillaries, mitochondria, the respiratory enzymes.

Group 2 - plastic proteins provide N - and Z-chain myosin myofibril proteins and enzymes muscle cell membranes.

Group 3 - neurofibrils ensure regulatory proteins, membrane proteins and enzymes of the nerve cells forming the mediator - noradrenaline.

↓

↑ energy, plastic, regulatory provision ↑ function units myocardial mass.

↓

If you have time to develop hypertrophy - a man will live if - no:

IFS will decline → IFS↓ → heart failure → can be fatal.

2 stage - stable compensatory hyperfunctional heart (CHH) and complete cardiac hypertrophy.

At this stage, the load on the heart ↑ 2-fold,

heart function as a whole also increased by 2 times,

but now completed hypertrophy and heart mass also increased by 2 times.

↓

IFS = 1 function (works without overload)

↓

Sustainable CHH (provided the energy, plastic and nervous regulation).

Stage 3 - progressive infarction, and congestive heart failure itself

It begins in the 2 stages:

The load on the heart, in general, constant

↓

Activation of the genetic apparatus of cells of the heart is constant

↓

On the unit myocardium ↓ the power supply

(↓ATP↓) Plastic software

(↓H chain↓) regulatory provision (↓noradrenalin).

Unbalanced growth of cardiac mass (K <d)

↓

↓ IFS - heart

failure: ↓SV

MECHANISMS decompensation in CHF

Hypertrophy of the heart in heart failure

1. ↓ power supply → hypoxia → ↓ATP → Ca is not included in the SR → ↑Ca in sarcoplasm →of muscle contracture heart fibers → ↓SV

2. ↓ plastic support (↓membranes, ↓enzymes, H-chains) → ↓O2 proceeds, nutrients in the cell heart + ↑ to end products + exchange disenzyms → muscular dystrophy heart fibers → ↓SV
3. ↓ regulatory provision (↓ nerve cells, their membranes, enzymes) → noradrenaline → ↓ adaptation to stress → dysfunction → ↓SV
4. As a result of the relative increase in the synthesis of long-lived proteins → ↑ cardiomyocytes volume ↑connective tissue →formation cardiosclerosis at the site of dying cells → ↓↓SV

↓

If the reason is valid - can occur irreversible changes of the myocardium - decompensated heart

failure

↓

↓SV

Mechanisms of compensation of hemodynamic disturbances in patients with chronic heart failure

The main link in the pathogenesis of heart failure is, as you know, gradually increasing reduction in myocardial contractility and cardiac output fall. What is happening at the same time a decrease in blood flow to organs and tissues is the last hypoxia, which can initially be compensated by increased tissue oxygen utilization, stimulation of erythropoiesis, etc. However, this is not enough for a normal oxygen supply of organs and tissues, and increasing hypoxia becomes a trigger compensatory hemodynamic changes.

As with acute heart failure, all of endogenous mechanisms for compensation of hemodynamic disturbances in heart failure can be divided into intracardiac (mechanism Frank - Starling, compensatory hyperactivity and myocardial hypertrophy) and extracardiac (handling reflexes Bainbridge and

Kitaeva). This division is somewhat arbitrary, since the implementation of both intra- and extracardiac mechanisms is under control of regulatory neurohumoral systems.

Extracardiac mechanisms of cardiac function compensation. In contrast to acute heart failure role reflex mechanisms of regulation of emergency cardiac pump function in heart failure is relatively small, because of hemodynamic instability develops gradually over several years. More or less can definitely talk about Bainbridge reflex, which is "turned on" at the stage quite severe hypovolemia.

A special place among the "unloading" noncardiac reflexes takes Kitaeva reflex that "run" in mitral stenosis. The fact is that in most cases of right ventricular failure associated with stagnation in the large circulation and left ventricular - small. An exception is the mitral valve stenosis, in which the congestion in the pulmonary vessels are not due to decompensation of the left ventricle, and blood flow obstacle; through the left atrioventricular opening called the "first (anatomical) barrier." This stagnation of blood in the lungs contributes to the development of right heart failure, in the genesis of which Kitaeva reflex plays an important role.

Reflex Kitaeva - a reflex spasm of the pulmonary arterioles in response to increased pressure in the left atrium. The result is a "second (functional) barrier," which was originally played a defensive role, protecting the lung capillaries from excessive blood overflow. But then this reflex leads to a marked increase in pulmonary artery pressure - develops acute pulmonary hypertension. Afferent link of this reflex is represented n.vagus, and efferent sympathetic component of the autonomic nervous system. The downside of this adaptive response is a rise of pressure in the pulmonary artery, which leads to increased stress on the right heart.

However, the leading role in the genesis of a long-term compensation and decompensation impaired cardiac function did not play reflex, and neurohumoral mechanisms, the most important of which is the activation simpatoadrenalovoj (SAS) and the renin-angiotensin-aldosterone system. Speaking about the activation of SAS in patients with CHF, it is necessary to point out that most of them catecholamine levels in blood and urine is in the normal range. CHF This differs from AHF.

Intracardiac mechanisms of cardiac function compensation. These include hyperactivity, and compensatory hypertrophy of the heart. These mechanisms are essential components of most adaptive reactions of the cardiovascular system of a healthy body, but under pathological conditions can become a link in the pathogenesis of heart failure.

Compensatory heart hyperfunction (CHH). CHH acts as an important factor in compensation for heart diseases, hypertension, anemia, pulmonary hypertension and other diseases. Unlike physiological hyperfunction it is prolonged and that substantially continuous. Although the continuity, the CHH may persist for many years without obvious signs of decompensation of heart pump function.

The increase in external work of the heart associated with the rise of the pressure in the aorta (isometric hyperactivity), leads to a more pronounced increase in myocardial oxygen demand than the overload of the myocardium caused by an increase in the volume of circulating blood (isotonic hyperthyroidism). In other words, to carry out work in the conditions of a pressure load of the heart muscle uses more energy than to perform the same work associated with the load capacity, and therefore, when persistent hypertension cardiac hypertrophy develops faster than the increase in VCB. For

example, when physical work, high altitude hypoxia, all kinds of valve failure, arteriovenous fistula, anemia, myocardial hyperfunction ensured by increasing cardiac output. Thus myocardial systolic pressure and the pressure in the ventricles increases slightly, and hypertrophy develops slowly. At the same time, hypertension, pulmonary hypertension, valvular stenosis holes hyperfunction development is associated with increased myocardial tension with small changes amplitude contractions. In this case, hypertrophy progressing fast enough.

Hypertrophy of the myocardium - is an increase in heart weight by increasing the size of cardiomyocytes. There are three stages of compensatory hypertrophy of the heart. First, emergency, stage is characterized, above all, an increase in the intensity of the functioning myocardium structures and, in fact, is a compensatory hyperactivity has not hypertrophied heart. The intensity of functioning of structures (IFS) - is the mechanical work per unit mass of the myocardium. Increased IFS naturally entails the simultaneous activation of energy production, synthesis of nucleic acids and proteins. Said activation of protein synthesis takes place in such a way that the first increases weight energyformation structures (mitochondria), and then - the mass of functioning structures (myofibrils). In general, an increase of myocardial mass leads to the fact that the IFS is gradually returned to normal levels.

The second stage of hypertrophy is characterized concluded IFS normal myocardium and thus a normal level of energy production and synthesis of nucleic acids and proteins in the cardiac muscle tissue. In this case the oxygen consumption per unit weight of the myocardium remains normal limits, and the oxygen consumption of cardiac muscle in general increased in proportion to increase in heart weight. An increase in myocardial mass CHF conditions is due to the activation of the synthesis of nucleic acids and proteins. Starting mechanism of this activation is insufficiently studied. It is believed that a decisive role is played here by strengthening the trophic influence sympathoadrenal system. This stage of the process is the same with a prolonged period of clinical compensation. ATP and glycogen content in the cardiomyocytes is thus also within the normal range. These circumstances give relatively stable hyperfunction, but at the same time does not prevent the gradually developing in this stage of myocardial metabolism and structure violations. The earliest signs of such disorders are a significant increase in the concentration of lactate in the myocardium, and Moderate cardio.

The third stage of progressive decompensation infarction, and is characterized by impaired synthesis of proteins and nucleic acids in the myocardium. As a result of violation of the synthesis of RNA, DNA and protein is observed in cardiomyocytes relative decrease in mitochondrial mass, which leads to inhibition of ATP synthesis per unit mass of tissue, reduce cardiac pump function and progression of CHF. The situation is exacerbated by the development of dystrophic and sclerotic processes that contribute to the appearance of signs of decompensation of heart failure and total ending at the death of the patient. Compensatory hyperfunction, hypertrophy and subsequent

decompensation of heart - these are links in a single process. The mechanism of decompensation hypertrophied myocardium includes the following links:

Process hypertrophy does not apply to coronary arteries, so the number of capillaries per unit myocardial volume in the hypertrophied heart is reduced. Consequently, blood flow to the heart muscle is hypertrophied insufficient to perform mechanical work.

Due to increased hypertrophied muscle fiber cells decreases the specific surface, thereby worsening conditions for entry into cells nutrient and isolating cardiomyocytes from the metabolic products.

In hypertrophic heart broken relationship between the amount of intracellular structures. Thus, the increase in mass of the mitochondria and the SR behind the increase in the size of myofibrils, which contributes to the deterioration of supply of cardiomyocytes and is accompanied by violation of the accumulation of Ca2 + in the SR. Ca2 + occurs –overload cardiomyocytes that provides cardiac contracture formation and contributes to a decrease in stroke volume. Furthermore, Ca2 + - overload myocardial cell increases the likelihood of arrhythmias.

The conducting system of the heart and autonomic nerve fibers that innervate the myocardium, are not subject to hypertrophy, which also contributes to the dysfunction of hypertrophied heart.

Activated individual cardiomyocyte apoptosis, which contributes to the gradual replacement of muscle fibers of the connective tissue (cardio).

Ultimately hypertrophy loses adaptive value and ceases to be useful for the organism. The weakening of the contractility of the hypertrophied heart occurs sooner, the more pronounced hypertrophy and morphological changes in the myocardium.

The concept of hypertrophy of athletes and pathological cardiac hypertrophy.

It is important to distinguish between hypertrophy of athletes as the adaptive response to regulatory intense exercise of hypertrophy develops in certain pathological conditions, an overload of the heart chambers (persistent elevation of blood pressure, valve defects, etc.).

Regular intense exercise leads to the fact that the size of the heart in athletes alone significantly more than in untrained people: the athletes alone heart can hold the amount of 3-4 times greater than the systolic (the average person - only 2 times higher). The load conditions of athlete's heart under the influence of sympathetic nerves and adrenaline increases cardiac output in a much greater extent than the heart of an ordinary person, fraction ejection during exercise in athletes increased significantly more, than in untrained persons. Thus, the hypertrophy of the athlete contributes to a significant increase in cardiac functional reserve and plays an essential role in adaptation to intense physical activity.

Signs	Normal hypertrophy (athlete's heart)	Pathological hypertrophy
Load	Increased load only during exercise - for several hours a day	constantly

The prevalence of hypertrophy	all heart uniformly	the hypertrophied heart department, which is experiencing an increased load
End-diastolic pressure in the wall of the ventricles and other chambers of the heart hypertrophied	not excessive	higher than normal
Ability to myocardial	no violations	Disturbed myocardial

Disturbance of system level blood pressure. Hypertension.

Fundamentals of the regulation of blood pressure levels.

Blood pressure (BP) in the population has a normal (Gaussian) distribution, and therefore it is impossible to draw a clear boundary between normality and pathology. Long-term observation of the target population have shown that at any level of blood pressure is a risk of death from cardiovascular disease. However, this risk is increased in accordance with an increase in blood pressure. Therefore, it is assumed that hypertension (AH) - a blood pressure above 140/90 mm Hg. Art., since in this case the risk of death doubled.

Monitoring of blood pressure is carried neurohumoral factors via autoregulation with the participation of baro- and chemoreceptors, and vasomotor centers in the medulla oblongata. Transmission of nerve impulses via adrenaline and noradrenaline is due to stimulation of α- and β-adrenergic receptors. Stimulation of the alpha-receptors causes vasoconstriction, β1-receptors - vasodilation. Adrenergic transmission pulses to the heart via the β1-receptors. In the regulation of vascular tone and hormones are involved with the properties of vasopressors or vasodilators.

Vasopressor function is performed by:

1. The renin-angiotensin-aldosterone system

The proteolytic enzyme renin is produced and stored in the juxtaglomerular cells of the kidney. When released into the bloodstream, where it remains active for 30-60 minutes, the enzyme cleaves angiotensinogen (α2 - globulin synthesized in the liver) to form the decapeptide angiotensin I. Under the influence convertases plasma angiotensin I to the octapeptide angiotensin passes II; This reaction proceeds advantageously in the lungs. After 1-2 minutes angiotensinase to inactive peptides.

Running this reaction sequence closely related to the magnitude of renal blood flow. By reducing the blood supply to the kidneys of any etiology (for example, when SAD narrowing of the renal arteries, and its lesions, etc.) is increased renin release.

Products renin cells juxtaglomerular apparatus is also increased by reducing the concentration of sodium ions into the lumen of the distal convoluted tubule.

Angiotensin II increases the blood pressure resulting from:

1) A spasm of arterioles and to a lesser extent due to the large veins:

- Direct binding to angiotensin II receptor on the surface of smooth muscle respective vessels;
- Stimulation of the sympathetic nervous system at different levels - the central sympathetic activation structures; increased activity of the sympathetic ganglion neurons; increasing the release of noradrenaline from the nerve endings of the sympathetic and its synthesis in the adrenal glands; increase adrenoceptor sensitivity to catecholamines;
- Increasing sensitivity to vasopressin receptors on the surface of vascular smooth muscle cells;

2) Enhancement of production of aldosterone zona glomerulosa cells of the adrenal cortex, which further increases the reabsorption of sodium ions in the distal convoluted tubules of nephrons and the excretion of potassium and hydrogen;

3) Enhancement of sodium and water absorption in the intestine.

As a result of these mechanisms of action of angiotensin II occurs GPR increase, increase in extracellular fluid volume and VCB, increasing venous return, the CO and the increase in SBP.

In order to activate the renin-angiotensin-aldosterone system has reached a maximum, it takes about 20 minutes. Further, this activity is maintained for a long time, is only slightly attenuated. Renin-angiotensin system plays an important role in normalization of blood circulation in pathological decrease of SBP and / or blood volume. This system causes increasing concentrations of renin and angiotensin blood.

2. Vasopressin

Vasopressin or antidiuretic hormone (ADH) plays a special role in the regulation of fluid volume (due to water reabsorption in the distal renal tubules) as reflex changes the contents of this hormone provide maintaining intravascular volume aqueous space. With an increase in blood

volume within 10-15 minutes decreasing excretion of vasopressin, which increases liquid discharge kidneys. In the fall of SBP process is reversed: the release of vasopressin increases, and the allocation of kidneys fluid decreases.

With a significant drop of the SBP posterior pituitary thrown enough of vasopressin, which causes contraction of the smooth muscle cells of vessels (most pronounced at the level of arterioles) and increased GPR.

3. Catecholamines

Changing the circulatory parameters captured receptors located in different parts of the cardiovascular system. Afferent impulses from them arrive in the cardiovascular center of the medulla oblongata, which sends regulatory signals to the heart and blood vessels in the central nervous system and the endocrine system involved in the regulation of blood flow.

Activation of the sympathetic nervous system accompanied by increased secretion of catecholamines adrenaline noradrenaline, acting through the α- and β-adrenergic receptors.

Activation of adrenaline and noradrenaline α-adrenergic receptors, located mainly on the surface of smooth muscle cells of the skin blood vessels and internal organs (stomach, liver, kidney), leads to a reduction, a decrease in vessel radius, improvement of GPR and SBP.

Effects of β-adrenergic activation depend on the type of receptor (β1, β2) and their location. Further, β-adrenergic receptors of various systems and organs reacted differently to adrenaline and noradrenaline. B1-adrenergic receptors have the same affinity for the catecholamines and mediate their stimulating effect on the heart; β2-adrenoreeptory have a stronger affinity for the adrenaline, providing relaxation of vascular smooth muscle.

Adrenaline is primarily the decrease in peripheral resistance in the coronary and cerebral blood vessels as a result of excitation of β2-adrenergic receptors. Norepinephrine causes a marked increase in the GPR and increasing SBP.

4. Endothelin.

This factor is released during endothelial damaged cells. With the release of endothelin is associated spasm of the umbilical artery of the newborn. Endothelin is the most potent of the peptides having vasoconstrictive activity. Receptors to endothelin were found in the heart, blood vessels, kidney (mezangly), adrenal and others. The greatest sensitivity to the vasoconstrictor action of endothelial factors have a kidney. Detection of endothelin in the cerebrospinal fluid and its connection with the human mental activity will include the peptide to neuropeptides.

Vasodilator function is provided

by 1. Prostaglandins (PGL2, prostacyclin)

Localization and level of biosynthesis of prostaglandins (PGs) in the different structures of the kidneys are not the same. The main part of PG is synthesized in the medulla. Expression of physiological effects have PGE2, PGI2, PGA2.

Increased production of most of the PG (or introduction into the body) causes an increase in diuresis and natriuresis, vasodilation and reduces the SAD. The direct influence of the renal system PG level of the whole organism is insignificant. Natriuretic and diuretic effects of PG have the immediate vicinity of the synthesis places - on the elements of the medullary concentrating mechanism (collecting tubes, thick ascending loop nephron otdl and straight vessels). While working on the vessels, PG regulate blood flow in the inner zone of the cortex and medulla, increasing his or contributing to the normalization, if it is reduced.

Kidney PG contribute to strengthening the separation of water by the kidneys:

- Reducing the ADH ability to increase permeability of the collecting duct epithelium for water; Increased blood flow to the vessels of the zone;
- Inhibiting the reabsorption of sodium and chloride in the thick ascending loop of the nephron. 2. The kinin-kallikrein system;

Vasodilator and natriuretic effect of kinins (activation products kallikrein-kinin system) mediated by their ability to stimulate the synthesis of renal PG (especially PGE2).

3. Atrial natriuretic peptide;

This peptide is synthesized in cells of the atria. Its main effects are: a decrease in the reabsorption of sodium and water in the collecting ducts, inhibition of production of aldosterone and vasopressin, as well as inhibition of sympathetic activity and a direct vasodilator effect. When the VCB is an increase in the formation of natriuretic peptide. This causes an increase in the excretion of sodium and water by the kidneys, vasodilation and decrease in SBP.

4. Endothelial vasodilator factor (N0).

On vascular tone affects nitric oxide, synthesized by endothelial cells in the amplification of pressure on them and their extension. Acting on the enzymatic system cells, nitric oxide accelerates the return tube of calcium ions into the sarcoplasmic reticulum, and accelerates the removal of these ions from the cells. Reducing the concentration of intracellular calcium ions leads to the relaxation of vascular smooth muscle cells, and reduce the decrease in SBP GPR. It is believed that through the formation of nitric oxide acting vasodilators such as acetylcholine and bradykinin.

General description, definitions, terminology.

All kinds of systemic blood pressure changes its orientation is conventionally divided into two groups: the arterial hyper-and hypotension.

To adequately indicate different states and reactions characterized by changes in systemic blood pressure, use special terms and concepts. In particular, it is important to distinguish between the value of terminological elements "tonia" and "tensor".

Terminology element "tonia" is used to describe the tone of muscles, including - the vascular wall. Hypertension (from the Greek hyper - over, above + Greek tonos - stress, tension) is excessive muscle tension, manifested by increasing their resistance to stretching; hypotension (from the Greek hypo -, below + tonos) involves reduction of muscle tension, manifested by a decrease in their resistance to stretching.

Terminology element "tensor" is used to indicate the pressure of fluids in the cavities and blood vessels, including blood. Hypertension (from the Greek hyper + lat tensio - pressure) is increased, and hypotension - low blood pressure in the cavities of the body, his hollow organs and vessels. Appropriate to refer to hyper- or hypotensive states is to use the "tensor" element, as the level of blood pressure depends not only on vascular tone muscles (in some types of hypertension, he not only does not increase, and may even be below normal), but also on the size of the minute ejection heart and circulating blood mass.

Drugs that decrease blood pressure, antihypertensive call regardless of their mechanism of action (vascular tone, cardiac output, blood volume). Substances that cause an increase in blood pressure is called hypertensive.

To identify relevant clinical entities retained their "historical" names - hypertension (essential) and hypotension.

It is necessary to distinguish between the notions of "hyper" - or "hypotensive response" from the concept of "arterial hyper- or hypotension." Under hyper- or hypotensive reactions understand transient (temporary) reaction of the cardiovascular system, in which the blood pressure to normal after termination of the agent that caused them. These reactions are generally regulated by physiological mechanisms. According to its biological value they tend to be adaptive. In contrast, arterial hyper- or hypotension are persistent. They usually are not removed after the termination of the causal factors that caused them. The components of the mechanism of their development can be pathologic reactions and processes. As a rule, they are accompanied by damage to the organs and tissues and decrease the adaptive capacity of the organism.

According to statistics arterial hypertension (AH) is a cause of death in 4 to 5% of deaths.

Approximately 40% of all diseases and disease states of the cardiovascular system is hypertension.

Under hypertension understand the persistent increase in blood pressure above normal. For individuals 20 to 60 years lower limits blood pressure norm (systolic and diastolic) are respectively 100 and 60 mm Hg .; Upper - 139 mmHg and 89 (WHO data). Border (between normal and hypertensive synonym - borderline hypertension) is considered a systolic pressure - 140-159 mm Hg, diastolic 90 - 94 mm Hg Hypertensive blood pressure - systolic and diastolic - are, respectively,

160 and 95 mm Hg and more. For persons under 20 years of blood pressure rate of 10 - 20 mm Hg below, and for those over 60 years by 10-15 mm Hg above mentioned rules.

Types of arterial hypertension

Arterial hypertension is differentiated by several characteristics:

1. cardiac volume (cardiac output) on the hyperkinetic - with an increase in cardiac output; eukinetic - with normal cardiac output; hypokinetic, with reduced cardiac output;
2. Change in total peripheral resistance (TPR) - on the hypertension with high, normal and reduced TPR;
3. In terms of volume of circulating blood (CBV) - on hypervolemic ("volumodependent", such as primary hyperaldosteronism - Conn's disease) and normovolemic ("volumonondependent") hypertension;

4. According to the type of high blood pressure - a predominantly systolic, diastolic and mixed - systolic-diastolic hypertension (most commonly found);
5. When blood levels of renin and its effects - on hyperreninogenic, normoreninogenic and hyporeninogenic AH;
6. The clinical course - to benign (slow developing for many years) and malignant (fast progressing, leading for 1 - 2 years in death). For malignant hypertension is characterized by significant damage to the vessel walls and the formation of fibrinoid necrotic changes, the rapid development of renal failure;
7. By origin - primary, essential, hypertension, or hypertension (abroad often use the term "Essential" hypertension), and a secondary, symptomatic hypertension.

Hypertensive heart disease (essential hypertension)

The difference between hypertensive disease from other types of hypertension. There are a number of features that differentiate hypertonic diseases (HD) from all other arterial hypertension:

1) increase in blood pressure when HD occurs in the absence of any known diseases that cause the development of symptomatic hypertension; 2) the importance of the development of HD has a genetic predisposition. HD is often a "family" disease; 3) the etiology and pathogenesis of HD are very complex and relatively poorly understood.

The above (and other) factors suggest HD independent nosological form. HD frequency on the data given by different authors, is 78 - 95% of all hypertension.

Stages of hypertension. According to the WHO, there are three stages of slowly progressive ("benign") hypertension.

Stage I (mild course HD). Systolic pressure alone ranges from 160 to 179 mm Hg.; diastolic - from 95 to 104 mm Hg or may remain within normal limits. Occasionally there are rises in blood pressure (BP) above these limits. It is also possible periodic normalization of blood pressure.

Stage II (moderate severity HD). Systolic pressure alone ranges from 180 to 200 mm Hg, diastolic - from 105 to 114 mm Hg Characterized hypertensive crises with a sharp rise in blood pressure, combined with headaches, dizziness, feeling of stupor, nausea, visual impairment (the appearance of "flies" in front of the eyes), angina, paresthesias, and sometimes paresis, and others. On the electrocardiogram and fluoroscopic study of signs of marked hypertrophy of the left ventricle of the heart. Spontaneous normalization of blood pressure in stage II HD, as a rule, is not observed.

Stage III (HD with severe). Systolic pressure - 200 - 230 mmHg and more. High blood pressure is stable. Often develop hypertensive crises. Their possible outcome in stroke or myocardial infarction. At this stage, usually, in addition to left ventricular hypertrophy, arteriosclerosis develops expressed vessels of the heart, brain, kidneys and other organs, leading to the development of ischemic damage and failure functions of these organs.

Causes of hypertension. Presumably HD causes are chronic psychoemotional overstrain, repeated negative emotions, genetic defects in cell membranes and ion pumps, as well as structures of the autonomic nervous system, regulating blood pressure.

Risk factors for hypertension. By HD of risk factors include: 1) overweight (about 1/3 of all obese people have hypertension at the same time); 2) diabetes mellitus (data driven by different authors, 30 - 40% of cases of diabetes in the elderly is combined with hypertension); 3) systematic excessive consumption of common salt; 4) re-tightening stress during natural disasters and social excesses - earthquakes, floods, fires, collapses buildings in times of war, etc .; 5) lack of exercise.

The pathogenesis of essential hypertension. To explain the pathogenesis of essential hypertension many hypotheses proposed that the subject of the discussion which is primarily the essence of the trigger (an initial) pathogenetic link HD. Chief among these are the following hypotheses.

Hypothesis Gellgorna E. et al. An initial pathogenetic factor is the persistent increase in excitability and reactivity (hyperergia) higher sympathetic nerve centers (in particular, located in the posterior hypothalamus). The factors that cause persistent hyperergia these centers is long, repeated emotional arousal centers, closely associated with the sympathetic hypothalamic nuclei. A certain importance is the hereditary hyperergia centers synaptic nervous system. Hyperergic state of these structures is on the one hand, increased tone pressor centers (also inherently non-sympathetic), which leads to vascular spasm, increase cardiac output and raise blood pressure, and on the other hand, causes hyperproduction humoral factors with pressor effect of epinephrine, norepinephrine, vasopressin, ACTH, corticosteroids, and hypersecretion of renin in the juxtaglomerular apparatus (south) of the kidneys. All these factors potentiate arteriolar spasms and promote even greater increase in cardiac output. This leads to an increase in diastolic pressure (as a result of increasing the tone of the vessel walls), and systolic (cardiotropic due to the stimulating effect of these agents). Depending on the size of their cardiotropic action and its relations with the vasoconstrictor effect can develop

various types of hypertension, differentiable largest cardiac output: hyper-, eu-, and hypokinetic. With the described hypothesis hyperergic able sympathetic centers is similar to a certain extent the hypothesis of pressor dominant in the vasomotor center (formulated by prof. A. Magnitsky). The formation of such a dominant leads to results, basically similar to the changes seen in hyperergia sympathetic centers.

Hypothesis prof. G.F. Lang and Prof. A.L. Myasnikov. An initial pathogenetic factor in the development of HD is to reduce the inhibitory effect of the cortex, it exerted in normal subcortical autonomic nerve centers, first of all - on the pressor. This leads, on the one hand, to a spasm of arterioles and increase blood pressure, and on the other - to the conditionality of spasm of the renal arteries and the inclusion of other changes in renal pressor pathogenetic factors, endocrine and blood pressure increase reflexogenic mechanisms. According to the hypothesis of Professor G.F. Lang and Prof. A.L. Myasnikov, the cause of reducing the inhibitory effect of the cortex on the subcortical centers pressor (which leads to the development of hypertensive disease) is the weakening of its "tone" (activity) under the influence of excess signals from extero- and interoceptors.

Hypothesis E. Muirad, Gaitopa A. et al. An initial factor for hypertension, according to these authors, is a genetically determined low level of sodium chloride and waterexcretory renal function. This leads to an excess accumulation in the body of sodium and water, including the vascular wall tissue, including their smooth muscle. Therefore it develops hypervolemia, increased vascular tone and sensitivity of their walls to pressor hormone and other biologically active factors. This is (eventually) leads to the development of hypertension.

The hypothesis of violation of functions of membrane ion pumps prof. Y. Postnov. An initial factor in the pathogenesis of hypertension is a generalized inherited defect of membrane ion pump cells, including smooth muscle cells of arterioles. This defect is to reduce the activity of the calcium pump localized in the membranes of the endoplasmic reticulum, and - sodium pump localized in plasmolemma. This reduces on the one hand, the "pumping" of calcium ions from the cytoplasm to the endoplasmic reticulum (which leads to the accumulation of excess cations in hyaloplasm) and on the other hand, to reduce "pumping" of sodium from the cytoplasm to the extracellular space (which results in its accumulation in the cytoplasm). Excess sodium and calcium ions in the

cytoplasm of vascular smooth muscle cells causes them spasm, and increased sensitivity to pressor factors. This leads to the development of hypertension.

Symptomatic (secondary) arterial hypertension

Symptomatic hypertension are due (hence the name - secondary) primary lesion of any organ or physiological systems involved in maintaining systemic blood pressure, and account for about 5% of all the varieties of hypertension.

Among the most common human symptomatic hypertension are renal (3 - 4% of all hypertension), endocrine (about 0.3%), neurogenic (centrogenic reflex and - about 0.2% in total). In addition, secondary hypertension may develop as a result of prolonged use of excess salt ("salt"

hypertension), or hypertensive drugs with action: sympathomimetics, thyroid hormone, vasopressin, and synthetic analogues mineralocorticoid other ("medicated" hypertension).

Renal arterial hypertension

Kidneys have a significant role in the regulation of systemic blood pressure. They take part in the hypertensive and hypertensive organ systems. In this regard, many chronic renal disease is often accompanied by the development of hypertension. Moreover, in most of other origin hypertension including essential hypertension, renal arterial pressure regulation system are involved in the formation of hypertension as potentiating mechanisms.

There are two varieties of renal hypertension: 1) renovascular (renovascular, renal ischemic) and 2) renoprival.

Renovascular hypertension. The reason for it is the reduction of blood perfusion pressure in the blood vessels of the kidneys of various origins. This may be due to compression of the main renal artery from the outside (tumor, scar); narrowing or complete closure of the inside (thrombus, emboli, tumors, atherosclerotic plaque); hypovolemia (post-hemorrhagic, with burn disease); Compression of the renal artery branches and at the most kidney inflammation in her parenchyma (e.g., glomerulonephritis).

The mechanism of development of renovascular hypertension can be schematically represented as follows. Reducing the amount of flowing blood is perceived by specialized receptors

- voluumoreceptors (from the English volum - volume, value) cells juxta - glomerular apparatus (JGA). With a decrease in perfusion pressure in the afferent arterioles of the glomeruli of the kidneys below 100 mmHg renin production in cells JGA quickly and significantly increased. It should be noted that the processes of renin and incretion biosynthesis to the blood are stimulated as well (in addition to the fall in perfusion pressure) in reducing blood sodium level and (or) the increase of the potassium content, increasing the concentration of catecholamines and vasopressin reducing angiotensin-II levels and aldosterone content increases antidiuretic hormone. Renin substrate is blood plasma protein alpha-2-globulin synthesized by the liver cells. He called angiotensinogen. Cleavage with renin it leads to the formation of the decapeptide - angiotensin-I, which has no effect on vascular tone. Under the influence converting enzyme (factor converting) angiotensin-I is cleaved to form the octapeptide, referred to as angiotensin-II (AT-II). This process is carried out mainly in the lung (approximately 50% of the resulting AT-II), in blood plasma and interstitial kidney tissue (which produces about 10 - 20% AT-II). AT-II - one of the most potent pressor human factors. It is inactivated under the influence of a complex of enzymes of oxidative and proteolytic nature (angiotensinase). AT-II has a range of effects, leading to increased blood pressure: 1) directly causes contraction of the smooth muscle of the arterioles; 2) activates the release of catecholamines from sympathetic neurons axonal vesicles; 3) increases the sensitivity of the vascular wall to catecholamines and other vasoconstrictor agents. Product metabolism AT-II - angiotensin-II gives a significant chronotropic effect, manifested a significant increase in heart rate, cardiac output and blood pressure. In addition, the AT-II stimulates the production of and access to the blood cells of the glomerular zone of the adrenal cortex hormones - aldosterone. Last potentiates process reabsorption into the blood from the primary urine sodium in the distal tubules of the kidneys and the urine excretion of potassium ions. This process is due to the activation of the

enzyme succinate dehydrogenase. Increase in plasma sodium concentration causes an increase in its osmotic pressure. This in turn activates vascular osmoreceptors, neurosecretion antidiuretic hormone (ADH) and its output in the blood. ADH causes increased permeability of the wall of the renal tubular fluid (believe that this effect is due to the activation of hyaluronidase, which is involved in the hydrolysis of the basic substance of the basement membrane of the tubules). Latency excess liquid increases its volume in the already narrowed bloodstream. In this regard, increased diastolic blood pressure. In addition, the increased inflow of venous blood to the heart, and as a result it increases stroke volume, and therefore increased systolic blood pressure, ie, developing hypertension.

In addition to the above-mentioned renal effects of aldosterone it has also extrarenal action. The latter plays a very significant role in the development of hypertension. This action of aldosterone is to control the exchange of sodium and potassium ions between intra- and extracellular fluid by reversibly altering cell membrane permeability. High concentration stimulates aldosterone excess sodium ions transport in cells of tissues, including blood vessels. The latter causes a number of effects: swelling of the walls of the arterioles, increasing the tone of the muscle layer, increased vascular sensitivity to vasoconstrictor agents (catecholamines, AT-II, vasopressin, prostaglandins, and others.).

Taken together, these changes provide the vascular lumen narrowing, increase the tone of the walls and, consequently, diastolic blood pressure. This in turn increases the blood return to the heart and stroke volume. Elevated blood released into the bloodstream narrowed potentiates the increase in blood pressure. Develops hypertension. Thus, aldosterone is the end product of the interaction of effector cascade factors unified functionally system "of the renin - angiotensin-II - aldosterone system." This system of "specialized" in the regulation of vascular tone, the osmotic pressure, blood volume, and ultimately the level of systemic blood pressure. Excessive activation of this system leads to the development of resistant hypertension.

Renoprival AH (from Latin ren -. + kidney, latin privo - reduce). The reason renoprival AH is to reduce the weight of the kidney parenchyma, generating compounds with hypotensive effect, which are components of depressant ("hypotensive") system of the body. These include prostaglandins with vasodilating effect (groups A and E) and kinins (bradykinin and mainly kallidin). Reduced renal mass may be the result of removing a portion of a kidney, one or both kidneys of necrosis, total nephrosclerosis, hydronephrosis, cystic changes, and other processes.

The mechanism of development renoprival AH is to reduce the synthesis and release into the blood of antihypertensive factors - prostaglandins and kinins. Prostaglandins of A and E are formed in the medullary interstitial cells located in the countercurrent system of the nephron. Of the two groups of renal prostaglandin A and E the last has largely local effects on renal hemodynamics due to its rapid destruction. Prostaglandins Group A, having long half-life, are involved in the regulation of systemic blood pressure. Furthermore, prostaglandins stimulates excretion of sodium ions and fluid from the tissues and cells of the whole organism. A significant vasodilator effect is also bradykinin and kallidin. In general, the components of kinin prostaglandin and renal "antihypertensive system" considered as a physiological antagonist "of the renin - angiotensin - aldosterone - ADH" system. Reducing the "power" of these components antihypertensive system in case of reduction of renal mass of tissue leads to the dominance of kidney and other "hypertensive" systems and the development of hypertension. It is this mechanism underlies the formation of hypertension in patients who for one reason or another had a one- or two-sided nephrectomy. It is important to note that "antihypertensive" kidney function is associated with pressor agents excretion in the urine as hemodialysis does not prevent the development of hypertension.

In general, various functional and organic damaged kidney tissue, on the one hand, activate "renopressor" system ("renin - angiotensin - aldosterone - ADH"), on the other, at the same time (or sequentially) are first stimulated, then leads to the depletion and (or) reduction in material substratum "renodepressor" kidney mechanisms. Taken together, this leads to the development of persistent renal hypertension.

Endocrine arterial hypertension

Endocrine (endocrinogen, hormone) AH fundamentally developed with the participation of the two mechanisms. The first is realized through increased production, incretion and (or) activity of hormones with hypertensive effect. Second - by improving the sensitivity of blood vessels and heart to their influences. The first way often leads to the formation of the corresponding AH, the second - to "consolidate" the stabilization of hypertensive blood pressure in hypertension of different origin, including hypertension. In chronic hypertension during both mechanisms are implemented, usually friendly.

AH with adrenal endocrinopathy. The adrenal glands are the main endocrine organ that provides regulation of systemic blood pressure. Adrenal hormones are all more or less related to the regulation of blood pressure, and in pathology - involved in the formation and fixing of hypertension. Among the main varieties of "adrenal" AG include: "corticosteroid" and "catecholamine".

Among the "corticosteroid" AG identified two clinical varieties AG: mainly caused by the overproduction of mineralocorticoids and glucocorticoids.

"Mineralocorticoid" hypertension due to overproduction mainly aldosterone. It is a major human mineralocorticoid. In addition, similar effects have corticosterone and deoxycorticosterone. However, their "capacity" is significantly lower (for example, corticosterone about 25 times).

The cause overproduction of aldosterone is often hyperplasia or a tumor of the adrenal cortex (of the glomerular zone). Aldosteronism such origin was first described in 1955 and was named A.Conn primary (or Conn's syndrome) in contrast to the secondary, which develops as a result of pathological processes in other organs and physiological systems (for example, cardiac, renal, hepatic insufficiency).

Hyperaldosteronism any genesis is accompanied, as a rule, an increase in blood pressure.

At the heart of the development of hypertension with hyperaldosteronism is the implementation of two of its effects: kidney (renal) and extrarenal (extrarenal). The renal effects of aldosterone can be schematically represented as follows: overproduction of aldosterone → reabsorption of excess sodium ions (in exchange for potassium ions) of provisionally urine in the distal tubules of the kidneys → increase in the sodium concentration in the blood plasma of → its hyperospheresia → activation of vascular osmoreceptors → stimulation process neurosecretion ADH and release it into the blood → proportional hyperosmia fluid reabsorption in the renal tubules

→ normalization of (temporary) osmotic homeostasis → volume expansion in the non-cellular fluid + increase in cardiac output → increase in blood pressure. Simultaneously realized and extrarenal effect aldosterone: hyperproduction aldosterone → enhancing transport across the cell membrane

(including muscle vascular cells and heart) sodium → accumulation of excess sodium in the cells of tissues and organs, combined with a decrease in its concentration of potassium and increase in the latter in the extracellular → cell swelling liquid + including vessel walls + luminal narrowing + tonicity enhancing their increased sensitivity to blood vessels and heart action effect hypertensive agents (catecholamines, vasopressin, aT-II, prostaglandins and others.) → raising blood pressure.

"Glucocorticoid" AH - a consequence of the overproduction of glucocorticoids (cortisone, hydrocortisone), combined, as a rule, with an increase in the blood level of aldosterone.

The cause of hypersecretion of corticosteroids are most often hyperplasia or a hormone-active tumors of the adrenal cortex - corticosteroma. Various forms of hypercortisolism caused by a primary lesion of the beam zone of the adrenal cortex, producing mainly glucocorticoids are known as Cushing syndrome - Cushing. It is shown that in the adrenal cortex (after disposal in patients with Cushing syndrome - Cushing) 62 - 85% of the corticosteroid is hydrocortisone, 5 - 12% - cortisone, 4 - 12% and corticosterone gidrooksiandrostendiol. Often the development of hypertension is the result of long-term administration to patients large doses of glucocorticoids (such as homograft after transplantation in the treatment of diffuse lesions of connective tissue immunoallergic genesis: systemic lupus erythematosus, scleroderma, etc.).

Mechanism of development of hypertension in syndrome Cushing two effects associated with glucocorticoids: 1) may themselves have a direct glucocorticoid hypertensive effect (without changing the level of sodium in the blood and the cells of organs and tissues). Furthermore, in high concentrations in plasma glucocorticoids observed increased sensitivity to vascular vasoconstrictor action of catecholamines; angiotensinogen increase in production in the liver; activation of the synthesis of pressor amines - serotonin; 2) possess mineralocorticoid glucocorticoids (such as aldosterone like) effects. In addition, excess corticosteroma usually produce not only glucose but also mineralocorticoids. Thus, the development of hypertension in Cushing syndrome - Cushing is the result of hypertensive actions as glucose, and mineralocorticoid.

"Catecholamine" adrenal AH develops due to a significant increase in chronic blood levels of catecholamines - adrenaline and noradrenaline are produced in the adrenal medulla. The latter is the equivalent of a nerve ganglion of the sympathetic nervous system. However, there is between them and contrast if in sympathetic neurons catecholamine biosynthesis stage is preferably up to noradrenaline in the adrenal medulla, but some cells produce norepinephrine. In other cells containing methyltransferase enzyme, the conversion is carried out in norepinephrine epinephrine.

Cause significant and persistent increase in blood catecholamine level, as a rule, is a tumor of the adrenal medulla - pheochromocytoma.

The mechanism of action of an excess of hypertensive catecholamines is dual magnification under their influence the tone of the vessel walls and heart function. Norepinephrine stimulates mainly alpha-adrenergic receptors and to a lesser extent, beta-adrenergic receptors, resulting in increased blood pressure primarily through vasoconstriction effect. Epinephrine acts as alpha - and beta-adrenergic receptors. In this regard, there is not only vasoconstriction, but also significantly increase work of the heart (due to positive chronotropic and inotropic effects) and ejection of blood in their bloodstream. This leads to the development of hypertension. It should be noted, that in itself hypertension due to overproduction of catecholamine pheochromocytoma usually transient. This is

due to the fact that adrenaline and noradrenaline are rapidly destroyed and monoamine oxidase ortometiltransferase. In connection with this increase in blood pressure in pheochromocytoma has an important feature - it is transient, transient in nature (within a few minutes, maximum - hours). However, catecholamines, causing narrowing of the afferent arterioles of the glomeruli of the kidneys and reducing the perfusion pressure in them, activate "the renin - angiotensin - aldosterone - ADH" system. Last potentiates hypertension and may make it stable.

Hypertension in hyperthyroid states. Long-term increase in blood levels of iodine-containing thyroid hormones (thyroxine, triiodothyronine) and (or) increase in tissue sensitivity to them is often accompanied by the development of arterial hypertension.

The cause of hyperthyroid conditions include hyperplasia or tumor of the thyroid, accompanied by an increase in the production and release into the blood of excess hormones it.

At the heart of the development of hypertension in hyperthyroid states is cardiotonic effect of thyroxine and triiodothyronine, shows a significant increase in the release of minutes of the heart. The latter is carried out due to severe tachycardia (due to positive chronotropic effect), often reaching 120 - 160 heart beats per minute, and - an increase in cardiac output (due to the positive inotropic effect of thyroid hormones). Therefore AH is hyperkinetic character with hyperthyroid conditions. Along with high systolic blood pressure is often observed normal or even decreased diastolic pressure, which is due to two factors: a compensatory (in response to increased cardiac output) extension resistance vessels; direct damaging effect of excess thyroid hormones on the vascular wall (and other tissues). It is accompanied by a weakening of the tone and decrease the resistance of resistive vessels.

AH in disorders of the hypothalamic-pituitary system. By increasing the secretion of neurons and supraoptic nuclei of hypothalamus paraventricular ADH (vasopressin) and output it from the posterior pituitary into the bloodstream hypertension develops as a result of a significant increase in the volume of liquid in the bloodstream. This is because under the influence of ADH activation process fluid reabsorption from the primary urine in the kidney distal tubules. In addition to the hypertensive effect of the increased volume of circulating fluid, increased blood pressure under these conditions is due to also increase Cardiac output, in excess flowing to the heart. Last, stretching the myocardium increases (according to the law of Frank - Starling) the strength and speed of his cuts, and as a result the value of the cardiac output. The main mechanism of

hypertensive effect of vasopressin is its vasoconstrictor effect and to a lesser extent - increase circulating blood volume.

Improved product and incretion of adrenocorticotropic hormone (ACTH) of the anterior pituitary cells leads to the development of a complex of symptoms, one component of which is hypertension. In general, a symptom called pituitary -Kushinga.

The cause of the disease can be hyperplasia or tumor basophil cells of the anterior pituitary, as well as increased production of corticotropin-releasing factor neurons in the hypothalamus. This is followed by ACTH hypersecretion (unlike Cushing syndrome - Cushing's is caused by overproduction of corticosteroids in hyperplasia or tumor lesion of the adrenal cortex).

The development of hypertension in conditions of increase in the blood level of ACTH is mainly the result of overproduction of adrenal cortex glucocorticoid and mineralocorticoid.

Antigens can develop in some other endocrinopathy, particularly in hormonally-active tumors of argentophile intestinal cells - Kulchytskyy cell (in connection with the production of excess pressor amine - serotonin) or pancreatic injury (apparently due to the formation under the influence her hormones - glucagon muscle arterioles in myocardium increased amount of cyclic AMP, enhances vascular tone and increase in cardiac blood output). However, their share among all hypertension is very small.

Neurogenic arterial hypertension

Neurogenic hypertension can be divided into centrogenic and reflex (reflex).

Centrogenic AH. Cortical and subcortical neurons and nerve centers that regulate blood pressure levels, are complex functional association, consisting of two multi-neural systems: hypertensive and hypotensive. The main structure, regulating the level of systemic blood pressure in the body, is cardiovasomotor (vasomotor) center. Its change both efferent influence vascular tone and function of the heart. Significantly, the number of "pressor" cardiovasomotor central neurons in approximately 4-fold more than "depressant". In the evolution of the relative predominance received regulatory mechanisms, mobilizing the physiological systems of the body, including the cardiovascular. On the whole, we have created an environment of relative dominance hypertensive mechanisms.

The causes of hypertension Centrogenic origin (including - hypertensive disease) are the most common or functional disorders of higher nervous activity, or organic lesion brain structures that regulate systemic hemodynamics.

The mechanism of hypertension resulting from disorders of higher nervous activity - neurosis

- is schematically represented as follows: the action of the causal factor (often repeated, prolonged stress situations with negative emotional coloring) → stress and often frustrating cortical nervous processes, violation of their balance and mobility → Development neurotic state (neurosis is, apparently, an initial pathogenetic factor AH centrogenic nature, emerging as a result of chronic stress effects) → formation of cortical-subcortical complex excitation (a dominant excitation) with the involvement of his sympathetic posterior hypothalamic nuclei adrenergic structures of the reticular formation, cardiovasomotor center → strengthening effects of the sympathetic nervous system on organs and tissues, manifested by excess release of epinephrine and norepinephrine → increased tone of arterial vessels + stimulation of the heart and increase blood minute ejection → increase in systolic and diastolic blood pressure. At the same time the excitation of subcortical centers, causes excessive activation of other systems, particularly systems, "the hypothalamus - pituitary gland - the adrenal glands." This is accompanied by an increase in the concentration of blood products and physiologically active substances including hypertensive action: vasopressin, corticosteroids (including mineral and glucocorticoids, catecholamines). The complex of these substances causes (involving mechanisms described above) an increase in the extent and duration of constriction of arterioles and increasing cardiac output, leading to persistent significant increase in blood pressure - hypertension develops. As you can see, the above Centrogenic pathogenesis of hypertension in general very similar to the mechanisms of initial stages of hypertension. Therefore, hypertensive disease at its early stage is a variant of neurogenic (Centrogenic) hypertension. At subsequent stages of GB included other "hypertensive" mechanisms: renal, endocrine, hematic. The

sequence of inclusion and "share" in the development of GB weight of each patient has their own individual characteristics.

Development Centrogenic hypertension often occurs as a result of organic damage of brain structures involved in the regulation of blood pressure levels. Most often this is due to compression of the brain tumor, his injury, hemorrhage, inflammation (encephalitis), shake it. These (and other) factors can directly damage the structures involved in the regulation of blood pressure levels (sympathetic nucleus of the hypothalamus, the reticular formation of the structure, cardiovasomotor center) and (or) their cause ischemia. This (as well as the formation of a neurotic state under stress) activates the sympathetic nervous system and (or) "the hypothalamus - pituitary - adrenal" system, causing eventually increase in vascular tone and heart function with the formation of resistant hypertension.

Reflex AH. Reflex (reflex) AH are divided into two groups: the conditioned reflex and unconditioned.

Conditioned reflex hypertension develops during the second combined action of indifferent ("conventional") agents irritants that cause hypertension. After a certain number of combinations already recorded an increase in blood pressure only when exposed to indifferent. After some time, can develop a persistent increase in blood pressure. So, prof. N.I. Graschenkova described the case of hypertension in people taking to the lectures and reports of caffeine ("for psychological doping"). After a while he recorded an increase in blood pressure of 180 and 115 mm Hg at the thought of the upcoming lecture. Several years later, this man developed hypertension. In the experiment, the conditioned reflex hypertension also develop after repeated combinations of "conventional" effects (light, objects, sound) in combination with a pain stimulus, excessive physical activity, introduction of substances with a hypertensive effect.

Unconditioned reflex AH can be divided into two groups: 1) AH, developing as a result of chronic irritation extero- and interoceptors or nerve trunks (it is frequently observed in patients with painful duration of the current, causal, syndromes, such as injury or inflammation of the trigeminal, facial, and other sciatic nerves); 2) AH, formed as a result of the termination of afferent impulses, is in normal braking ("chilling", "depressor") effect on the tonic activity cardiovasomotor (pressor) center.

Normally, even small fluctuations in blood pressure cause an increase (if increase) or decrease (with a decrease in blood pressure) of the impulses. Receptors "containment", reacting to their stretching, are located in different regions of the vascular system, but most of them in the area of the aortic arch (from the zone moves "depressor" nerve Ludwig-Zion), and the ramifications of the carotid arteries - the carotid sinus (hence moves "depressor "Hering nerve). Long-term reduction or cessation of "depressant" impulses from these and other areas, "releasing" cardiovascular vasomotor center of constraints and influences may lead to the development of hypertension. Most often this is due to: 1) the destruction of the aortic arch baroreceptors and (or) of the carotid sinus (resulting in toxicity, trauma, infections); 2) reduction of distensibility of the aorta or carotid artery walls (baroreceptors in functional safety) by atherosclerotic changes in them, calcification, etc .; 3) violation of the afferent impulses depressant resulting from damage to nerve trunks (tumor, trauma,

inflammation); 4) adaptation ("addiction") baroreceptors to increased blood pressure for a long time, they begin to perceive as normal.

Arterial hypertension associated with changes in blood condition

Changing the state of the blood [increase its mass and (or) viscosity] may also determine the development of hypertension. So, when Vakeza disease, polycythemia, erythrocytosis, hyperproteinemia and other such states often (in 25 - 50%) recorded a persistent increase in blood pressure. The reasons for this are to increase the mass of circulating blood (which tends to raise its flow to the heart and as a consequence of cardiac output), and - the viscosity of the blood. The latter creates additional resistance to its current vessels. This activates the contractile function of the myocardium, further contributing to the increase in cardiac output that potentiates appears, AG development.

Arterial hypotension

Hypotension, decrease in blood pressure below 100/60 mm Hg in men and 95/60 mm Hg women (limit of normal in good health and full operability).

Types hypotension

There are physiological and pathological arterial hypotension.

Physiological hypotension

- Individual version of the rules (so-called normal low blood pressure).
- Hypotension high fitness (sports hypotension).

- Adaptive (compensatory) hypotension (characteristic of the inhabitants of the highlands, the tropics, the Arctic).

Pathological hypotension

1. Acute

- Collapse (acute circulatory failure that occurs as a result of a sharp decrease in heart function, rapid fall of vascular tone and / or reduce the VCB, shows sharp downstroke arterial and venous pressure, cerebral hypoxia and depression of vital body functions).

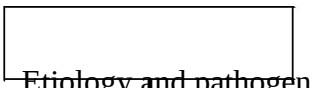
- Continued decline in systolic blood pressure below 90 mm Hg, accompanied by anuria, symptoms of disorders of the peripheral circulation and consciousness, eg in shock.

2. Chronic

Chronic primary arterial hypotension.

- Hypotension neurocirculatory (with reversible unstable current and persistent severe form - hypotension).
- Hypotension orthostatic idiopathic (primary autonomic failure).

Chronic secondary (symptomatic) hypotension with or without orthostatic syndrome him.



Etiology and pathogenesis

On an initial link of the mechanism isolated neurogenic, endocrine and metabolic arterial hypotension.

Neurogenic arterial hypotension

Among neurogenic hypotension isolated centrogenic hypotension and reflex.

Centrogenic arterial hypotension.

Hypotension Centrogenic neurogenic origin or result from the functional disorder higher nervous activity (HNA) or organic brain damage structures involved in blood pressure regulation.

1. Arterial hypotension due to violations of HNA.

The reason: a long, repeated stress caused by the need to keep the motor and emotional manifestations. This will lead to the development of a neurotic state.

Development Mechanism.

- Overvoltage (and failure) of HNA - a neurosis. It is an initial link in the pathogenesis of hypotension.
- Neurosis characterized by the formation of cortical-subcortical complex excitation. It extends to the parasympathetic nucleus of the anterior hypothalamus and other structures of the parasympathetic nervous system (eg, the dorsal motor nucleus of the vagus nerve).

- The activation of parasympathetic effects on the cardiovascular system leads to reduction of myocardial contractile function, cardiac output, blood and tone of resistance vessels. Develops hypotension.

The argument above ideas is a large proportion of people with a weak type of GNI (with a high frequency of their neurotic states) among patients with arterial hypotension.

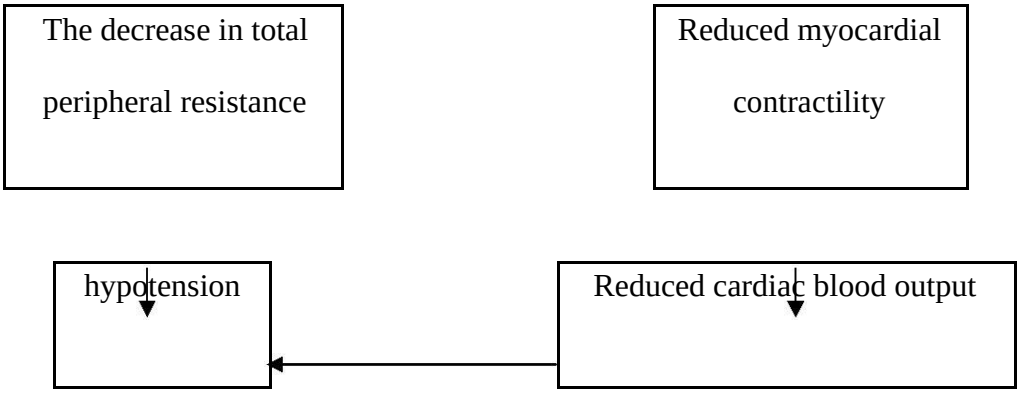
It is believed that this mechanism underlies the development of hypotension. In chronic course of its included and other pathogenetic links, which helps stabilize blood pressure at a reduced level or even aggravates the extent of its loss.

Repeated stress

Activation of neurons:

- Parasympathetic nuclei of the anterior hypothalamus
- Other structures of the parasympathetic nervous system

Increased parasympathetic effects on the cardiovascular system



2. Arterial hypotension due to organic changes in the brain structures. There are at damage of the central (diencephalic-hypothalamic) and peripheral structures, involved in blood pressure regulation.

The most common causes: traumatic brain injury (if concussion or contusion), cerebrovascular accident (ischemia, venous hyperemia), degenerative changes in the brain substance (degeneration of neurons in the extrapyramidal system, basal brain nuclei, posterior nucleus of the vagus nerve), violation of the allocation in blood catecholamines during exercise, change in body position from horizontal to vertical (in this case, often develop orthostatic collapse and syncope), Shy-Drager syndrome.

Pathogenesis.

- Decreased activity of sympathetic-adrenal system and the severity of its effects on the cardiovascular system.
- Relative or absolute predominance of the parasympathetic nervous system effects on the heart and blood vessels.
- Decreased arteriolar tone walls, round, cardiac output of blood.

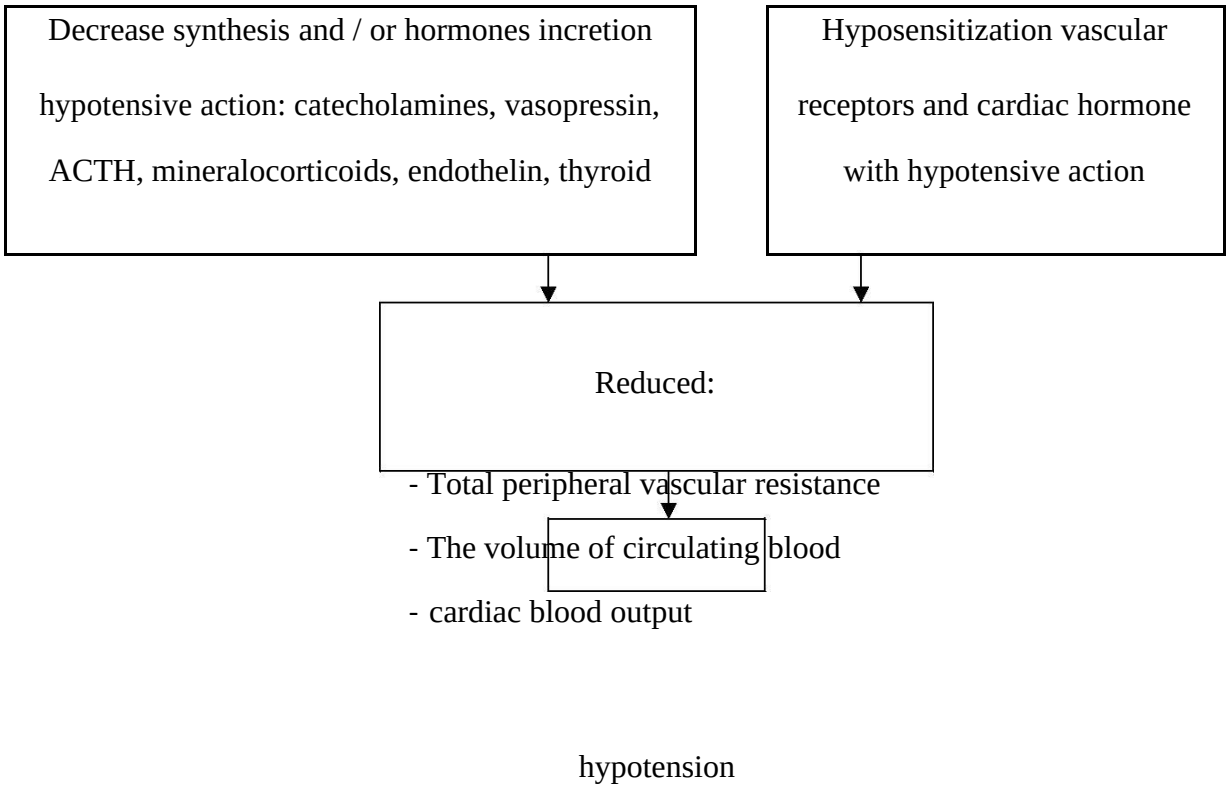
Reflex (reflex, conductor) centrogenic arterial hypotension.

Cause: violation of hypertensive efferent impulses from the vasomotor center of the medulla oblongata to the walls of blood vessels and heart. Most often it develops in neurosyphilis, amyotrophic lateral sclerosis, syringomyelia, peripheral neuropathies of various origins (eg, diabetes, infectious, neurotoxic).

Development Mechanism. It consists in a substantial reduction or termination of the tonic effects of the sympathetic nervous system to the walls of blood vessels and heart. This leads to a decrease in peripheral vascular resistance and consequently - diastolic blood pressure, as well as to a

decrease in contractile function of the heart, cardiac output, and systolic blood pressure. As a result of developing hypotension.

Endocrine arterial hypertension



Distinguish arterial hypotension adrenal, pituitary, hypothyroid genesis.

1. Arterial hypotension adrenal origin.

Causes: wasting adrenal tumor of the adrenal cortex with the destruction of the parenchyma, bleeding in the adrenal gland (one or both), tuberculous lesion of the adrenal glands, the adrenal destruction as a result of the reactions of the immune self-aggression and injury, leading to damage or destruction of the adrenal glands.

Pathogenesis. Deficiency of catecholamines, mineral-and glucocorticoids and / or failure of their effects cause a decrease arteriolar tone walls and round, bcc and cardiac output.

2. Arterial hypotension in the defeat of the pituitary gland. **Causes**: pituitary hypothyroidism.

Pathogenesis. The development of arterial hypotension with pituitary failure is the result of

lack of effect of vasopressin, ACTH, TTH, growth hormone. As a result of pituitary insufficiency leads to a decrease in arteriolar tone and round, bcc, cardiac output. Taken together, these changes cause sustained reduction in both systolic and diastolic blood pressure.

3. Hypotension with hypothyroid conditions.

- Bradycardia. Developed due to the reduction or absence of the positive chronotropic effect of thyroid hormones due to their scarcity, reduce the activity of the sympathetic-adrenal system.

- Decreased cardiac output.

- Reduced tone of the vessel walls due to their degenerative changes and as a result - reduction in systemic vascular resistance.

Metabolic arterial hypotension

Arterial hypotension, metabolic disorders caused by substances with hypo- and hypertensive action, are rare.

Possible reasons.

- Degenerative changes in organs and tissues (eg, chronic intoxications, infections, starvation). This results in reduction of production and / or effects of metabolites from the hypertensive effects (eg, endothelin, PgF, thromboxane A2, angiotensinogen, etc.), Falling tone myocytes walls of arterioles, decreased myocardial contractility.
- Hydropenias body. It causes a decrease in the fluid volume in the body due to a decrease in metabolic rate. The latter, as is known, is accompanied by the formation of water.

Pathogenesis. The basic functioning of pathogenesis are decreased tone smooth muscle cells vessel walls and thereby - TPR falling contractile function of the heart, leading to a decrease in cardiac blood ejection, reducing the water content in the body, including the volume of the circulating fluid. Taken together, these factors lead to sustained reduction in blood pressure below normal - hypotension.

Hypotonic disease.

Hypotonic disease - a condition in which a long, sustained reduction in blood pressure (no apparent reason for this decline) is a leading, and for a long time and the only symptom of the disease.

Hypotonic disease affects people of different ages, more women than men. Blood pressure is usually at the same time <110/70. For a long time a lowering of blood pressure may not be accompanied by any other symptoms, however, is gradually beginning to emerge long headaches (and in contrast to hypertensive disease, which is characterized by pain in the occipital region, with hypotension are usually localized in the fronto-parietal part of the head) , muscle weakness, drowsiness, nausea, decreased ability to work.

In contrast to the pathogenesis of essential hypertension hypotension little studied (perhaps due to the fact that hypotension is not dangerous for life and health consequences and complications). It is believed that patients with hypotension, all systems that support the blood pressure at the required level for the body to function at the lower border of physiological norm. The coincidence of the "

lower of level " functioning of a number of systems of regulation of blood pressure and leads to its persistent decline.

Therapy hypotension has not been developed. Typically, patients in the diet is recommended to increase the salt content, as well as to drink more coffee, to increase locomotor activity, etc.

DISORDER OF CARDIAC RHYTHM

RHYTHMICAL EXCITATON OF THE HEART

The heart is endowed with a specialized electrogenic system for (1) generating rhythmical impulses to cause rhythmical contraction of the heart muscle and (2) conducting these impulses rapidly throughout the heart. When this system functions normally, the atria contract about one sixth of a second ahead of ventricular contraction, which allows filling of the ventricles before they pump the blood through the lungs and peripheral circulation. Another special importance of the system is that it allows a11 portions of the ventricles to contract almost simultaneously, which is essential for most effective pressure generation in the ventricular chambers.

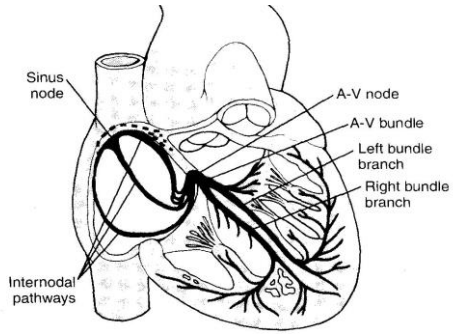


Fig 1. Specialized excitatory and condactive system of the heart

This rhythmical and conductive system of the heart is susceptible to damage by heart disease, especially by ischemia of the heart tissues resulting from poor coronary blood flow. The consequence is often a bizarre heart rhythm or abnormal sequence of contraction of the heart chambers, and the pumping effectiveness of the heart often is affected severely, even to the extent of causing death.

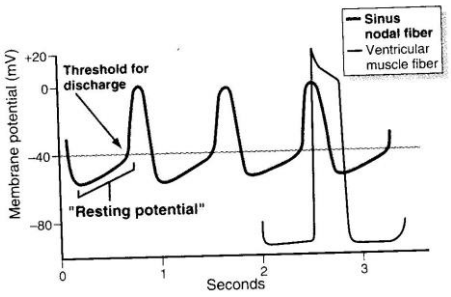
Automatic Electrical Rhythmicity of the sinus Fibers

Some cardiac fibers have the capability of self-excitation, a process that can cause automatic rhythmical discharge and contraction. This is especially true of the fibers of the heart's specialized conducting system. Figure 1 shows the specialized excitatory and conductive system of the heart that controls cardiac contractions. The portion of this system that displays self-excitation to the greatest extent includes the fibers of the sinus node. The impulse normally arises in the sinus node. The sinus node ordinarily controls the rate of beat of the entire heart. These rates are in contrast to the normal rate of the sinus node of 70 to 80 times per minute. Therefore, the sinus node is the normal pacemaker of the heart.

Mechanism of Sinus Nodal Rhythmicity. Figure 2 shows action potentials recorded from inside a sinus nodal fiber for three heart beats and, by comparison, a single ventricular muscle fiber action potential. Note that the so-called resting membrane potential of the sinus nodal fiber between discharges has a maximum negativity of only -55 to -60 millivolts in comparison with -85 to -90 millivolts for the ventricular muscle fiber.

In cardiac muscle, three types of membrane ion channels play important roles in causing the voltage changes of the action potential. They are (1) fast sodium channels, (2) slow calcium-sodium channels, and (3) potassium channels. Opening of the fast sodium channels is responsible for the rapid upstroke spike of the action potential observed in ventricular muscle, because of rapid influx of positive sodium ions to the interior of the fiber. Then the plateau of the ventricular action potential is caused primarily by slower opening of the slow calcium-sodium channels. Finally, increased opening of the potassium channels allows diffusion of large amounts of positive potassium ions outward from the inside of the fiber and returns the membrane potential to its resting level.

Figure 2. The action potentials from inside a sinus nodal fiber for three heart beats and the single ventricular muscle fiber action potential



The ends of the sinus nodal fibers connect directly with the surrounding atrial muscle fibers. Therefore, action potentials originating in the sinus node travel outward into these atrial muscle fibers. In this way, the action potential spreads through the entire atrial muscle mass and, eventually, to the A-V node.

The conductive system is organized so that the cardiac impulse does not travel from the atria into the ventricles too rapidly; this delay allows time for the atria to empty their blood into the ventricles before ventricular contraction begins. It is primarily the A-V node and its adjacent conductive fibers that delay this transmission of the cardiac impulse from the atria into the ventricles. After penetrating the fibrous tissue between the atrial and ventricular muscle, the distal portion of the A-V bundle passes downward in the ventricular septum Then the bundle divides into left and right bundle branches that lie beneath the endocardium on the two respective sides of the ventricular septum. Each branch spreads downward toward the apex of the ventricle, progressively dividing into smaller branches. These branches in turn course around each ventricular chamber and back toward the base of the heart. The ends of the Purkinje fibers penetrate into the muscle mass and finally become continuous with the cardiac muscle fibers.

In abnormal conditions if a rhythmical discharge rate some other part of the heart is more rapid than that of the sinus node they can develop rhythmical excitation. The A-V nodal fibers, when not stimulated from some outside source, discharge at an intrinsic rhythmical rate of 40 to 60 times per minute, and the Purkinje fibers discharge at a rate somewhere between 15 and 40 times per minute. In either of these cases, the pacemaker of the heart shifts from the sinus node to the A-V node or to the excited Purkinje fibers. Under rarer conditions, a point in the atrial or ventricular muscle develops excessive excitability and becomes the pacemaker.

Another cause of shift of the pacemaker is blockage of transmission of the impulses from the sinus node to the other parts of the heart. The new pacemaker then occurs most frequently at the A-V node or in the penetrating portion of the A-V bundle on the way to the ventricles A pacemaker elsewhere than the sinus node is called an ectopic pacemaker.

Control of Heart Rhythmicity and Impulse Conduction by the Cardiac Nerves:

The Sympathetic and Parasympathetic Nerves

The heart is supplied with both sympathetic and parasympathetic nerves. The parasympathetic nerves (the vagi) are distributed mainly to the S-A and A-V nodes, to a lesser extent to the muscle of the two atria, and very little directly to the ventricular muscle. The sympathetic nerves, conversely, are distributed to all parts of the heart, with strong representation to the ventricular muscle as well as to all the other areas.

Effect of Parasympathetic (Vagal) Stimulation to Slow or Even Block. Stimulation of the parasympathetic nerves to the heart (the vagi) causes the hormone acetylcholine to be released at the vagal endings. This hormone has two major effects on the heart. First, it decreases the rate of rhythm of the sinus node and, second, it decreases the excitability of the A-V junctional fibers between the atrial musculature and the A-V node, thereby slowing transmission of the cardiac impulse into the ventricles.

Effect of sympathetic stimulation on Cardiac Rhythn and Conduction. Sympathetic stimulation causes essentially the opposite effects on the heart to those of caused by vagal stimulation, as follows: First, it increases the rate of sinus nodal discharge. Second, it increases the rate of conduction as well as the level of excitability in all portions of the heart. Third, it in creases greatly the force of contraction of all the cardiac musculature, both atrial and ventricular.

CARDIAC ARRHYTHMIAS

Cardiac arrhythmia - a typical form of heart disease, characterized by loss of coordination between different parts of the cuts or infarction of the heart, changes in the frequency and rhythm of heartbeats. Pathogenetic basis of arrhythmias are various changes in the basic electrophysiological properties of the heart: automatism, excitability and conductivity.

In arrhythmias, abnormal electrical conduction or automaticity changes heart rate and rhythm. Arrhythmias vary in severity, from those that are mild, asymptomatic, and require no treatment (such as sinus arrhythmia, in which heart rate increases and decreases with respiration) to catastrophic ventricular fibrillation, which requires immediate resuscitation. Arrhythmias are generally classified according to their origin (ventricular or supraventricular). Their effect on

cardiac output and blood pressure, partially influenced by the site of origin, determines their clinical significance.

Causes:

I. Diseases of the myocardium, its anomalies, congenital or hereditary defects in electrogenic membrane damage or destruction of cellular structures.

II. Disorder of neurogenic, endocrine regulation, changing over electrical processes in specialized or contractile myocardial cells.

III. Disorder of the electrolyte composition of plasma.

Common causes of arrhythmias include: congenital defects, myocardial ischemia or infarction, organic heart disease, drug toxicity, degeneration of the conductive tissue, connective tissue disorders, electrolyte imbalances, cellular hypoxia, hypertrophy of the heart muscle, acid-base imbalances, emotional stress. However, each arrhythmia may have its own specific causes.

Classification of cardiac arrhythmias I. Disorder of formation impulse:

1. Nomotopic arrhythmia (disturbance of sinoatrial node automaticity): - Sinus tachycardia;

- Sinus bradycardia;
- Sinus arrhythmia;

- Sick sinus syndrome

2. Heterotopic arrhythmia (ectopic center of automaticity display):
- The migration of a pacemaker;
- Slow slip systems and rhythms;

- Accelerated ectopic rhythms And:

1. Disorder of the SA-node automaticity;

- Sinus tachycardia;

- Sinus bradycardia;

- Sinus arrhythmia;

- Sick sinus syndrome

- Rigid sinus rhythm;

- Stop (failure) the sinus node.

2. Disorders of excitability; - Extrasystole;
- Paroxysmal tachycardia;
- Atrial flutter;

- Flicker (atrial fibrillation) atrial

- Atrial flutter and atrial (fibrillation) ventricular

II. Impulse conduction disorders; In character:

- Slowing down;
- Blockade;

- Acceleration

For the duration of: -
Temporary (transient)
- Continued

Localization: -
Sinoauricular;

- Intraauricular (intraatrial)
- Atrioventricular

a) in a bundle-branch block or its branches ("longitudinal" slowing down or block).

III. Combination of formation and disorder of the impulse

- atrioventricular
dissociation - parasystole

Pathogenesis

The main types of arrhythmias result from such electrophysiological phenomena as:

- Acceleration or delay self-excitation and transmission the impulse throughout the heart

- Triggered activity

- Phenomenon of Re-entry ("Circus Movements")

Acceleration self-excitation and transmission the impulse In the sinus node, an increase a sodium permeability causes a more positive resting potential, resulting in increased rate of upward drift of the membrane potential to the threshold level for self-excitation, thus accelerating self-excitation and, therefore, increasing the heart rate. In the A-V node, increased sodium permeability makes it easier for the action potential of the conducting fiber, thereby decreasing the conduction time from the atria to the ventricles. The increase in permeability to calcium ions can arise under the influence of sympathetic stimulation.

Delay self-excitation and transmission the impulse

The increasing permeability of the fiber membranes to potassium results in rapid leakage of potassium out of the conductive fibers. This causes increased negativity inside the fibers, an effect called hyperpolarization. The state of hyperpolarization decreases the "resting" membrane potential of the sinus nodal fibers to a level considerably more negative than usual, to -65 to -75 millivolts rather than the norm level of-55 to -60 millivolts. This greatly slow the rate of rhythmicity of these nodal fibers. In the A-V node a state of hyperpolarization decreases transmission of the cardiac impulse into the A-V nodal fibers. The state of hyperpolarization can be caused by vagal stimulation

In abnormal condition triggered activity can arise. Triggered activity is activation ectopic center of the excitation, arising because of premature depolarization membrane under action superthreshold and subthreshold occillations (phenomena at oscillatoiry afterpotentials and afterdepolarizations)

Superthreshold occillations (fig. 3) arise when the potential is in a phase 3 and has not fallen below threshold. Such occillations are capable to cause a new impulse of excitation (early afterdepolarizations) in a cell and development of ectopic rhythm.

Subthreshold occillations (fig. 4) is fluctuations of transmembrane potential in a phase 4. Under certain conditions they can achieve of threshold and cause ectopic impulse. (delayed afterdepolarization)

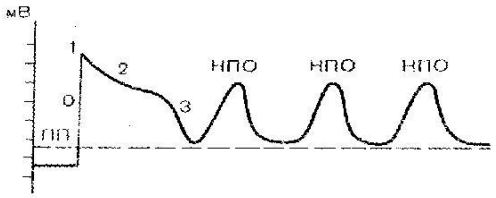


Fig 3 Superthreshold occillations

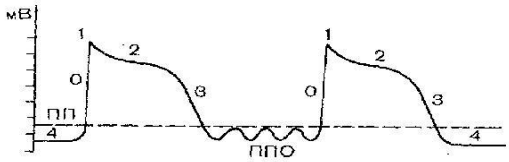


Fig 4 Subthreshold occillations

Phenomenon of Re-entry-"Circus Movements"

When the normal cardiac impulse in the normal heart has traveled through the hart, it then has no place to go because all the hart muscle is at that time refractory and cannot conduct the impulse further. Therefore, that impulse dies, and the heart awaits a new action potential to begin in the sinus node. Under some circumstances, however, this normal sequence of events does not occur. There are three different conditions that can cause this impulse to continue to travel around the circle, that is, to cause "re-entry" of the impulse into muscle that has already been excited. This is

First, if the pathway around the circle is long, by the time the impulse returns, the originally stimulated muscle will no longer be refractory and the impulse will continue around the circle again and again.

Second, if the length of the pathway remains constant but the velocitv of conduction becomes decreased enough, an increased interval of time will elapse before the impulse returns. By this time, the originally stimulated muscle might be out of the refractory state and the impulse can continue around the circle again and again.

Third, the refractory period of the muscle might become greatly shortened. In this case, the impulse could also continue around and around the circle.

All of these conditions occur in different pathological states of the human heart as follows (1)

A long pathway typically occurs in dilated hearts. (2) Decreased rate of conduction frequently results from blockage of the Purkinje system, ischemia of the muscle, high blood potassium levels, or many other factors. (3) A shortened refractory period commonly occurs in response to various drugs, such as epiaephrine, or after repetitive electrical stimulation. Thus, in many cardiac disturbances, re-entry can cause abnormal patterns of cardiac contraction or abnormal cardiac rhythms that ignore the pace-setting effects of the sinus node.

There are two types of re-entry:

-"Ordered" re-entry, or macrore-entry (circulation of impulse over a closed loop of large diameter);

- Microre-entry (circulation of impulse over random, short pathways).

Signs and symptoms of arrhythmias result from reduced cardiac output and altered perfusion to the organs, and may include: dyspnea, hypotension, dizziness, syncope, and weakness, chest pain, cool, clammy skin, altered level of consciousness, reduced urinary output.

Complications Possible complications of arrhythmias include: sudden cardiac death, myocardial infarction, heart failure, thromboembolism.

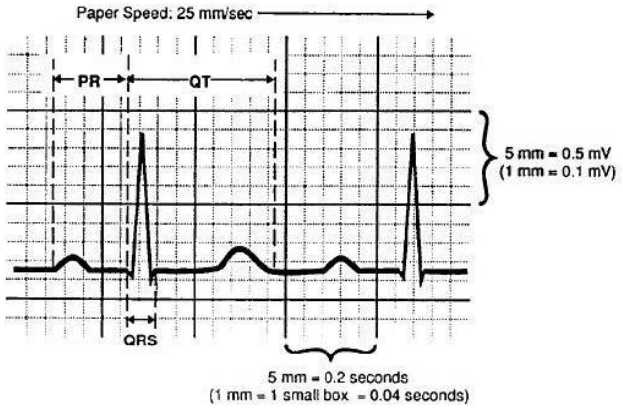
Diagnosis Electrocardiography detects arrhythmias as well as ischemia and infarction that may result in arrhythmias. Electrophysiologic testing identifies the mechanism of an arrhythmia and the location of accessory pathways; it also assesses the effectiveness of antiarrhythmic drugs.

Laboratory testing may reveal electrolyte abnormalities, acid-base abnormalities, or drug toxicities that may cause arrhythmias.

Treatment Follow the specific treatment guidelines for each arrhythmia.

Charateristics of the normal electrocardigram

The normal electrocardiogram (Figure 5) is composed of a P wave, a QRS complex, and a T wave. The P wave is caused by electrical potentials generated when the atria depolarize before atrial contraction begins. The QRS complex is caused by potentials generated when the ventricles depolarize before their contraction, that is, as the depolarization wave spreads through the ventricles. Therefore, both the P wave and the components of the QR complex are depolarization waves.



The T wave is caused by potentials generated when the ventricles recover from the state of depolarization. The T wave is known as a repolarization wave.

Characteristics of normal sinus rhythm include: ventricular and atrial rates of 60 to 100 beats/minute, regular and uniform QRS complexes and P waves, PR interval of 0.12 to 0.20 second, QRS duration < 0.12 second.

Some Types of Cardiac Arrhythmias and their Electrocardiographic Interpretation

The causes of the cardiac arrhythmias are usually one or a combination of the following abnormalities in the rhythmicity-conduction system of the heart:

1. Abnormal rhythmicity of the pacemaker
2. Shift of the pacemaker from the sinus node to another place in the heart
3. Blocks at different points in the spread of the impulse through the heart
4. Abnormal pathways of impulse transmission through the heart
5. Spontaneous generation of spurious impulses in almost any part of the heart.

I. Disorder of formation impulse:

At abnormal sinus rhythms the impulses are generated in the Sinus Node and they are called nomotopic.

Sinus tachycardia

Sinus tachycardia (ST) - the increase in heart rate to 100 per minute or more, while maintaining normal sinus rhythm. ST is due to increased automaticity CA site. ST may by is:

1. Physiological

Physiological sinus tachycardia is a normal response of the cardiovascular system:

- Physical activity,
- Psycho-emotional excitation,
- The use of coffee, etc.

In these cases, sinus tachycardia is temporary in nature and are usually not accompanied by unpleasant sensations.

Restoration of normal heart rate occurs shortly after the termination of the factors causing the tachycardia.

2. Pathological

Extracardiac factors

• hyperthyroidism;

• fever;

• acute vascular insufficiency;

• respiratory insufficiency;

• anemia;

• Some versions of neurocirculatory dystonia, accompanied by activation of the CAC;

• Use of certain medications (sympathomimetic, aminophylline, caffeine, corticosteroids, peripheral vasodilators, calcium channel blockers slow, α-blockers, diuretics, chime, etc.).

Some of these drugs (dihydropyridine calcium antagonists group) have no direct effect on the function of the SA-node, causing the so-called reflex tachycardia.

Intracardiac factors.

• chronic heart failure;

• myocardial infarction;

• a severe attack of angina pectoris in patients with coronary artery disease;

• acute myocarditis;

• cardiomyopathy, etc.

Pathogenesis The listening factors can cause the sympathetic nervous system to excite the heart. For instance, when a patient loses blood and passes into a state of shock or semishock, sympathetic reflex stimulation of needed the heart can increase the rate spontaneous diastolic depolarization and the heart rate to 150 to 180 beats. Also, simple weakening of the myocardium

usually increases the heart rate because the weakened heart does not pump blood into the arterial tree to a normal extent, and the elicits sympathetic reflexes to increase the heart rate.

Electrophysiological mechanism of sinus tachycardia.

The leading mechanism electrophysiological ST is to accelerate the spontaneous diastolic depolarization (phase 4 transmembrane potential) cells sinoatrial node, that the following factors:

- Activating effect on the heart of the sympathoadrenal system;

- Reduced impact on the heart of parasympathetic nervous system;

- The direct action of factors of different nature (physical, chemical, biological) into cells sinoatrial node

Main electrocardiographic sign sinus tachycardia:

1. Heart rate exceeds the upper limit age norm in the rest state.

2. Pacemaker - the sinus node.

3. The rhythm is correct, rapid.

4. Shortened intervals R-R, and T-P.

5. Sometimes the tooth can be layered on P-T wave

6. The tendency to rigidity of rhythm

Sinus bradycardia

Bradycardia - a type of disorder of sinus rhythm

By sinus bradycardia understand this change of heart rhythm, which is a decrease in heart rate below 60 beats per minute due to a decrease in sinus node automaticity.

Causes:

1. Physiological sinus bradycardia uncommon in healthy, physically trained especially for people (sportsmen) alone.

- 25% of healthy young men in heart rate from 60 to 50 per minute, during sleep there is a decrease in heart rate by 30% due to physiological fluctuations in a vegetative status.

Sinus bradycardia may also be a manifestation of neurocirculatory dystonia occur when carotid sinus massage, pressure on the eyeballs (Aschner reflex).

2. Pathological sinus bradycardia.

- Increased intracranial pressure (such as meningitis, cerebral contusion, subarachnoid hemorrhage, cerebral edema).
- Some infections (viral hepatitis, influenza, typhoid fever, sepsis).
- Hypercalcemia and severe hyperkalemia.

- Metabolic alkalosis.
- Obstructive jaundice.
- Peptic ulcer and duodenal ulcer.
- Hypothermia.
- Uremia.
- Poisoning by organophosphorous compounds.

- Myocardial infarction, especially the lower location.
- Atherosclerotic or postinfarction cardio.
- Other heart diseases with an organic or functional damage to the CA site, including the sick sinus syndrome.

Pathogenesis

- In healthy people, sinus bradycardia indicates good fitness of the cardiovascular system.
- Noncardiac causes cause toxic effects on the sinus node or the predominance of the activity of the parasympathetic nervous system (vagal effect).
- Intracardiac form of sinus bradycardia occurs when an organic or functional damage to the sinus node. Intracardiac form of sinus bradycardia is often accompanied by other symptoms of sick

The electrophysiological phenomena underlaying sinus bradycardia is decreased rate spontaneous diastolic depolarization

Any circulatory reflex that stimulates the vagus nerve can cause the heard rate to decrease because of the inhibitory effect of acetylcholine on heart function. Perhaps the most striking example of this occurs in patients with the carotid sinus svndronie. In the patients, an arteriosclerotic process in the carotid sinus causes excessive sensitivity of the pressure receptors (baroreceptors) located in the arterial wall. As result, mild external pressure on the neck elicits a strong baroreceptor reflex, causing intense vagal-acetylcholine effeci. on the heart, including extreme bradycardia.

Clinical manifestations of sinus bradycardia

A disturbance of sinus rhythm occurs in a patient without any symptoms.

However, as a rule, the symptoms of bradycardia, heart appear as follows:

- dizziness;
- cold sweat;
- weakness;
- syncope (as a result of oxygen starvation);

• reduced heart rate (less than 40 beats per minute).

Define one or another type of arrhythmia can use the ECG. The electrocardiogram shows a significant decrease in heart rate and increased intervals (PQ or TP).

The electrocardiogram

Regular atrial and ventricular rates decreased the rate spontaneous diastolic depolarization. Rate < 60 beats/minute

Normal P waves preceding each QRS complex.

Sinus Arrhythmia

Sinus arrhythmia is various heart rate. Sinus arrhythmia can result from reflexes that alter the strength of the Sympathetic and Parasympathetic nerve signals to the heart sinus node.

Sinus arrhythmia can result from any one of many circulatory reflexes that alter the strength of the Sympathetic and Parasympathetic nerve signals to the heart sinus node. The respiratory type of the sinus is synchronized with respiration. It results mainly from of signals from the medula respiratory center into the adjacent vasomotor center due the inspiratory and expiratory cycles of respiration. The signals cause alternate increase and decrease in the nomber of impulses transmitted to the heart through the sympathetic and vagus nerves. Heart rate increases during inspiration and slows down during expiration.

The electrocardiogram at sinus arrhythmia is characterized by normal complexes and various intervals between beats (various intervals between QRS complexes)

At sinus disorders of rhythm parameters of hemodynamic usually changes no much.

2. <u>Disorders of excitability;</u>

Disorders of excitability include:

1. Extrasystolic arrhythmia
2. Tachycardia (paroxysmal and no paroxysmal)
3. Atrial flutter and fibrillation
4. Ventriclar flutter and fibrillation

Extrasystolic arrhythmia is disorders of rhythm, when Premature Contractions, that is independent of the normal rhythm, arises.

According the site of arises the Premature Contractions (extrasystoles) may be sinus (in sinus node), atrial (in atrium), supraventricular (in any part above A-V node and in A-V node), atrio-ventricular (in A-V node), ventricular (in any part below A-V node).

trasystole

Extrasystole (ES) is a premature excitation of the heart or any of his department, due to the extraordinary momentum that comes from the atria, AV connection or ventricles.

Classification extrasystole

1. Classification extrasystole localization:
• Sinus arrhythmia.

• Atrial arrhythmias.

• Extrasystole of AB compounds.

• Left ventricular arrhythmia and right ventricular

2. Classification extrasystole at the time of appearance in diastole:

• Early arrhythmias.

• Average arrythmia.

• Late arrhythmia.

3. Classification extrasystole frequency:

• Rare beats - less than 5 to 1 min.

• Average beats - from 6 to 15 in 1 min.

• Frequent extrasystole - 15 in 1 min.
4. Classification extrasystole density

• Single arrythmia.

• Pair beats.

Classification extrasystole by etiology

- extrasystole functional character.
- beats organic.

- beats of toxic origin.

The etiology of functional extrasystole (disregulation) character.

Functional extrasystole occurs as a result of the autonomic response of the human body at one of the following actions:

- Emotional stress.
- Smoking.
- Abuse of coffee.
- Abuse of alcohol.
- In patients with neuro-circulatory dystonia.
- Also, functional beats can be observed in healthy individuals for no apparent reason (the so-called idiopathic premature beats).

Etiology extrasystole organic origin

Beats of organic origin, usually occurs as a result of morphological changes in the cardiac muscle in the form of necrosis, degeneration, or metabolic disorders cardiosclerosis. Can be observed in the following diseases:

- coronary artery disease, acute myocardial infarction.
- Arterial Hypertension.
- Myocarditis.
- Postmyocardial cardiosclerosis.
- Cardiomyopathy.
- Congestive heart failure.
- Pericarditis.
- heart disease (especially with mitral valve prolapse).
- Chronic pulmonary heart.
- Surgical interventions on the heart.
- «The heart of an athlete."

Etiology extrasystole toxic origin.

Beats of toxic origin when the following pathological conditions:

- fever.
- intoxication.
- The impact of anti-arrhythmic drugs (proarrhythmic side effect).

- thyrotoxicosis.

- Reception of aminophylline, inhalation betamimetics.

Pathogenesis extrasystole

Basic mechanisms of arrhythmias:

• Re-entry waves of excitation (re-entry) in the areas of infarction or cardiac conduction system, characterized by varying the speed of impulse conduction and unidirectional block of the development.

• Increased the oscillator (the trigger), the activity of cell membranes of individual sections of the atria, AV connection or ventricles.
• Ectopic impulse from the atria extends down to the conduction system of heart.

• Ectopic impulse arising in the AV-connection extends in two directions: top to bottom on the conduction system of the ventricles and from the bottom up (retrograde) on the atria.

Features of the pathogenesis of ventricular arrhythmia:

- Single monomorphic ventricular arrhythmia may occur as a result of the formation of re-entry waves of excitation (re-entry), and the mechanism post depolarization.
- Repetitive ectopic activity in the form of several consecutive ventricular premature beats are usually caused by a mechanism re-entry.
- The source of ventricular premature beats in most cases the branching bundle of His and Purkinje fibers. This leads to a significant disruption of the spread of excitation wavelength on the right and left ventricles, resulting in a significant increase in the total duration of ventricular extrasystolic complex QRS.
- If ventricular arrhythmia also changes the sequence of repolarization.

Common ECG signs of arrhythmia

- The main electrocardiographic signs of arrhythmia is premature ventricular complex QRST and / or P wave, that is, shortening the interval linkage.
- Interval linkage - the distance from the preceding beats of the next cycle P-QRST basic rhythm to extrasystoles.

Compensatory pause - the distance from the beats to the next cycle of her P-QRST basic rhythm

Different between part-and full compensatory pause:

- Incomplete compensatory pause - a pause that occurs after atrial extrasystoles or extrasystoles of the AB compound, the duration of which slightly more than the usual interval of P-P (R-R) of the basic rhythm. Incomplete compensatory pause include the time required to ectopic impulse reached the CA node, and "discharged" him, as well as the time required to prepare it the next sinus impulse.

- Complete compensatory pause. Complete compensatory pause - a pause that occurs after ventricular extrasystoles, and the distance between the two complexes, sinus P-QRST (preextrasystolic and postextrasistolic) is equal to twice the R-R interval of the basic rhythm.

ECG signs of atrial (supraventricular) arrhythmias

- The beats from the upper atrial P wave is not very different from the norm. With beats from the middle divisions - P wave is deformed, while the lower parts of the arrhythmia-negative.
- Lower atrial extrasystole with aberrant form of the complex QRS, due to the blockade of transient right bundle branch block.
- Extrasystolic QRS complex widened in front of him in lead III is determined by the negative prong of P. compensatory pause is not complete.

ECG signs of ventricular arrhythmia

- The premature appearance of ECG changes of ventricular complex QRS, before which there is no P wave
- Significant expansion (up to 0.12 or more) and the deformation of the QRS complex extrasistolic
- The presence of ventricular arrhythmia after a full compensatory pause

Clinical manifestations of arrhythmia

- When single extrasystoles at the time of occurrence of brain blood flow may be reduced by 40%.
- Multiple extrasystoles leads to a significant decrease in cardiac output.
- If a subsequent extrasystole falls on the compensatory phase of the preceding, it may be ventricular fibrillation of the heart

Premature Atrial Contractions.

The causes. Premature atrial contractions occur frequently in healthy people and indeed are often found in athletes whose hearts are in very healthy condition. Mild toxic conditions resulting from such factors as smoking, lack of sleep, ingestion of too much coffee, alcoholism, and use of various drugs can also initiate such contractions.

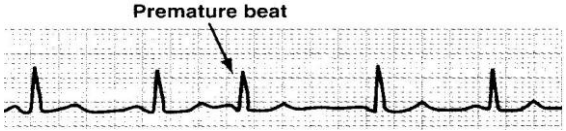


Fig 6

Figure 6 shows the single premature atrial contraction. The P wave of this beat occurs too soon in the heart cycle, and the P-R interval is shortened, indicating that the ectopic origin of the beat is near the A-V node. Also, the interval between the premature contraction and the next succeeding contraction is slightly prolonged, which is called a compensatory pause. One of the reasons for this is that the premature contraction originated in the atrium some distance from the sinus node, and the impulse had to travel through a considerable anount of atrial muscle before it discharged the sinus node. Consequentialy, the sinus node discharged late in the premature cycle and this made the succeeding sinus node discharge also late in appearing.

Pulse Deficit. When the heart contracts ahead of schedule. the ventricles will not have filled with blood normally and the stroke volume output during that contraction is depressed or almost absent Therefore, the pulse wave passing to the peripheral arteries after a premature contraction may be so weak that it cannot be felt in the radial artery. Thus, a deficit in the number of radial pulses occurs when compared with the number of contractions of the heart.

A-V Nodal or A-V Bundle Premature Contractions

In general, A-V nodal premature contractions have the same significance and causes as atrial premature contractions.

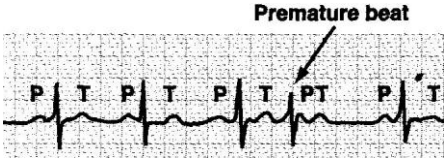
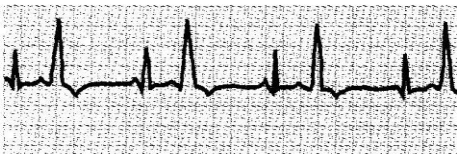


Fig 7

Figure 7 shows a premature contraction that originates in the A-V node or in the A-V bundle. The P wave is missing from the electrocardiographic record of the premature contraction. Instead, the P wave is superimposed onto the QRS-T complex because the cardiac impulse travels backward into the atria at the same time that it travels forward into the ventricles; this P wave distorts the QRS-T complex. but the P wave itself cannot be discerned as such.

Premature Ventricular Contractions

The causes. Some PVCs are relatively benign in their origin and result from factors such as cigarettes, coffee, lack of sleep, various mild toxic states, and even emotional irritability. Conversely, many other PVCs result from stray impulses or re-entrant signals that originate around the borders of infarcted or ischemic areas of the heart. Therefore, the presence of such PVCs is not to be taken lightly. Statistics show that people with significant numbers of PVCs have a much higher than normal chance of developing spontaneous lethal ventricular fibrillation, presumably initiated by one of the PVCs. This is especially true when the PVCs occur during the vulnerable period for causing fibrillation, just at the end of the T wave when the ventricles are coming out of refractoriness.

II  Figure 8

The electrocardiogram of Figure 8 shows a series of Premature ventricular contractions (PVCs) alternatine with normal beats

Premature ventricular contractions (PVCs) demonstrated by the wide and distorted QRS complex premature, usually followed by a compensatory pause, QRS complex, usually > 0.14 second. Premature QRS complexes occurring singly, in pairs, or in threes, alternating with normal beats; focus from one or more sites.

The mechanisms of originating of extrasystoles may be

1. Increase of rate spontaneous diastolic depolarization
2. re-entry
3. trigger activity (superthreshold and subthreshold oscillation)

At rare extrasystoles hemodynamic don't suffer. Frequent extrasystoles can reduce the stroke volume and the cardiac output, a coronary and brain blood flow. There is risk of developing spontaneous lethal ventricular fibrillation, initiated by one of the PVCs (Premature Ventricular Contractions)

Paroxysmal tachycardia

The term "paroxysmal" means that the heart rate becomes rapid in paroxysms, with the paroxysm beginning suddenly and lasting for a few seconds, a few minutes, a few hours, or much longer.

Rapid rhythmical discharge of impulses that spread in all directions throughout the heart can be caused by abnormalities in any portion of the heart, including the atria, the Purkinje system, or the ventricles and tachycardias are difference at site of origin.

<u>Paroxysmal supraventricular tachycardia (PSVT)</u>

Atrial or A-V nodal paroxysmal tachycardia, both of which are called supraventricular tachycardias,

The *causes* of supraventricular tachycardias may be intrinsic abnormality of atrioventricular (AV) conduction system, physical or psychological stress, hypoxia, hypokalemia, cardiomyopathy, congenital heart disease, MI, valvular disease, Wolff-Parkinson-White syndrome, cor pulmonale, hyperthyroidism, and systemic hypertension, digoxin toxicity; use of caffeine, marijuana, or central nervous system stimulant

Paroxysmal supraventricular tachycardia usually occurs in young, otherwise healthy people. Supraventricular tachycardia frightens a person tremendously and may cause weakness during the paroxysms, but only seldom does permanent harm come from the attacks

The electrocardiogram

Atrial and ventricular rates regular

Heart rate > 100 beats/minute; rarely exceeds 250 beats/minute

P waves regular but aberrant; difficult to differentiate from preceding T wave

P wave preceding each QRS complex

Ventricular Paroxysmal Tachycardia

The *causes*. Myocardial ischemia, MI, or aneurysm; coronary artery disease; rheumatic heart disease; mitral valve prolapse; heart failure; cardiomyopathy; ventricular catheters; hypokalemia; hypercalcemia; and pulmonary embolism. Digoxin, procainamide, epinephrine, or quinidine toxicity.

Sometimes digitalis intoxication causes irritable foci the lead to ventricular tachycardia. Conversely, quinidine, which increases the refractory period and threshold for excitation of cardiac muscle, may be used to block irritable foci causing ventricular tachycardia.

Ventricular paroxysmal tachycardia is usually a serious condition for two reasons. First, this type of tachycardia usual does not occur unless considerable ischemic damage is preser in the ventricles. Second, ventricular tachycardia frequenrly initiates the lethal condition of venticular fibrillation becaus of rapid repeated stimulation of the ventricular muscle.

The electrocardiogram

Ventricular rate 140 to 220 beats/minute, regular or irregular

QRS complexes wide, bizarre, and independent of P waves

P waves not discernible

May start and stop suddenly

Pathogenesis of the tachycardia. The paroxysmal supraventricular tachycardia and the ventricular tachycardia may be began with premature contractions This is believed to be caused most frequently by re-entrant circus movement feedback pathways that set up local repeated self-reexcitation. Because of the rapid rhythm in the irritable focus, this focus becomes the pacemaker of the heart

The hemodynamic characteristic. At paroxysmal tachycardia in fist all the stroke volume decrease because of insufficient filling of ventricles during short diastole. At a proceeding attack the minute volume and arterial pressure decreases. This lead to disorders of regional hemodynamics (brain, heard and so on)

Paroxysmal tachycardia often can be stopped by eliciting a vagal reflex. A type of vagal reflex elicited for this purpose is one that occurs when painful pressure is applied to the eyes.

Also, sometimes pressure on the carotid sinuses can elicit enough of a vagal reflex to stop the paroxysm. Various drugs may also be used. Two drugs frequently used are quinidine and lidocaine, both of which depress the normal increase in sodium permeability of the cardiac muscle membrane during generation of the action potential, thereby often blocking the rhythmical discharge of the focal point that is causing the paroxysmal attack.

Ciliary arrhythmia

Ciliary arrhythmia is clinical manifestation of atrial fibrillation or atrial flutter, when ventricular contraction occurs without atrial contraction.

Atrial flutter

Atrial flutter is an atrial dysrhythmia that occurs when the atria begin to contract at a rate of 160 to 400 beats/minute. The ventricles may not be able to keep up.

The causes may be heart failure, tricuspid or mitral valve disease, pulmonary embolism, cor pulmonale, inferior wall MI, and pericarditis, digoxin toxicity

The Pathogenesis Atrial flutter is caused by a circus movement (re-entry) in the atria. The electrical signal travels as a single large wave in one direction around the atrial muscle mass. The signals reach the A-V node too rapidly for all of them to be passed into the ventricles because the refractory period of the A-V node and A-V bundle is too long to pass more than a fraction of the atrial signals. Therefore, there are usually two to three beats of the atria for every single beat of the ventricles.

The electrocardiogram

Atrial rhythm at regular rate; 160 to 400 beats/minute

Ventricular rate variable, depending on degree of atrioventricular (AV) block (usually 60 to 100 beats/minute)

Sawtooth P-wave configuration possible (F waves)

QRS complexes uniform in shape, but often irregular in rate

Atrial flutter leads to *hemodynamic* instability. Atrial flutter causes no effective contraction of the atria. However, because one side of the atria is contracting while the other side is relaxing, the amount of blood pumped by the atria is slight. Ventricular filling does not totally depend on organized atrial contractions; therefore, blood flow in and out of the ventricles is usually sufficient to meet normal energy needs, but not those encountered at high demand times such as during exercise.

Atrial fibrillation

Atrial fibrillation is an atrial dysrhythmia that occurs when the atria beat at more than 400 (up to 600) beats/minute.

The *causes*. Heart failure, chronic obstructive pulmonary disease, thyrotoxicosis, constrictive pericarditis, ischemic heart disease, sepsis, pulmonary embolus, rheumatic heart disease, hypertension, mitral stenosis, atrial irritation, or complication of coronary bypass or valve replacement surgery. Nifedipine and digoxin use

The Pathogenesis Atrial fibrillation is also caused by a circus movement in the atria but in atrial fibrillation many separate and small contractile waves spreading at the same time in different directions over the cardiac muscle. The dilated atrial walls provide ideal conditions

a long conductive pathway as well as slow conduction, both of which predispose to atrial fibrillation. The re-entrant impulses in fibrillation are not simply a single impulse moving in a circle. They have degenerated into a series of multiple wave fronts that have the appearance of a "chain reaction." When the atria are fibrillating, impulses arrive from the atrial muscle at the A-V node rapidly but also irregularly. because the A-V node will not pass all impulses to ventriculars.

The electrocardiogram at atrial fibrillation

Atrial rhythm grossly irregular; rate > 400
beats/minute Ventricular rate grossly irregular

QRS complexes of uniform configuration and
duration PR interval indiscernible

No P waves, or P waves that appear as erratic, irregular, baseline fibrillatory waves

Pumping Characteristics During Atrial Fibrillation. The atria will not pump blood during in atrial fibrillation. Therefore, the atria become useless as primer pumps for the ventricles. Blood flows passively through the atria into the ventricles, and the efficiency of ventricular pumping is decreased only 20 to 30 per cent. Therefore, a person can live for months or even years with atrial fibrillation, although at reduced efficiency of overall heart pumping.

Ventricular fibrillation

At ventricular fibrillation absent any coordinate contraction of the hart. It is most serious of all cardiac arrbythmias, which, if not stopped within 2 to 3 minutes, is almost invariably fatal.

The causes. Myocardial ischemia, MI, untreated ventricular tachycardia, R-on-T phenomenon, hypokalemia, hyperkalemia, hypercalcemia, alkalosis, electric shock, and hypothermia, digoxin, epinephrine, or quinidine toxicity

A person may have a normal heartbeat one moment, but 1 second later the ventricles are in fibrillation. Especially likely to initiate fibrillation are (1) sudden electrical shock of the heart or (2) ischemia of the heart muscle, of its specialized conducting system, or both.

The pathogeneses.The Basis for Ventricular Fibrillation is phenomenon of Re-entry-"Circus Movements**".** Ventricular fibrillation results from cardiac impulses that have gone berserk within the ventricular muscle mass, stimulating first one partion of the ventricular muscle, then another portion, then another, and eventually feeding back onto itself to re-excite

the same ventricular muscle over and over-never stopping. When this happens, many small portions of the ventricular muscle will be contracting at the same time, while equally as many other portions will be relaxing. Thus, there is never a coordinate contraction of all the ventricular muscle at once, which is required for a pumping cycle of the heart.

The electrocardiogram

Ventricular rhythm rapid and chaotic

QRS complexes wide and irregular; no visible P waves

Pumping Characteristics Despite massive movement of stimulatory signals throughout the ventricles, the ventricular chambers neither enlarge nor contract but remain in an indeterminate stage of partial contraction, pumping either no blood or negligible amounts. Therefore, after fibrillation begins, nconsciousness occurs within 4 to 5 seconds for lack of blood flow to the brain, and irretrievable death of tissues begins to occur throughout the body within a few minutes.

In the same manner ventricular fibrillation can be converted back to a normal rhythm by electroshock. The procedure is essentially the conversion-passage of a single strong electric shock through the ventricular which throws the entire heart into refractoriness for a few seconds,

a normal rhythm usually will follow if the heart is capable of this.

Asystole

The causes Myocardial ischemia, MI, aortic valve disease, heart failure, hypoxia, hypokalemia, severe acidosis, electric shock, ventricular arrhythmia, AV block, pulmonary embolism, heart rupture, cardiac tamponade, hyperkalemia, and electromechanical dissociation Cocaine overdose

The electrocardiogram

No atrial or ventricular rate or rhythm

No discernible P waves, QRS complexes, or T waves

Disorder conduction

Normal functioning of the heart depends on:

1) The parasympathetic neurotransmitter acetylcholine, which slows impulse conduction in all divisions of the vascular system and the neurotransmitter norepinephrine, which speeds impulse conduction.
2) myocardial ischemia, which slows impulse conduction in all divisions of the vascular system due to local acidosis.
3) Set to the level of hormones (glucocorticoids) and catecholamines.

4) Increasing concentrations of K + slows the conduction of impulses, and hypokalemia (but with a certain limit!) Speeds.
If you violate the conductivity occur various kinds of heart block, there is slowdown or complete cessation of impulse conduction in the conduction system of heart.

The etiology of heart block

1. Organic heart disease: cardio, myocardial infarction, myocarditis everything, especially rheumatic origin, syphilis, congenital heart defects, injuries of the heart, especially surgical.

2. Changing the tone of the sympathetic and parasympathetic nervous system: neuroses, vagotonia athletes, brain tumors, due to drug therapy:
a) The overdose of cardiac glycosides,

b) an overdose of antiarrhythmics (betaadrenoblokator).

3. Electrolyte disturbances, particularly hyperkalemia: medication, some pathological conditions associated with an increase in potassium in the body.
The separate or combined effect of the above factors may cause various types of closures.

Sinoatrial Block

In rare instances, the impulse from the sinus node is blocked before it enters the atrial muscle, and the lack of atrial excitation and contraction eliminates the atrial P wave. AT the electrocardiogram the cessation of P waves, with resultant standstill of the atrium. However, the ventricles pick up a new rhythm, the mpulse usually originating in the atrioventricular (A-V) node.

Atrioventricular Block

The impulses can pass from the atria into the ventricles through the *A-V bundle*, also known as the *bundle of His*:

Atrioventricular Block may cause an extra long delay between the P wave and the QRS complex, or may totally uncouple the P wave from the QRS. Blocks are described as first degree (each QRS follows a P but with an extended delay), second degree (occasionally, a P wave fails to

cause a QRS complex), or third degree (complete block, in which the link between the P wave and the QRS complex is lost). .

Different conditions that can rither decrease the rate of conduction of the impulse through this bundle or block the impulse entirely are as follows

1. *lschemia of the A-V node or A-V bundle fibers* often delays or blocks conduction from the atria to the ventricles. Coronary insufficiency can cause ischemia of the A-V node and bundle in the same manner that it caп cause ischemia of the myocardium.

2. *Compression of the A-V bundle* by scar tissue or by calcified portions of the heart can depress or block conduction from the atria to the ventricles.
3. *Inflammation of the A-V node or A-V bundle* can depress conductivity between the atria and the ventricles.
4. *Stimulation of the heart by the vagus nerves* in rare instances blocks impulse conduction through the A-V node, Such vagal excitation occasionally results from strong stimulation of the baroreceptors in people with the *carotid sinus syndrome,* discussed earlier in relation to bradycardia.

First-degree AV block

The causes May be seen in healthy persons; Inferior wall MI or ischemia, hypothyroidism, hypokalemia, and hyperkalemia Digoxin toxicity; use of quinidine, procainamide, or propranolol

The electrocardiogram

Atrial and ventricular rates regular
PR interval > 0.20 second

P wave precedes QRS
complex QRS complex normal

The normal lapse of time between *beginning* of the P wave and *beginning* of the QRS complex is about 0.16 second when the heart is beating at a normal rate. This so-called P-R *interval* usually decreases in length with faster heartbeat and increases with slower heartbeat In general, when the P-R interval increases above a value of 0.20 second in a heart beating at normal rate and excitation of the ventricles still elicited by the delayed A-V bundle signal, the P-R interval is said to be prolonged and the patient is said to have *frst degree incomplete heart block.*Thus, first degree block is defined as *a delay* of conduction from the atria to the ventricles but not actual blockage of conduction.

Second Degree Block**.**

When conduction through the A-V junction is slowed until the **P-R** interval rises to 0.25 to 0.45 second, sometimes the action potential traveling through the A-V node is strong enough to pass on through the A-V node and at other times not strong enough. In this instance, it is said that there are "dropped beats" of the ventricles. This condition is called *second degree heart block.* A"2:1 rhythm" develops in the heart, with the atria beating twice for every single beat of the ventricles. Sometimes other rhythms such as 3: 2 or 3: l also develop

Two type of second-degree AV block may be

Second-degree AV block Mobitz I (Wenckebach)

The causes Inferior wall MI, cardiac surgery, acute rheumatic fever, and vagal stimulation, Digoxin toxicity; use of propranolol, quinidine, or procainamide

The electrocardiogram

Atrial rhythm regular

Ventricular rhythm irregular

Atrial rate exceeds ventricular rate

PR interval progressively, but only slightly, longer with each cycle until QRS complex disappears (dropped beat); PR interval shorter after dropped beat

Second-degree AV block Mobitz II

The causes Severe coronary artery disease, anterior wall MI, and acute myocarditis Digoxin toxicity

The electrocardiogram

Atrial rate regular

Ventricular rhythm regular or irregular, with varying degree of
block P-Q interval constant

QRS complexes periodically absent

Third-degree AV block (complete heart block)

A conduction of impulses through the A-V junction is absent.

The causes Inferior or anterior wall MI, congenital abnormality, rheumatic fever, hypoxia, postoperative complication of mitral valve replacement, Lev's disease (fibrosis and calcification that spreads from cardiac structures to the conductive tissue), and Lenugre's disease (conductive tissue fibrosis) Digoxin toxicity

At complete AV block some part of the Purkinje system beyond the block, usually in the distal part of the A-V node beyond the blocked point in the node, or in the A-V bundle, begins discharging rhythmically at a rate of 15 to 40 times per minute and acting as the pacemaker of the ventricles. This is called *ventricular escape.*

The electrocardiogram

Atrial rate regular

Ventricular rate slow and regular

No relation between P waves and QRS complexes

No constant PR interval

QRS interval normal (nodal pacemaker) or wide and bizarre (ventricular pacemaker)

After sudden A-V bundle block, the Purkinje system does not begin to emit its intrinsic rhythmical impulses until 5 to 20 seconds later because, before the blockage, the Purkinje fibers had been "overdriven" by the rapid sinus impulses and, consequently, are in a suppressed state. During these 5 to 20 seconds, the ventricles fail to pump blood, and the person faints after the first 4 to 5 seconds because of lack of blood flow to the brain. This delayed pickup of the heart beat is called Stokes-Adams syndrome. If the delay period is too long, it can lead to death.

III. Combination of formation and disorder of the impulse.

Atrioventricular dissociation

Atrioventricular dissociation is the lack of a consistent excitation and contraction of the atria and ventricles.

Atrioventricular dissociation is complete when atrial impulses are not conducted to the ventricles, and underemployment, when some atrial impulses reach the ventricles, "capture" the ventricles. When dissociation occurs with capture of the correct sequence of excitation and contraction of the heart.

Dissociation has 2 independent sources of automatism: atrial excited from the sinus node or atria, ventricles - of the atrioventricular node or a low center. Thus, the atria and ventricles separately, each at their own pace. This rhythm disturbance caused by the increase of automaticity

of the atrioventricular node. Thus there is blockade for retrograde pulses from the atrial side node, so the impulse for the atrium is not transmitted. Independent, dissociated existence of two rhythms at times replaced by one for the heart rhythm of the sinus node with the correct sequential contraction of the atria and ventricles.

Atrioventricular dissociation is usually not self-pathology, as a consequence of other disorders of rhythm and conduction. It may occur during deceleration or inhibition of the formation of impulses in the sinus node, such as sinus bradycardia, "refusal" of the sinus node, and so on. E., As well as in violation of sinuauricular or atrioventricular conduction and increase the activity of the atrioventricular node.

Dissociation can develop as a result of the processes, inhibits the formation or conduct of sinus impulses, while increasing the activity of automatic centers of the second and third order.

Atrioventricular dissociation is rarely observed in healthy subjects with bradycardia with severe vagotonia. Much more often it occurs in severe lesions infarction: myocardial infarction, myocarditis and other diseases. It can occur when toxic drugs digitalis, quinidine, and others.

Since the effect of changes in the atrial functions on systemic hemodynamics is relatively small, the disorder is often observed circulation are not associated with arrhythmia and a major disease (myocardial infarction, myocarditis and so on. D.).

In patients with atrioventricular dissociation observed different sonority of tone and I periodically auscultated very loud, "cannon" tone (Strazhesko), resulting from the coincidence in time of systole the atria and ventricles. At the same time the difficulty of blood from the atria to the ventricles outflow causes increased pulsation of neck veins.

ECG P wave while positive (sinus) and is followed regardless of the QRS complex. Form QRS is not changed. The rhythm of the atria slower ventricular rhythm. Independent reduce the atria and ventricles are replaced periodically coordinated, correct. They are so-called reductions in the capture, since the momentum of sinus passes through the atrioventricular system and drives (captures) the ventricles. These cuts appear somewhat premature, the interval P - Q constant and higher than 0.12 seconds. Acronyms with the seizure may be single or multiple.

The ECG of the patient with atrioventricular dissociation duration of intervals R - R is equal to 0.84 (frequency of contractions of the atria 71 per minute), the duration of intervals R - R is equal to 0.70 (ventricular rate of 85 per minute). In the cycles of 1.6 is a "capture" ventricular atrial pulses, atrio-ventricular conduction is slowed down (PQ = 0,32 s), in cycles 2 and 7 ventricular capture is uncertain, in the rest - no.

Sometimes dissociation of the atria and ventricles are excited and almost reduced to the same frequency. This is called a complete dissociation isorhythmic.

Treatment of atrioventricular dissociation is determined by the underlying disease (myocarditis, myocardial infarction, and so on. D.). When dissociation induced intoxication drugs, they should be withdrawn and potassium supplements.

Forecast arrhythmia in healthy face vagotonia favorable, the main pathology is determined by organic heart disease prognosis.

Parasystole

Parasystole (Greek para - about at; systole - reduction) is called an arrhythmia in which the heart, in addition to the main sinus rhythm, there is an additional center of automatism. An additional center located heterotopic automaticity brings parasystole with arrythmia. Parasystolic center of automatism often located in one of the legs ramifications atrioventricular bundle, at least - in the atrio-ventricular or atrial compound. This center produces, in most cases 20 - 60 pulses per minute. It is believed that parasystole center consists of a group of cells that have automatism. Unlike sinus node cells, they have a different rate of spontaneous activity. automatism Center protected with a group of cells with an altered perception of excitement. These cells block the pulse input from the sinus node in parasystolic center. This condition is called "entry blockade." Parasystolic individual pulses can not go beyond the limits of the center and not to cause myocardial contraction. This phenomenon is called "blockade exit."

In parasystolic rhythm, unlike arrhythmia, no communication with the main clutch in sinus rhythm. Both excitation chamber running in automatic mode, and each of them causes a reduction in its whole (or part) of the heart. If the pulse is one focus of excitation coincides with the refractory period, it goes without causing excitation and contraction of the myocardium.

Parasystole rarely found in healthy individuals, but more often - in various heart diseases:

myocarditis, myocardial infarction, with heart defects and others.

ECG form parasystolic pulse determined by the place of its origin. If parasystolic focus of excitation is in the ventricle, the shape is the same as that of ventricular extrasystoles, ie legs blockade type atrioventricular bundle; if atrial or atrioventricular connection, - the shape is maintained normal ventricular complex. Sometimes sinus and parasystolic pulses stimulate the heart, almost simultaneously, the ECG obtained "drain" reduction. Such reductions have traits normal and parasystolic rhythms, forming a deformed QRS complex preceded. positive tooth R.

If individual parasystolic impulses are not conducted and formed a long interval between them, it is always a multiple of the number of times (2, 3, and so on. D.) Higher than the lowest parasystolic interval. Parasystole better detected with prolonged ECG monitoring, for example, monitor the observation of the patient. Parasystole responds poorly to anti-arrhythmic therapy.

Disorder of myocardial contractility.

Alternating pulse

Alternating pulse - a form of arrhythmia in which the first broken contractile function of the myocardium, while there is a regular alternation of large and small pulse waves. Pulsus alternans is not a form of arrhythmia, which comes to the fore and has independent significance, like arrhythmia, atrial fibrillation. This form of arrhythmia temporary or permanent, it occurs in coronary atherosclerosis, hypertension during the pronounced heart failure, acute myocarditis, myocardial infarction, acute infectious diseases and intoxications.

As temporary alternating pulse appears during and after an attack of angina pectoris, after extrasystoles, after experimental ligation of the coronary vessels, upon exposure to large doses of digitalis, nicotine, veratrine, barium chloride. The pathogenesis of this form of arrhythmia is not fully set. There are many different theories as to the mechanism of alternating pulse. With high probability we can assume that the alternation of the heart caused by a partial asystole. In such cases, part of the attack is not reduced. By this provision W. Gaskell came on the basis of experimental studies on the frog heart. This position supports the IA Montenegro, who observed in the experiment with alternation partial ventricular asystole.

At the heart of the counter form of the arrhythmia, apparently, it is a heavy defeat of the myocardium in violation of its contractile function. After the systole of the heart during diastole dramatically altered heart muscle does not have time to recover their motility and the second systole is more weak. So begins the alternation of strong and weak systole of the heart, in accordance with this there is an alternation of large and small pulse waves. Recognition of alternating pulse does not cause much difficulty. Most often it is taken for extrasystole arrhythmia (bigemia). However, a careful study of palpation pulse can be detected by bigeminy that the pause between the large and small pulse

wave is considerably smaller than that between the smallest and next largest. Patients with alternating pulse pause between the waves of the same. Physical tension and compression blurred hands cuffed in determining blood pressure clearly identify this form of arrhythmia.

The strength of the tone and intensity of heart murmurs, depending on the strength of cardiac contraction changes. Forecast at alternating pulse is a serious and indicative of severe myocardial damage.

Since this arrhythmia occurs in patients with severe heart, it has the appearance of a very serious prognostic significance.

The paradoxical pulse

Paradoxical pulse - disturbance of a rhythm, which consists of a sharp decrease, and sometimes the disappearance of the pulse wave during inspiration and an increase in the pulse wave

during expiration, is described for the first time when the adhesive pericarditis (Kussmaul, Kissmano, 1973) and was named paradoxical as ironic that when it not observed respiratory arrhythmia.

Distinguish (Wenckebach, 1918), three forms of paradoxical pulse, due to various reasons:

- Extrathoracic;
- Dynamic;
- Mechanical.

Extrathoracic form of paradoxical pulse is due to abnormality of the structure of the chest or in the presence of her tumors and scarring.

Dynamic form created due to inspiratory negative pressure in the chest.

These paradoxical pulse shape not associated with the state of blood flow.

Mechanical form of paradoxical pulse caused by strong seam between the heart and its surrounding organs: lungs, diaphragm and chest. When you inhale lifting of the chest and the lowering of the diaphragm due to spikes dramatically complicate both systole and diastole and cause a decrease in systolic volume and the pulse wave. When you inhale a negative effect on cardiac adhesions activity ceases and the pulse wave begins to gradually increase. The highest waves are observed during breathing pauses.

Paradoxical pulse is also observed in a significant omission of the diaphragm when the heart is hanging, losing pad on which it rests - the diaphragm.

The clinical picture of a paradoxical pulse is determined by the underlying disease, a form of paradoxical pulse and state of circulation. Feeling the radial artery gives an opportunity to establish

the presence of a paradoxical pulse. Sphygmograms, combined with pneumogram, it gives a clear idea about this kind of rhythm disturbance. Dents electrocardiogram at high and low pulse waves differ little from each other.

The diagnosis of paradoxical pulse is usually no difficulty. For a paradoxical pulse can take respiratory arrhythmia.

For the differential diagnosis should be introduced atropine: it stops the respiratory arrhythmia, and does not act on a paradoxical pulse.

Ability to work with paradoxical pulse is dependent on the underlying disease and the form of paradoxical pulse. Extrathoracic form on disability is not reflected. With dynamic and mechanical forms of earning capacity determined by the extent or impact of the affected myocardium powerful pericardial adhesions in the circulation. The treatment is to remove the causes of this rhythm disturbance.

PATHOPHYSIOLOGY DIGESTIVE SYSTEM

Vital activity of the organism is possible with the constant intake of nutritional substances: proteins, fats, carbohydrates and, in addition, water, mineral salts and vitamins. At the same time, water, mineral salts and vitamins are absorbed in an unchanged form, in which they enter the food composition. Proteins, fats and carbohydrates undergo physical and chemical transformations in the gastrointestinal tract, after which the products of their metabolism are absorbed from the digestive tract and enter the blood and lymph. Digestion is the transformation of food products into compounds that lack species specificity, their absorption and participation in interchange.

The functions of the digestive tract include: secretory - the production of enzymes, hydrochloric acid, bile, etc., which provide digestion due to physical and chemical effects and enzymatic food processing; Motor and evacuation - mechanical processing of food due to grinding, mixing and movement along the gastrointestinal tract; Suction - active penetration of the final products of digestion, water, salts, vitamins, minerals through the mucosa of the gastrointestinal tract into the blood and lymph; Excretory (excretory) - first, it is one of the extrarenal ways of excretion of metabolites from the bloodstream to provide homeostasis (for example, uremia urea is excreted through the mucosa of the digestive tract, causing the formation of symptomatic ulcers); second, the excretory function ensures the participation of the digestive system in Interorganic metabolism of nutrients (nutrients are not food, but nutrients, in a day in the norm in the gastrointestinal tract is released up to 80 g of protein and 20 g of fat, which together with exogenous proteins and fat mi digested, absorbed and used by the body); Endocrine - the synthesis of their own hormones (cholecystokinin, secretin, enterogastron, etc.), as well as the function of the digestive tract, which is closely related to the blood system - the synthesis of the internal factor of Castle, with a lack of which develops B12-deficiency anemia.

Insufficiency of digestion - the state of the gastrointestinal tract, which does not provide sufficient assimilation of food coming into the body. As a result, the body develops a negative nitrogen balance, hypoproteinemia, hypovitaminosis, the phenomenon of incomplete starvation, exhaustion of the body, a violation of reactivity. Insufficiency of digestion can develop if the entire

digestive tract or its departments are disrupted. Another IP Pavlov noted the remarkable coherence and regularity in the work of the digestive glands. This interdependence stands out particularly vividly in conditions of pathology, when the disruption of the activity of any part of the digestive tract causes, naturally, the breakdown of the functions of its other departments.

The main causes of digestive disorders

For digestive disorders can lead to:

1) congenital digestive tract;

2) inaccuracies in nutrition (poor quality, rough food, dry eating, unbalanced nutrition with protein deficiency, vitamins, trace elements, intake of excessively hot or cold food, etc.);
3) pathogens of certain infections (typhoid fever, dysentery, food poisoning, etc.);

4) entry into the gastrointestinal tract of poisons (salts of heavy metals, poisons of plant origin, etc.);
5) the effect of ionizing radiation;

6) tumors;

7) postoperative conditions;

8) psychotrauma, negative emotions, physical overstrain;

9) drug addiction, alcoholism, smoking.

Pathology of the gastrointestinal tract can develop as a result of direct or mediated damaging effects of etiological factors.

An example of a direct damaging effect of the etiologic factor may be the development of esophagitis and necrotic changes in the esophagus with the subsequent formation of stricture (cicatrical narrowing) of this organ after taking acetic essence.

The mediated damaging effect of the etiological factors is realized through disorders of the neurohumoral regulation of the digestive organs. At the same time, the damage can initially be

formed either in the nervous system or in some other organ of the gastrointestinal tract. If in the beginning there are disorders in the nervous system under the influence of poisons, chemicals, stressors, etc., it can lead to pathological impulses from the central nervous system to the periphery, which contributes to the disruption of the digestive system, for example, the development of a gastric ulcer after a head injury or contusion . If in the beginning there is damage to any organ of the gastrointestinal tract, this results in abundant afferent impulses from the diseased organ in the central nervous system. In the central nervous system a persistent pathological dominant is formed, pathological response impulse from the central nervous system to the periphery arises, which leads to a disruption of the function of other digestive organs. Disorder of the function of one part of the gastrointestinal tract causes disturbances in other departments by the mechanism of the viscero-visceral reflex. For example, if the stomach ulcer develops reactive pancreatitis or reactive hepatitis.

The main pathogenetic factors of insufficiency of digestion

The main pathogenetic factors in the development of digestive failure include:

1. Disorder of appetite.
2. Disruption of food processing in the oral cavity and its passage through the esophagus.
3. Disturbance of digestion in the stomach.
4. Disturbance of digestion in the intestine.

Disorders of appetite

The sensations of hunger and satiety are determined by the activity of the food center, which represents the functional union of several nerve formations at various levels of the central nervous system. It is a complex hypothalamic-limbic-reticulocortical complex. An important role in this complex is assigned to the hypothalamus. Normally, the process of food intake is regulated by two hypothalamic centers: ventrolateral - "hunger center" and ventromedial - "saturation center", which are in reciprocal relations. Leading department - the center of hunger, from him goes the excitation of the entire food center. There are several theories of the emergence of hunger.

It is considered, in particular, that the excitation of neurons of the center of hunger can arise as a result of a decrease in blood glucose (glucostatic theory) or in the action of metabolites of the Krebs cycle (metabolic). The feeling of hunger also comes with a decrease in the amino acid content (aminoacidostatic theory) and the level of fatty acids and triacylglycerols in the blood (lipostatic), and also with a decrease in body temperature (thermostatic) and as a result of impulse from the mechanoreceptors of the stomach with its "hungry" contractions (local theory) .

Peptide hormones play an important role in regulating food intake, creating hunger and feeling saturated. Strengthening of food motivation and activation of food behavior cause an excess of insulin, pentagastrin, oxytocin, activation of the parasympathetic nervous system. When the saturation center is activated, on the contrary there is a restraining impulse to the center of hunger, and the activity of the latter falls. Excitation of neurons of the saturation center is caused by glucose, leptin, cholecystokinin, pancreatic glucagon, somatostatin, sympathetic nervous system activation, and serotonin. The level of cerebral serotonin especially increases after eating foods rich in carbohydrates and proteins, when the passage through the blood-brain barrier of the precursor of serotonin - the amino acid tryptophan - increases. It is known that many depressions are caused by a decrease in the level of cerebral serotonin, and then hyperphagia develops in depression.

There are the following disorders of appetite: pathological exacerbation - hyperrexia (from Greek hyper - over, excessive, orexis - appetite), pathological decline right up to anorexia (from Greek an - denial) and aversion to food.

Pathological appetite enhancement is often combined with increased food intake - polyphagia (from the Greek poly - a lot, phagein - eat). With a sharp increase in appetite, they speak of bulimia (bus - bull, linos - hunger, a synonym - wolf hunger). In the experiment, hyperrexia is caused by

destruction of the ventromedial nuclei of the hypothalamus or chemical damage by their aurotic glucose (C6HnAuSO5) administered parenterally. Pathological increase in appetite can be observed in a number of diseases of the central nervous system (dementia, neurosis, tumors of the posterior

cranial fossa) and endocrine glands (diabetes mellitus, pancreatic tumors producing insulin, insulomas, thyrotoxicosis).

A pathological decrease in appetite right up to anorexia can be reproduced in an experiment, destroying the ventrolateral nuclei of the hypothalamus. At the same time, the feeling of hunger disappears, and the animals refuse to eat until aphagia - a complete cessation of food intake.

There are the following types of anorexia:

1. Dynamic anorexia. It is one of the symptoms in diseases of the gastrointestinal tract and hepatobiliary system. It can be associated with a violation of the functions of the receptors of the digestive tract, and also have a conditioned reflex character, i.e. Cause pain, discomfort. This kind of dyspepsia can be a symptom of a number of stomach diseases (for example, stomach cancer) and intestines. In the latter case, it must be clearly differentiated from sitophobia, or Emcomfft's disease when the appetite is preserved, but eating can be reduced. Sitophobia develops, for example, in Crohn's disease (regional ileitis), especially in cases of partial intestinal obstruction, or in patients with gastric ulcer after partial or total gastrectomy. Anorexia may also precede jaundice syndrome with hepatitis.

2. Intoxication anorexia. It is noted for a number of intoxication poisonings and due to severe long-term diseases (tumors, infections). It is based on a decrease in the excitability of the food center. It is an important symptom in patients with chronic renal insufficiency, and is noted with intoxications with drugs, in particular cardiac glycosides, hypnotics, narcotic drugs.

3. Neurotic anorexia. The reason for its development are negative emotions, stressful situations, a strong brain stimulation.

4. Neuropsychiatric anorexia. It manifests itself in psychogenic disorders, in particular, with residual-organic lesions of the central nervous system. In these cases, anorexia often accompanies a depression syndrome and can be a manifestation of a consciously severe restriction of food intake with an obsessive idea of excessive completeness.

5. Neurodynamic anorexia. It develops as a result of reciprocal inhibition of the food center during vomiting, pain syndromes (hepatic, renal, intestinal colic, myocardial infarction, etc.).

In some cases, anorexia is difficult to attribute to one of the listed species, it often has a mixed character. For example, severe anorexia in severe chronic heart failure and pulmonary insufficiency is explained not only by the lack of oxygen in the organs of the gastrointestinal tract and the hepatobiliary system, but also by severe metabolic disorders, often the presence of drug intoxication.

Disorders of food processing in the oral cavity and its passage through the esophagus

Impaired chewing

The pathology of digestion can be caused by violations of its initial phase - chewing. Chewing is a mechanical process of grinding food in the mouth, performed by the temporomandibular joints, as well as teeth, the presence of which determines the area of the chewing surface. The most common cause of masturbation is tooth disease - caries and periodontitis. Caries is a bacterial-induced progressive deterioration of the mineral and organic components of the outer enamel and the

underlying dentin and the main cause of tooth loss. The progressing course of caries is complicated by inflammation of the pulp and periodontal disease.

Parodontosis is a serious disease of the oral cavity, in which there are dystrophic changes in the periodontal, which leads to loosening and loss of teeth. The pathogenesis of caries and periodontitis is not completely clear. They play a role of disturbance in metabolism, especially protein, hypovitaminosis, nutrition imbalance, digestive disorders, absorption and other factors.

Disturbance of chewing is associated with a decrease in the number of teeth that experience functional overload. This leads to deformation of the dentition and bite, which further aggravates the chewing disorder. Chewing food is disturbed by anomalies of bite, injuries, gunshot wounds to the lower part of the face, when there are fractures of the jaw bones, dislocations and fractures of the teeth.

The violation of chewing arises in the pathology of the chewing musculature. Its function suffers with infections, innervation disorders, injuries, gunshot wounds. So, with tetanus, meningitis, there is a tonic spasm (trismus) of the chewing musculature. With trigeminal neuritis, there is a sharp pain when chewing (which can cause erroneous removal of healthy teeth), in a number of cases, peripheral paralysis of the masticatory muscles develops.

The chewing process is affected by disturbances in the temporomandibular joints, which occur, for example, in rheumatoid arthritis.

Inflammatory processes in the oral cavity - pulpitis, stomatitis, gingivitis disrupt the process of chewing, are the focus of infection, can cause sensitization of the body and allergic diseases of internal organs.

If there is a violation of the chewing food, there are changes in the activity of the stomach: his motor skills suffer, since poorly chewed food is slower to digest and lasts longer, causing changes in the mucosa. This is facilitated by a decrease in the reflex compartment of gastric and pancreatic juices. Rough, poorly crushed food injures the mucous membrane of the digestive tract, especially the esophagus and stomach, causing damage to the superficial epithelium.

Disturbance of salivation

Saliva secretion is important for the act of swallowing, as well as for wetting and forming a food lump. This is due to the content in the saliva of mucins (glycoproteins of saliva) enveloping the food lump. Saliva, except mucin, contains amylase (ptyalin), involved in the digestion of carbohydrates, lysozyme. Its secretion is also necessary for cleansing the oral cavity, which prevents the accumulation of bacteria. The bicarbonate buffer contained in it maintains a pH value of about 7 in the mouth. Saliva serves as a solvent for nutrients.

The increase in salivation (hypersalivation) occurs as a result of direct or reflex stimulation of the center of salivation in the medulla oblongata or the secretory nerves of the salivary glands. The strongest stimulants of salivation are taste sensations. When hypersalivation in an adult person for a day can stand up to 8-14 liters of saliva, which entails dehydration and loss of bicarbonates and potassium, which are in large quantities found in saliva. Hypersalivation is possible with the defeat

of the central nervous system, inflammatory processes in the oral cavity, diseases of the esophagus (reflux-esophagitis), helminthiases, toxicosis of pregnant women, action of certain drugs (pilocarpine, physostigmine).

Salivation usually decreases at night. The volume of saliva released per day is 1000 ml or more, and about 90% of it is produced by the parotid (secretion of serous secretions with a small amount of organic components) and the submandibular glands (secretion of the mixed secretion - serous and mucous components). The composition of saliva is affected by the rate of its secretion and the action of hormones (estrogens, androgens, glucocorticoids, peptide hormones). When a large amount of saliva is ingested, the gastric juice is neutralized and digestion is disturbed in the stomach. A prolonged loss of saliva causes metabolic disorders, an acid-base balance, an exhaustion of the body. Usually, when hypersalivation of saliva is not completely swallowed. It flows outward, causing maceration and inflammation of the mucous lips and facial skin. It is possible that saliva enters the respiratory tract and infection with microbes in the oral cavity.

Reduction of salivation (hyposalivation) can occur in pathological processes in the tissues of salivary glands (siladenite, tumors). Inflammation of the salivary glands (siladenite) is usually associated with the presence in the duct of one of them salivary stone (sialolithiasis). Salivary stones have a mechanical impediment to the current of saliva and increase the pressure in the salivary ducts. At the same time, the current of saliva is disturbed, pain and swelling of the gland occur during meals; The parenchyma of the gland can atrophy. Hyposalivation noted when the central inhibition of the secretion of the salivary glands, which occurs with stress, pain. It is observed under the influence of a number of medications of anticholinergic action (atropine, metacin, scopolamine), some antidepressants. Salivation decreases with fever, a number of endocrine diseases (thyrotoxicosis, diabetes mellitus), lesions of the nervous system (damage to the base of the brain, spinal cord, etc.), exposure to ionizing radiation (due to radiotherapy of head and

neck tumors), dehydration. When the saliva secretion decreases or stops, xerostomia develops - dryness in the oral cavity. There is a violation of chewing food and swallowing it. Xerostomia is caused by dysfunction of the salivary glands and can be temporary or permanent. Factors that cause temporary xerostomia are emotional stress, certain medications, such as atropine, antihistamines, tricyclic antidepressants and phenothiazines. The development of persistent xerostomia occurs when the oral cavity is irradiated, which is associated with the atrophy of the salivary glands.

Hyposalivation and xerostomia are symptoms of Sjogren's disease - a systemic autoimmune disease, in which the secretion of the glands of the digestive tract, salivary glands is sharply reduced, the dryness of the synovial membranes (pleura, pericardium) is noted.

When hyposalization in the oral cavity - on the tongue and gums formed a plaque from the lowered epithelium, which serves as a nutrient medium for microflora. Normally, 1-10 ml of saliva contains 108-109 bacteria: streptococci, diplococci, spirochaetes, lactobacilli, actinomycetes, fungi of the genus Candida, often the Herpes simplex virus etc. In hyposalivation and xerostomia, the microflora of the oral cavity strengthens its growth and inflammatory processes of the oral cavity, Worsening digestion and serving as a hotbed of infection for possible septic complications.

Disturbance of swallowing

Swallowing is a complex reflex act having three phases: oral (arbitrary), pharyngeal (involuntary fast), and esophageal (involuntary slow).

Dysphagia (violation of swallowing) is defined as a feeling of "getting stuck" or obstructing the passage of food through the mouth, throat or esophagus.

Normal transport of the food lump through the swallowing canal, formed by the pharynx and esophagus, depends on the size of the food lump, the diameter of the lumen of the canal, its peristaltic contraction, the state of the swallowing center.

Dysphagia caused by too large a size of the food lump or narrowing the lumen of the swallowing canal is called mechanical dysphagia. Dysphagia associated with uncoordinated or weak peristaltic contractions of the canal walls, as well as with disturbance of the swallowing center, is called motor dysphagia.

Mechanical dysphagia can be caused by internal or external compression of the lumen of the swallowing canal. The esophagus of a healthy person due to the elasticity of its wall has the ability to stretch up to 4 cm in diameter. If this ability is limited to 2.5 cm, dysphagia is possible, and with restriction to 1.3 cm, dysphagia will always develop. The causes of the development of mechanical dysphagia are numerous. They can be associated, first of all, with a change in the lumen of the canal (with too large a size of a food lump or foreign body entry). Possible internal narrowing of the channel due to the inflammatory process (stomatitis, pharyngitis, epiglottitis, esophagitis), benign strictures (peptic - under the influence of alkalis, acids or drugs, inflammatory - Crohn's disease, candidiasis, ischemic, postoperative, radiation, congenital), malignant Primary cancer, metastases) or benign (angioma, papilloma, polyp) tumors. External compression of the swallowing can be associated with cervical spondylitis, osteophytes of the spine, retropharyngeal abscess, mediastinal abscess, thyroid gland enlargement, aortic aneurysm, mediastinal tumors, pancreas, hematoma (after vagotomy), etc.

Motor dysphagia occurs due to a violation of the initiation of the swallowing reflex, damage to the skeletal muscles of the pharynx and esophagus or smooth muscles of the esophagus. So, many diseases of the central nervous system lead to dysphagia. The most severe disorders of swallowing are noted when the brainstem is damaged, where the nerve structures responsible for the innervation of the pharyngeal part of the passage of the food lump are located. At the same time, there are serious violations of the initial phase of swallowing, often difficult to reverse. In cerebrovascular diseases, aspiration pneumonia, dehydration of the body, loss of mass can become the results of dysphagia. The mechanisms of swallowing are disturbed in such diseases of the central nervous system as poliomyelitis and Parkinson's disease, which are characterized by dysarthria, dysphagia due to weakness of the pharynx and tongue muscles, amyotrophic lateral sclerosis with possible aspiration during or after swallowing. The cause of dysphagia can also be

dystrophy of the muscles of the tongue and pharynx, which is accompanied by nasopharyngeal regurgitation and nasal sound. Possible choke, aspiration of food because of the weakness of the muscles that raise the pharynx. Patients usually switch to slow reception of finely ground food, and with progression of swallowing disorders, feeding is done through the nasal probe. Similar conditions develop, for example, in dermatomyositis with disruption of the functions of the superior esophageal sphincter and the proximal striated musculature of the esophagus. With a number of diseases - tetanus, rabies, hysteria - there is a spasm of the swallowing musculature. With these diseases, phagophobia

can develop - fear of swallowing and therefore rejection of it, which may be due to fear of aspiration. To the refusal of swallowing can lead and painful swallowing, for example, in the inflammatory process. Globus histericus is a sensation of a "coma" in the throat. Some patients feel the passage of food through the esophagus, which may be due to psychosomatic disorders.

Swallowing disorder is noted with botulism, which is caused by a violation of the transfer of impulses from the nerves to the muscles involved in the swallowing act. In swallowing disorders, the swallowing of water is more difficult, since it requires the maximum closure of the holes leading to the nose and the trachea, which is possible with an intensive reduction of the swallowing musculature. The ingestion of water is severely impaired in rabies, which has led to a judgment about "rabies" in this disease.

The reasons for the development of motor (neuromuscular) dysphagia is the damage to the smooth muscles of the esophagus. This is noted with achalasia of the esophagus, a number of collagen diseases, especially with scleroderma and metabolic neuromyopathy associated with alcohol intake, diabetes mellitus.

Disturbance of the motor function of the esophagus

The motor function of the esophagus may be decreased (hypokinesis, or atony) or elevated (hyperkinesis). Atony is reproduced in the experiment by high cutting of n.vagus (IP Pavlov), which causes a decrease in the peristalsis of the esophagus and, in connection with this, a delay in the progression of the food lump. The difficulty of moving food through the esophagus can occur due to its spasmodic contraction. Experimentally, spasm of the cardial part of the esophagus can be obtained by stimulation of the sympathetic nerve.

The main motor disorders affecting the body of the esophagus are observed in achalasia, gastroesophageal reflux disease, diffuse spasm of the esophagus and scleroderma.

With achalasia (lack of normal patency of the cardiac esophagus), coordination of peristalsis is impaired due to loss of inhibitory nervous regulation of the smooth muscles of the esophagus body and lower esophageal sphincter. The latter can not relax sufficiently when swallowed. In this regard, food is delayed in the esophagus, and it stretches (mesophagy). The main causes of achalasia of the esophagus may be a primary neurological disorder with damage to the brainstem, a vagus nerve, degenerative changes in the intramural nerve plexuses: Meissnerian and Auerbachian, as well as smooth muscles of the esophagus. The main mechanism of these disorders is the deficiency of the neurotransmitter necessary for muscle relaxation. Most likely they are a vasoactive intestinal polypeptide (VIP), which is confirmed by a decrease in its level in patients with cardiac achalasia in comparison with healthy patients. Under the influence of VIP, nitric oxide is released from the neurons of the esophagus, which is a vasodilator and simultaneously a relaxant of smooth muscles. It has been established that, with achalasia, the level of nitric oxide in the distal smooth muscles of the esophagus decreases.

Quite early signs of the disease are feelings of filling and squeezing in the chest. With the progression of the disease, the difficulty in swallowing food increases, associated with a feeling of esophagus overflow, it is possible to throw (reflux, regurgitate) food into the mouth, indicating that it is delayed in the enlarged esophagus. These disorders increase with emotional stress and fast food. Delayed food in the esophagus causes aversion to it and leads to a decrease in the patient's weight.

Regurgitation of food increases with eating. Often in the mouth gets undigested food, eaten a few hours ago, it is possible to aspirate food in the respiratory tract (which can cause death or

cause aspiration pneumonia). Clinical manifestations of achalasia, in addition to dysphagia and regurgitation, may be pain in the chest, which is explained by the high contractile activity of the esophagus, as well as the inflammatory process in its mucosa due to stagnation of food. Secondary heartburn occurs, associated not with gastroesophageal reflux, but with enzymatic digestion of food in the esophagus itself and the formation of a large amount of lactic acid.

Another type of pathology - excessive relaxation of the lower esophageal sphincter (gastroesophageal sphincter), which contributes to gastroesophageal reflux. Decrease in pressure in the lower sphincter of the spine or an increase in the number of episodes of its spontaneous relaxation can be associated with a primary defect in the smooth muscles of the sphincter, including a conditioned violation of nervous regulation (with a decrease in the function of the vagus nerve) or a decrease in gastrin production regulating the function of this sphincter. In children of the first year of life, this sphincter is not developed enough, and therefore, after feeding, it is easy to regurgitate food, which increases with overfeeding. Insufficiency of the lower food sphincter, which contributes to gastroesophageal reflux, can be noted in systemic scleroderma, pregnancy, and also in smokers. Often underestimate the effect of a number of drugs that can reduce the tone of smooth muscles, including the lower food sphincter, and delay the emptying of the stomach, thus contributing to the appearance of gastroesophageal reflux. This can be the case with the use of nitrates, M-cholinolytics, tricyclic antidepressants, progesterone, prostaglandins, calcium antagonists, sedatives, euphyllin, β-adrenoblockers, narcotics. Reduces the tone of the sphincter and a number of foods, such as alcohol, chocolate, mint, fried and fatty foods, flour. Some drinks with a low pH increase the symptoms of reflux with esophagitis. Such beverages include Coca-Cola, Pepsi-Cola (pH 2.5), Red Wine (pH 3.25), Orange Juice (pH 3.5).

As a result of casting and prolonged exposure of gastric contents in the esophagus, inflammatory and degenerative changes occur, gastroesophageal reflux disease (reflux esophagitis) develops. In the development of this disease, an important role, in addition to reducing the tone of the lower sphincter of the spine, is the violation of esophageal peristalsis, the mechanisms of cleansing the esophagus from hydrochloric acid (esophageal clearance): chemical purification by reducing the neutralizing effect of saliva, bicarbonates of esophageal mucus; And volumetric purification - because of the inhibition of secondary peristalsis and a decrease in the tone of the wall of the thoracic esophagus. A certain value is attached to the damaging properties of the refluxant (hydrochloric acid, pepsin, bile acids), a decrease in the resistance of the mucosa of the esophagus to acido-peptic damage, an increase in the volume of gastric contents due to hypersecretion, food retention in the stomach, increased intra-abdominal pressure and a predisposition to sphincter failure.

The normal pH value in the esophagus (5.5-7.0) decreases in the case of reflux to below 4.0. Pathological reflux is indicated in the case when the number of episodes per day is more than 50 Thyles when the reflux duration exceeds 5 minutes, and the total duration of the period during which the intraepisitic pH drops below 4.0 is greater than 1 hour per day. When the degree of reflux-esophagitis is expressed, there are merging erosions, covered with exudate or rejecting necrotic masses, which are located in the distal esophagus. Erosive-ulcerative reflux esophagitis is complicated by strictures; Possibly replacing the flat nonkeratinized epithelium of the esophageal

mucosa with a cylindrical epithelium (Barrett's esophagus). The presence of Barrett's esophagus leads to the development of the most formidable complication of reflux esophagitis-adenocarcinoma.

Diffuse spasm of the esophagus, as well as achalasia, is associated with the loss of inhibitory control over the smooth musculature of the esophagus during the normal functioning of the lower sphincter of the sphincter. There are indiscriminate intensive contractions of all parts of the esophagus, which can cause chest pain. These pains resemble angina and are also removed with nitrates, which reduce the tone of the esophagus. As a secondary complication, dysphagia is observed.

The cause of motor dysphagia can be systemic scleroderma with esophageal involvement. This disease refers to collagenosis. Along with the damage to the skin and muscles, internal organs

change. Most often among the digestive organs is affected by the esophagus. There is a progressive replacement of the smooth musculature of the esophagus and the lower food sphincter with a dense fibrous tissue, which leads to a loss of peristalsis of the esophagus and a decrease in the pressure of the lower food sphincter. Dysphagia and acidic gastroesophageal reflux (heartburn, sour belch, regurgitation) occur. Barrett's esophagus is possible.

The violation of the passage of food through the esophagus occurs when it forms diverticula - protrusion of the wall. In the diverticulum, food masses can stagnate and decay. Perhaps the thinning of the wall of the diverticulum followed by rupture, bleeding and infection of the mediastinum.

Hernias of the esophageal opening of the diaphragm - in 10% of cases it is a constant, circular diaphragmatic hernia, more often (in 90% of cases) there is a fickle, sliding hernia that appears in the case of increased peristalsis. The causes of the formation of hernias are: a sharp increase in intra-abdominal pressure with increased physical exertion and an inborn underdevelopment of connective tissue structures. With the development of hernia of the esophageal opening, reflux-esophagitis develops, it is possible to infringe the hernia with the occurrence of esophageal-gastric bleeding.

Hypertrophy of cardia is a hereditary disease characterized by an increase in the mass of the circular muscles of the lower part of the esophagus and a simultaneous increase in their tone. As a result, the speed of food movement slows down, the esophagus stretches, there is a feeling of discomfort and retrosternal pain.

Varicose veins inside the esophageal wall occur with portal hypertension. In the case of a sharp stretching of the esophagus during vomiting, these thin vessels can be ruptured, which in 40% of cases leads to a lethal outcome.

Digestive disorders in the stomach

Disorders of digestion in the stomach are associated with the disorder of its functions:

secretory, reservoir, evacuation, motor, absorption, excretory, etc.

Violation of the secretory function of the stomach

Violation of the secretory function of the stomach includes changes in the amount of gastric juice, acidity, the formation of pepsin and mucus. Hydrochloric acid and pepsin are necessary for chemical processing of food. The main stimulator of the formation of hydrochloric acid is gastrin, produced G-cells of the gastrointestinal tract. Gastrin stimulates the release of HC1 and gastric enzymes, increases the blood circulation of the stomach (it is a trophic hormone), increases the motility of the antral stomach, but inhibits the emptying of the stomach, stimulates the release of insulin. The secretion of gastrin is increased: vagus irritation, protein intake, excess Ca ions, intake of caffeine, ethanol. The secretion of gastrin is reduced: hypersecretion of HC1, the action of somatostatin, secretin, glucagon.

The main stimulants of the secretion of hydrochloric acid in the stomach, in addition to gastrin, are histamine and acetylcholine. In response to n.vagus irritation, the concentration of gastrin produced by the G cells of the antrum of the stomach increases, which leads to an increase in the secretion of hydrochloric acid (a synthetic analogue of gastrin - pentagastrin is used as a stimulant for HC1 secretion). Gastrin and acetylcholine activate specific receptors associated with the calcium / protein kinase C system. After activation of the appropriate mechanisms, hydrogen-potassium (H + / K +) ATPase channels are stimulated, leading to production and release of hydrogen ions.

The stomach emits up to 2 liters of fluid per day. Quantitative changes in the secretion of gastric juice are expressed in an increase (hypersecretion) and a decrease (hyposecretion). This can be combined with changes in the production of hydrochloric acid by parietal cells and pepsinogen - the main cells located in the tubular glands mainly of the bottom and body of the stomach. The production of hydrochloric acid may increase (hyperchlorhydria) or decrease (hypochlorhydria).

Combinations of hypersecretion with hyperchlorhydria and hypoxecretion with hypo - and achlorhydria are possible.

Methods for the study of secretory function of the stomach include the method of fractional gastric sensing and PH-metry. The method of fractional gastric sounding is to obtain gastric juice through a probe injected into the stomach on an empty stomach 12 hours after ingestion. In this case, the following is obtained: a "rush" portion - the contents are sucked from the stomach 5 minutes after the introduction of the probe, "basal" secretion - 4 servings every 15 minutes for one hour, "stimulated secretion" - 4 servings every 15 minutes for one Hours after stimulation by the stimulus. Submaximal stimulation with histamine (0.01%, 0.1 ml / 10 kg of body weight) and maximum stimulation with pentagastrin (6 μg / kg of mass, synthetic preparation of gastrin) or histalkon (2 μg / kg) are used. In each serving of juice determine: volume, acidity (free, associated with proteins and total HC1), debit-HC1 - absolute acid production per hour, the content of pepsin (according to the ability of gastric juice to digest proteins), the stratification factor (by the ratio of liquid and dense Layers).

Normal indices of gastric juice

Indicator	On an empty stomach	Basal secretion	Stimulated secretion
Volume of gastric juice, ml	5-40		

Hourly voltage, ml		50-100	100-140
General HC1, titer. units	20-30	40-50	60-100
Free HO, title. units	0-15	20-40	65-85
The debit hour is HC1, meq / mmol / hr	Not determined	1,5-5,5 55-100	8-14 300-500
Debit hour of pepsin, mg / h	Not determined	10-40	50-90
Stratification coefficient, liquid / thick	Not determined	1:1-1:2	1:1-1:2

It should be noted that the term "free HC1" is conditional (hydrogen ions are bound by protein molecules and bicarbonate ions, so it is possible to separate hydrogen ions into bound and free ions). In this regard, the lack of free hydrochloric acid does not speak of achlorhydria, but only ascertains a decrease in the concentration of hydrogen ions to a pH of 3.5 or lower. To judge the increased or decreased acid-forming function of the stomach follows the definition of the absolute production (production rate) of hydrochloric acid (mmol / h), which takes into account the amount of secretion of gastric juice in milliliters (ml) and the concentration of total hydrochloric acid in millimoles (mmol) in each portion of the gastric Juice in the phases of basal and stimulated secretion.

The violation of acid formation is judged taking into account age, sex (in women acidity is lower by 20%) and the weight of the patient (with increasing mass, acidity increases). Considering the great variability in the parameters of the secretory function of the stomach, it is said to be disturbed only if there are gross deviations from the normal secretion parameters, taking into account the errors in the method for determining this function. The disadvantages of the method include: the need for continuous gastric juice sucking, in vitro research, the determination of mainly only the general HC1. In addition, when evaluating this method, the production rate of hydrochloric acid depends on what and what titrates (there may be impurities of mucus, bile, which has an alkaline pH).

A more accurate method for assessing the acid-forming function of the stomach is the pH-metry - the near-wall pH determination. It is carried out with the help of special instruments with pH probes, which are injected transnazalno (through the nose). It is possible to conduct a 3-hour pH-meter and 24-hour pH monitoring. The advantages of this method include: the ability to conduct pH-metry in each department of the stomach, functional stimulation and depressant tests and select

appropriate drug therapy, determine the true achlorhydria, which is of great importance in the diagnosis of precancerous state with atrophic gastritis.

Digestion in hypersecretion and hyperchlorhydria. When hypersecretion and hyperchlorhydria fasting is observed the presence of acidic gastric juice more than 50 ml with a concentration of hydrochloric acid up to 40 mmol.

Stimulation of the secretory function of the stomach is carried out with the participation of the vagus nerve through gastrin, histamine, glucocorticoids, insulin, thyroxine, etc. In addition, some drugs, acute and hot foods, specific food components such as peptides, amino acids, caffeine, alcohol, calcium, Which stimulate the production of gastrin, can stimulate gastric secretion.

In the reflex phase, the secretion of gastric juice increases from the species, smell and taste of food, which occurs through the influence of vagus. In the gastric phase of secretion there is a mechanical stretching of the stomach by the food, perceived by the stretch receptors in the wall of the stomach, which is realized through the reflex arcs, including the vagus nerve.

Hyperchlorhydria in the stomach is noted in the Zollinger-Ellison syndrome (gastrinoma) caused by a gastrin-forming tumor located in the pancreas (65-75%) or in other organs (stomach, duodenum, liver, testicles, mesentery, lymph nodes, Fatty tissue of the abdominal cavity). Usually it is a multiple tumor. The isolation of gastrin by tumor cells causes persistent gastric hypersecretion, which is associated with the main manifestations of the disease: ulceration, digestive disorders and diarrhea. More than 90% of patients with gastrinomas develop ulcers of the upper gastrointestinal tract. Ulcers are resistant to standard therapy, have a continuously-recurrent course, are prone to severe complications: perforation, penetration and bleeding. Even a surgical operation for complications of ulcers does not stop the recurrence of the disease. In addition to peptic ulcers, the common manifestations of the syndrome Zollinger-Ellison are diarrhea and maldigestia syndrome (violation of the cavity digestion). The pathogenesis of diarrhea in Zollinger-Ellison syndrome is complex and is mainly associated with hypersecretion of gastric juice, reaching several liters per day. In addition, the cause of diarrhea can be inactivation of pancreatic enzymes with gastric acid juice of increased acidity, which leads to steatorrhea and to maldigestia syndrome. Due to a decrease in pH in the small intestine, the mucosa is damaged with the development of malabsorption syndrome (impaired absorption). Perhaps the development of "secretory" diarrhea, as hypergastrinemia increases the secretion of potassium and reduces the absorption of sodium and water in the small intestine.

In addition to the stimulating effect on the secretion of acid, gastrin has a pronounced trophic effect on the tissues of the gastrointestinal tract. It enhances the synthesis of DNA and proteins in the cells of the gastric mucosa and in other tissues. Hypergastrinemia in the syndrome of Zollinger-Ellison causes two synergistic effects: hyperstimulation of parietal cells of the stomach and, as a consequence, a significant increase in the secretion of acid and the number of secreting parietal cells.

The main differential-diagnostic sign of this syndrome is hypergastrinemia. The average level of gastrin in healthy and peptic ulcer patients is less than 150 ng / ml, while the level of gastrin in patients with Zollinger-Ellison syndrome is much higher -> 1000 ng / ml. At the same time, it is necessary to know that hypergastrinemia can be not only primary, contributing to a rise in the level of hydrochloric acid (as is the case with the Zollinger-Ellison syndrome), but also secondary due to hypo- and achlorhydria. The most common cause of hypergastrinemia is atrophy of the underlying gastric mucosa, as hydrochloric acid is the main inhibitor of gastrin release. The absence of hydrochloric acid leads to ineffable secretion of gastrin, hyperplasia of cells of the antrum of the stomach, which often occurs with pernicious anemia. In connection with this, the determination of gastric juice acid plays an important role in the differential diagnosis of the syndrome of hypergastrinemia.

Early detection and removal of the tumor is the basis for the treatment of Zollinger-Ellison syndrome.

When hypersecretion of hydrochloric acid there are conditions for a persistent spasm of the pylorus, since it takes a long time to neutralize the excessively acidic stomach contents in the

duodenum. When the gatekeeper spasms, food is in the stomach for a long time, the stomach is full, there may be heartburn, sour stomach, sometimes vomiting, pain syndrome occurs, and the evacuation function of the stomach decreases. In the intestine comes a more homogeneous food, decreases the peristalsis of the intestine, there is a tendency to constipation, autointoxication.

Digestion with hypoxecretion and hypochlorhydria. Decrease in secretion of gastric juice develops with an increase in the tone of the sympathetic nervous system, the action of glucagon, secretin, cholecystokinin, enterogastron. Secretin, cholecystokinin, enterogastron are referred to as the duodenal inhibitory mechanism of gastric secretion. Somatostatin normally inhibits the release of gastrin and the secretion of hydrochloric acid in the stomach; Reduction of gastric juice secretion also develops with significant structural changes related to the glandular layer of the stomach, a decrease in the number of cells producing gastric juice.

With a decrease in acid formation, pepsin is not active, and proteins are not digested. Patients can complain of belching "rotten", as the bactericidal action of hydrochloric acid decreases, the processes of putrefaction and fermentation intensify. Decreased production of hydrochloric acid leads to excessive colonization of the gastrointestinal tract by bacteria. Evacuation of food chyme from the stomach is usually accelerated, as its neutralization in the duodenum occurs rapidly. Conditions are created for the gaping of the gatekeeper. Quickly entering the duodenum large portions of gastric contents are poorly saturated with duodenal juice. Duodenal digestion suffers from a decrease in gastric secretion and secretion of pancreatic juice, the release of which is stimulated by hydrochloric acid. Food rough chyme, not prepared for absorption, enters the lower parts of the intestine. The peristalsis that causes diarrhea increases, maldigestia syndromes increase (mainly cavitary digestion) and malabsorption (impaired absorption). The early sign of the latter is steatorrhoea (after taking fatty foods). The body weight decreases, hypovitaminosis develops, electrolyte metabolism disorders, dehydration, significant metabolic disorders.

Achlorhydria can be combined with achilia (absence in the gastric juice of pepsin). Allocate a functional and organic Achilles. With functional achilias, the gastric activity and activity of the main cells are preserved, but their function is inhibited. This is a reversible condition, the occurrence of which is possible under stressful situations, avitaminosis (scurvy, pellagra). The unstable character of the Achilles is noted, changing depending on the stimulus of secretion and the conditions of the study. Organic Achilles develops with a pronounced atrophic gastritis. Functional inferiority, and then structural changes in the activity of the main cells develop later than in the lining cells. Organic Achilles is always associated with a severe syndrome of maldigestion and is often combined with pernicious (B12-deficient) anemia.

Violation of the reservoir and evacuation functions of the stomach

Evacuation of food masses from the stomach in the duodenum occurs when the food becomes liquid, and the previous portion of acidic chyme is neutralized by duodenal juice. The pathology of evacuation is expressed in the acceleration or deceleration of evacuation.

Acceleration of evacuation is observed when hyposecretion of gastric juice, achilles, achlorhydria, the intake of hypoosmolar food, as well as food rich in carbohydrates.

Deceleration of evacuation is noted with hypersecretion of gastric juice, ingestion of a large amount of food in the stomach, especially poorly chewed, for grinding it (up to a size of less than 1

mm) takes a long time. When a large volume of food enters the stomach, the large particles of the particles are "sieved" and grinded by reducing the antrum, which in turn worsens the absorption of nutrients. Stretching the stomach with a large amount of food strengthens the peristaltic contraction of the antrum and pushes food to the gatekeeper and duodenum, which can be accompanied by pain. Deceleration of evacuation is also noted when taking hypertensive solutions and hyperosmolar, protein and especially fatty foods, which contributes to the production of enterogastron in the intestinal mucosa, which is referred to as a duodenal braking mechanism (inhibits motility). Slows the emptying of the stomach with overexertion of duodenum and a decrease in the secretion of pancreatic juice and bile, which neutralize the acidic chyme. The reservoir and evacuation functions suffer from surgical interventions on the abdominal organs, stomach, partial resection, gastroenteric

anastomosis, cicatricial changes due to peptic ulcer or after chemical burns. All this prevents the normal passage of food chyme and disrupts the functions of mixing and evacuation.

Evacuation function is reduced after abdominal injuries, with circulatory disorders of the abdominal cavity. In addition, sometimes with acute, especially intestinal infections, reflex inhibition of tonus and peristalsis of the stomach is possible with violation of the evacuation function. This function is worsened in elderly people due to atrophy of the gastric mucosa and, possibly, under the influence of medications, with pyloric stenosis in adults as a result of tumors, scar scarring or congenital pyloric stenosis - hypertrophy of the muscles of the layer of the stomach.

When deceleration of evacuation, there is a delay in the stomach of food masses, liquids, gases. The wall of the stomach is stretched, thinned, its peristalsis and tone are weakened, the secretion of gastric juice decreases. With prolonged delay of food masses, the enlarged stomach exerts pressure on the diaphragm, PDC, nausea, vomiting, which leads to loss of fluid, chlorides. As a result, acid-base balance may be violated towards alkalosis, dehydration, collapse and coma.

Violation of the motor function of the stomach

Normally, the movements of the stomach are expressed in the form of peristalsis - a wave-like contraction of the stomach wall, which promotes food from the cardiac to the pyloric section, and the peristals - the tonic tension of the musculature, which facilitates the crushing of food.

In pathological conditions, the peristalsis of the stomach can be strengthened (hypertonus) or weakened (hypotonic, atony).

The occurrence of abnormalities on the part of the motor activity of the stomach is mainly due to the direct response of smooth muscles to the influence of a number of neurotransmitters and hormones with the participation of receptors. Possible pathology of smooth muscles and pacemaker stomach (for example, with surgical cutting of the vagus nerve). Stem vagotomy leads to an increase in the tone of the proximal parts of the stomach with a simultaneous decrease in the phase activity of its distal sections. From the stomach, the evacuation of the liquid is accelerated and the evacuation of solid chyme is slowed down. When the tone of vagus increases, the rhythm and strength of the

stomach contractions increase, and the evacuation of its contents to the PDC is accelerated. On the contrary, the activation of sympathetic nerves reduces the rhythm, the force of the contractions of the stomach and the speed of the peristaltic wave.

The motor activity of the stomach is influenced by gastrointestinal hormones and hormones of general action. Secretin, cholecystokinin-pancreosimin, enterogastron, glucagon depress gastric motility and the rate of evacuation of food from it. Strengthening motility of the gastrointestinal tract occurs under the influence of gastrin, motilin, histamine, serotonin, insulin.

Oppress gastric motility hypoxecretion of gastric juice (hypo- and achlorhydria), bulbogastron, glucagon, fever, fasting.

Among other causes of gastric motility disorders, a number of drugs, particularly antihypertensive agents, especially calcium antagonists, more long-acting (prolonged), rauwolfia, a-methyldopa derivatives, psychotropic, anticholinergic drugs, nitrates, antispasmodics are often noted.

Violation of the motor activity of the stomach is noted for endocrine diseases (hypothyroidism, hyperparathyroidism, diabetes mellitus), nervous system (meningitis, encephalitis, brain tumor), a number of infectious diseases (Botkin's disease, intestinal infections), metabolic disorders, electrolyte disorders, often with mental illnesses (Neurogenic anorexia, indomitable vomiting). In each of these diseases, the presence of gastric motility disorders can be associated with a complex mechanism involving disorders of nervous, hormonal regulation, electrical rhythm, and smooth muscle functions of the stomach. So, for example, a violation of gastric emptying can develop with a prolonged course of diabetes mellitus, complicated by visceral neuropathy, which manifests itself in a disorder of the vegetative functions of not only the stomach, but also the gallbladder, bladder, and intestine. Gastroparesis in patients with diabetes is most often caused by visceral neuropathy, but the influence of sugar-lowering drugs, psychogenic factors, is not ruled out.

Primary change in the musculature of the stomach may occur with a number of collagenases, in particular with scleroderma and dermatomyositis. Significant violations of the motor activity of the stomach are noted during surgical operations.

Violations of the motor function of the stomach manifest such symptoms as heartburn, eructation, hiccups, nausea and vomiting.

Heartburn (pyrosis) - a sensation of heat or burning in the lower part of the esophagus (can be located behind the breastbone or in the upper part of the epigastric region), spreading from the bottom upwards - from the epigastric region to the neck. Heartburn is usually the result of throwing acidic (pH <4.0) contents of the stomach or bile into the esophagus with an anti-peristaltic wave with an open cardiac sphincter (ie associated with gastroesophageal reflux). At the level of contact with gastric contents there is a spasm of the esophagus, above - its antiperistaltic. The intensity of this manifestation depends on the concentration of acid in the gastric contents, the frequency and duration of its contact with the mucosa of the esophagus. Heartburn is worse after eating, especially abundant, with the torso in the supine position, with abdominal muscle abnormalities. It can be accompanied by a spontaneous appearance in the mouth of a liquid that may be acidic, brackish (stomach contents or "acidic eructation") or bitter, having a yellow or green color (bile).

Heartburn can occur after eating a number of foods: fats, sour fruit juices, tomatoes, garlic, onions, peppers, etc. Or medications that reduce the tone of the lower esophageal sphincter -

theophylline, progesterone, antidepressants, nitrates, calcium antagonists, etc. Heartburn usually decreases when swallowing saliva, drinking water and most clearly when taking antacid preparations.

Erythra (eructatio) - a sudden ingestion in the mouth of a small portion of the contents of the stomach or esophagus. Usually, the stomach contains a small amount of gas (gas bubble), stimulating its motor and secretory functions. A small amount of air is swallowed while eating. From 20 to 60% of the gas in the intestine is due to the amount of swallowed air (the proof of this is the presence of nitrogen and oxygen present in the atmosphere and not produced in the digestive tract). The accumulation of air in the stomach can cause a feeling of overflow, overstretching it after eating, which is proved by radiographic examination of the abdominal cavity. Acute stretching of the stomach with swallowed air often occurs after a plentiful meal and is accompanied by a marked pain syndrome resembling angina. In the supine position, the stomach bladder syndrome can develop when the air in the stomach is trapped (below the junction of the esophagus with the stomach) by the pressure of the liquid above it, so that this air can not be regurgitated.

Aerophagia (ingestion of air outside food intake) is more often observed with neurogenic conditions.

Distinguish eructation by air and burping food. Eating food can be acidic or bitter (an impurity of bile), as well as putrefactive (with food stagnation in the stomach). Resistant burping of food is a characteristic symptom of a deficiency of the cardiac sphincter and a number of diseases of the abdominal cavity organs: peptic ulcer of stomach and duodenum, active gastroduodenitis, gastroesophageal reflux disease, stomach cancer, esophagus. With atrophic gastritis, when the gatekeeper gapes, increased gas formation in the stomach is often associated with gassing in the intestine, with the gas freely entering the stomach. An eructation, especially bitter, often occurs in the pathology of the hepatobiliary system. In addition, eructation can occur reflexively, for example, in diseases of the cardiovascular system.

A portion of the swallowed air passes further through the gatekeeper into the intestines, which causes its swelling. Air may be trapped in the splenic flexure of the large intestine (this is the syndrome of left bend of the colon) when there is a feeling of overflow in the left upper quadrant of the abdomen with possible irradiation into the left half of the thorax. Pain relief often occurs after defecation or secretion of gases from the intestine.

Hiccup (singultus) occurs as a result of a combination of rapid spasm of the diaphragm, convulsive contraction of the stomach and sudden strong inspiration with narrowing of the glottis. Hiccups can be observed in diseases of the gastrointestinal tract and other organs of the abdominal cavity, with more often there is a reflex when the center of the diaphragmatic nerve is excited.

Hiccups are also observed in diseases of the mediastinum, pleura, peritoneum, when the diaphragm or diaphragmatic nerve is directly irritated.

Nausea (nausea) is an unpleasant, painless subjective feeling of an impending desire to perform an emetic act. Nausea often precedes vomiting than accompanies it. However, nausea and vomiting can occur independently of each other. With nausea, various physiological reactions occur. In connection with the close location of the vomiting of the nuclei of the glossopharyngeal and facial

nerves (which innervate the salivary glands), hypersalivation is often observed. With nausea, tachycardia often develops, probably as a result of a stressful reaction to possible vomiting. There is weakness, increased sweating, pale skin, cold extremities, a drop in blood pressure due to excitation of the parasympathetic, and then sympathetic parts of the autonomic nervous system. Possible development of hypotension with bradycardia (vasovagal syndrome). With nausea, the motor activity of the gastrointestinal tract is disrupted and the secretory function of the stomach decreases. The sensation of nausea is associated with anti-peristaltic movements of the stomach. Nausea is often accompanied by anorexia, i.e. A loss of desire to eat or a refusal to eat. Following the continuing for some time nausea and brief periods of urges for vomiting, a sequence of involuntary visceral and somatic motor acts, leading to the occurrence of vomiting, develops.

Vomiting (vomitus) is a complex reflex act, as a result of which the contents of the stomach erupt outward. In the process of vomiting, the stomach plays a relatively passive role. Pushing its contents is provided by the abdominal muscles. With the relaxation of the bottom of the stomach and gastroesophageal sphincter, there is an increase in intra-abdominal pressure due to an involuntary contraction of the diaphragm and the abdominal wall (external oblique muscles of the stomach). This reduction, together with the ongoing contraction of the gatekeeper, leads to the expulsion of the contents of the stomach into the esophagus. Increase in intra-abdominal pressure promotes further movement of the contents along the esophagus into the oral cavity. The reflex rise of the soft palate during vomiting prevents the contents of the stomach from getting into the nasal part of the pharynx, and the reflex closure of the glottis and respiratory depression inhibit the aspiration of the stomach contents into the respiratory tract.

When vomiting, there are violations of the motility of the gastrointestinal tract. The tone of the bottom of the stomach and the peristalsis of the stomach usually decrease, the tone of the DPC and the proximal jejunum increases, and the peristalsis may take the opposite direction (antiperistaltic). In the latter case duodenogastric reflux arises, and this explains the impurity of bile in the vomit from the duodenum. The role of anti-peristalsis in vomiting is well shown in experiments on animals (cats, dogs), which injected substances stimulating vomiting into the cavity of the ventricles of the brain. It has been established that before the act of emesis there is a change in the electrical activity of the intestine with an increase in the electro potential in the proximal direction. Clinically, the anti-peristalsis of the intestine is manifested by the frequent presence of intestinal contents in the vomit. With intestinal obstruction, vomiting with an admixture of feces is possible.

The emetic act is controlled by two functionally different centers located in the medulla oblongata: the vomiting center and the chemoreceptor trigger zone. These centers are located next to other centers of the brain stem that regulate autonomic functions. The afferent path of the emetic reflex follows the sensitive fibers of the vagus nerve into the center of vomiting, which is located in the lower part of the bottom of the IV ventricle, next to the respiratory and cough centers. Centrifugal impulses to the effectors spread along the motor fibers of the vagus nerve, along the diaphragmatic, dorsal and celiac nerves.

The vomiting center controls and unites the vomiting into a single whole. He receives afferent signals from the intestine, from other parts of the body, from the upper cortical centers, especially from the inner ear apparatus and the trigger chemoreceptor zone. Important efferent conductive pathways during vomiting are the diaphragm nerves (to the diaphragm), the spinal cord nerves (to the muscles of the abdominal wall), and the visceral efferent nerves (to the stomach and esophagus).

More often, vomiting occurs when gastric receptors are irritated by poor-quality food, toxic substances, in particular alcohol substitutes, and also with high excitability of these receptors in conditions of pathology. In such cases, vomiting is called gastric. Reflexogenic zones of the

vomiting act are also the posterior wall of the pharynx, the ileocecal region of the gut. It is possible to stimulate the center of vomiting from the peritoneal receptors, bile ducts, gallbladder, kidneys, urinary tract, coronary vessels, membranous inner labyrinth, etc. Vomiting caused by pulses from peripheral reflex zones is called peripheral vomiting.

Vomiting can be of central origin and occur in pathological processes in the region of the IV ventricle (tumor or inflammatory process). The center of vomiting can be irritated by poisons or toxins, with toxicoses of pregnant women, the use of toxic products, drugs, metabolic disorders in renal and hepatic insufficiency, in ketoacidosis, etc. Vomiting can occur by the mechanism of a conditioned reflex - with an unpleasant odor, a form of inedible food. In the laboratory of I.P. In 1914, Pavlov's conditional reflex vomiting was reproduced in a dog with a combination of an indifferent stimulus (sound of a pipe) with injections of apomorphine.

Vomiting can be acute, which is observed during poisoning as a protective reaction aimed at cleansing the gastrointestinal tract from toxins, substances of poor-quality food. Acute vomiting can be associated with an acute process in the abdominal cavity, such as intestinal obstruction, infringement of the hernia, which is also associated with pain syndrome. Acute pain with the phenomenon of vomiting occurs with perforation of the stomach and duodenal ulcers, acute appendicitis. Such a symptom is not always associated with the pathology of the gastrointestinal tract, but it can also be caused by a pathological process in the hepatobiliary system (acute cholecystitis, acute hepatitis, acute pancreatitis, cholelithiasis), cardiovascular pathology (acute myocardial infarction, exfoliating aortic aneurysm), kidneys (nephrolithiasis). Repeated vomiting, more often after a meal, facilitating the patient's condition, is typical for peptic ulcer of the stomach or duodenum during an exacerbation. With stenosis of the gatekeeper, vomiting occurs more often by evening and food, eaten the day before.

Vomiting, especially repeated, leads to a number of metabolic disorders. Most often it is metabolic alkalosis, hypokalemia and hyponatremia. Metabolic alkalosis is a consequence of an increase in the concentration of bicarbonates in the blood plasma, which is due to: 1) a decrease in the concentration of H + in the extracellular fluid; 2) loss of a liquid containing chlorides at higher concentrations than the concentration of bicarbonates in the extracellular fluid; 3) an increase in the concentration of bicarbonates when soda and other substances are converted into bicarbonate in the extracellular fluid.

Hypokalemia develops as a result of loss of potassium with vomiting and its small intake with food. Hyponatremia also develops as a result of excretion of sodium with vomit and, possibly, urine due to metabolic alkalosis.

Violation of the suction function of the stomach

Normally, this function is not large. With pathological conditions of the stomach, it can significantly increase. So, with food stagnation in the stomach, polypeptides can be absorbed through

its wall, which causes intoxication syndrome and allergic organism. Strengthening of this function can be noted in inflammatory-dystrophic processes, in particular in chronic gastritis, when the gastric mucosa becomes permeable to toxins and food digesting products.

Violation of the excretory function of the stomach

The excretory (excretory) function of the stomach is one of the extrarenal ways of excreting metabolites from the bloodstream to provide homeostasis. Into the cavity of the stomach are released metabolic products, as well as substances that have entered the body, the stay of which is unnecessary or harmful. Excretory function of the stomach favors the kidneys, preventing them from excessive stress. The role of this function especially increases with various pathological conditions of the body or with extreme effects on it, which cause pronounced changes in the metabolism. Excretory function of the stomach is closely interrelated with its other functions, which is provided by general regulatory mechanisms.

The stomach wall can be released into its cavity circulating in the blood metabolites (urea, uric acid, creatine, creatinine). I.P. Pavlov stressed the role of gastric excretory function as an

important detoxification factor of the body, as a "physiological measure of protection." So, for example, in chronic renal failure, the content of urea, creatinine in the gastric juice and in saliva increases significantly. With the increase in gastric wall excretion of cellular decay products, the development of gastritic changes in the gastric mucosa is associated with severe infectious diseases and other diseases.

In dogs subjected to overheating, the appearance of lactic acid in the gastric juice. Excretion of a large number of nitrogen-containing substances by the stomach is observed in experimental animals with complete starvation. A similar situation with prolonged hunger occurs in humans. These substances are then absorbed into the intestines and used by the body to feed vital organs. Thus, in patients with prolonged chronic purulent processes, continuous secretion of gastric juice is noted, where the concentration of hydrochloric acid is reduced, and a high content of nitrogenous substances is present. The latter are absorbed into the intestine. However, the absorption process lags behind excretion, and this is one of the factors that contribute to the so-called wound depletion.

Gastric secretion is regulated by cholinergic structures of the autonomic nervous system. Stimulation of α- and β-adrenergic receptors mobilizes the excretory function of the stomach. In the starting phase of gastric digestion, the excretory capacity of the gastric glands is lower than in the completed one, in the mechanism of which the leading role is played by humoral factors. Stimulants of the excretory function of the stomach include corticosteroids, prostaglandins E, hypoxia; The inhibitory effect on it has mineralocorticoids.

The excretory function of the stomach is judged by the speed of appearance in the gastric juice of an intravenously injected solution of neutral red (neutral) powder, which normally appears there in 12-15 minutes. With secretory deficiency of the stomach, especially with atrophy of the mucosa, the release of the paint is significantly delayed (up to 30-45 min), with increased acidity - somewhat accelerated (up to 8-10 min).

Peptic Ulcer

The peptic ulcer is a chronic, cyclically recurring disease in which general and local mechanisms of nervous and humoral regulation of the secretory trophic activity of the gastrohepatopancreatic system are violated and ulcerative mucosal defects in the stomach or in the duodenum are formed, often against the background of active gastritis and duodenitis associated With Helicobacter pylori, prone to the progression and development of complications that threaten the life of the patient.

Ulcer disease occurs in 6-10% of the adult population, more often in men under the age of 50 years. In 60-70% of patients, peptic ulcer is formed in adolescence and young age. In adolescents and young men, duodenal ulcer is more likely to develop, in women and men of older age groups - peptic ulcer. In 1/3 patients with peptic ulcer disease, duodenal ulcer develops further.

Peptic ulcer is an independent disease. Acute (symptomatic) ulcers are always secondary, for example, when treated with steroid hormones, salicylates, butadione, with cirrhosis, acute renal failure, etc.

Etiology and pathogenesis of peptic ulcer

The peptic ulcer is polyethiologic. The main etiological factors of peptic ulcer of the stomach and duodenum are the bacterium Helicobacter pylori and neuropsychic stress.

At present, there is every reason to consider peptic ulcer as an infectious disease, since the link between the development of peptic ulcer and infection of Helicobacter pylori (HP) has been proved. Australian scientists R. Warren and B. Marshall in 2005 received the Nobel Prize for the "unexpected and startling" discovery that they made in 1982: they found that the cause of gastritis and peptic ulcer of the stomach and duodenum is the bacterium - HP. When B. Marshall singled out the pure culture of the bacterium, he conducted an experience of self-infection, and developed a sharp gastritis. As a means of treatment, he used antibiotic therapy. As a result of this discovery, a reasonable opportunity to treat ulcerous disease with antibiotics appeared, which increased the frequency of cure for peptic ulcer and reduced the number of relapses of the disease.

It is established that in patients with peptic ulcer of the duodenum HP is found in 90-95% of cases, in patients with peptic ulcer of the stomach - in 80% of cases. Evaluation of the presence of a bacterium is carried out with the help of a serological blood test, an enzyme immunoassay, a bacteriological study of the mucosal biopsy, a breath test,

Helicobacter pylori is a gram-negative anaerobic rod that has a flagella and is capable of producing urease. This pathogen is found in the mucous membrane of the antral part of the stomach, appearing sometimes in healthy, without any pathological changes, but much more often (up to 95%) in patients with gastritis or peptic ulcer. If you get into the lumen of the stomach with swallowed saliva or from the surface of the gastroscope, the gastric (duodenal) probe HP is in a difficult habitat (acid content of the stomach). However, due to their urease activity, bacteria can exist under these conditions. Urea, coming from the bloodstream, by sweating through the wall of capillaries, urease turns into ammonia and CO2, which neutralizes hydrochloric acid of gastric juice, creating local

alkalinization around the bacterial cell. Ammonia acts irritatingly on the G cells of the APUD system, increasing the secretion of gastrin and, respectively, HC1.

Flagellum and spiral form of bacteria provide active advance, and HP in the environment of urease and ammonia penetrates from the lumen of the stomach into the layer of mucus, where the progress continues. In addition to local alkalization, around the bacteria there is a decrease in the viscosity of the gastric mucus - mucin is destroyed, and HP reaches through the protective mucous barrier of the gastrointestinal epithelium of the gastric mucosa. There is an adhesion of HP on the integumentary-pit epithelium of the antral part of the stomach. A part of the microbes penetrates into its own plate through interepithelial contacts. Dystrophic changes occur in the epithelial cells, which reduces their functional activity. Intensive reproduction and colonization of HP on the antrum mucosa of the stomach lead to damage to the epithelium due to the action of phospholipases. Isolate an ulcirogenous strain of HP, which synthesizes cytotoxins that activate the phospholipase. In this case, the probability of ulceration of the gastric mucosa is very high. There is a destruction of protective protein components, mucin, which opens the way of HP deep into the mucous membrane. Ammonia, affecting the endocrine cells of the antrum of the stomach, reduces the number of D-cells that produce somatostatin, and, accordingly, its concentration decreases. The release of gastrin leaves the control of D-cells, which leads to hypergastrinemia, an increase in the mass of parietal cells and hyperproduction of hydrochloric acid. Thus, infection with HP can be primary, and increased secretion of hydrochloric acid - a secondary link in the pathogenesis of gastric ulcer. In the submucosal layer, an inflammatory infiltrate is formed (consisting of neutrophils, lymphocytes, macrophages, plasma and mast cells), necrosis of the epithelium with the formation of a ulcerative defect.

Pathogenesis of duodenal ulcer is more difficult than stomach ulcers. HP selectively populates only the metaplastic epithelium and does not affect the normal mucosa of the duodenum. Gastric metaplasia (replacement of the cylindrical cells of the epithelium of the duodenum by cells of the gastric epithelium) is observed in 90% of patients with a duodenal ulcer. Metaplasia allows HP to penetrate the cells of the mucosa of the bulb of duodenum, making them less resistant to damage by hydrochloric acid, pepsin, bile. The prolonged casting of acidic gastric contents into the bulb of duodenum creates favorable conditions for the development of gastric metaplasia of its epithelium. The risk of developing duodenal ulcers with pronounced antral gastritis and proximal duodenitis associated with HP exceeds the control duodenal by 50 times, and in normal mucosa it is practically zero.

It is interesting to note that HP infection is high enough - infection in the north of Russia is 50%, in the south and east of Russia it reaches 80 and 90%, respectively. Only 1/8 of people infected with HP develop a peptic ulcer.

However, peptic ulcer is not a classic infection and one infection of HP is not enough for its occurrence.

The main etiological factors of peptic ulcer include neuropsychic stress. Under the influence of prolonged or often recurring psychoemotional overstrain (severe nervous shocks, professional failures and family dramas), the coordinating function of the cerebral cortex with respect to the

subcortical formations and especially the hypothalamus is disrupted. There is a persistent excitation of the centers of the autonomic nervous system. Abundant pathological parasympathetic impulse from the CNS leads to hypersecretion of HC1 and gastric hypermotorics. Abundant pathological sympathetic impulse from the central nervous system leads to the ejection of catecholamines in synapses and adrenal medulla that causes trophic and hemodynamic disturbances in the gastric mucosa. Activation of the hypothalamic-pituitary-adrenal system causes increased production of glucocorticoids, which entails hypersecretion of gastric juice, vasospasm, catabolic effect (increased disintegration and reduced protein synthesis). All of the above causes the formation of ulcerative defects, a decrease in mucus production and a decrease in regeneration.

Predisposing factors of peptic ulcer include genetic markers: high level of production of HC1

- maximum acid production of the stomach (as a result of genetically determined increase in the weight of the cells and their sensitivity to gastrin); High level of pepsinogen 1 in the blood serum - "ulcirogenic fraction of pepsinogen"; Excess gastrin release by G-cells in response to food intake; I blood group (these people have gastric adhesive mucosa with adhesive receptors for Helicobacter pylori); Genetically determined decrease in the production of a number of protective substances (protecting the mucosa from proteolysis), including α1-antitrypsin inhibitor of serine protease, and a2-macroglobulins (account for 97% of the total content of plasma macroglobulins - non-specific protease inhibitors and universal regulators of the immune system).

Factors contributing to the development of the disease are nutritional factors (acute, hot food, spices, seasonings), bad habits (smoking and abuse of strong alcoholic beverages, a role in the development of peptic ulcers take away coffee), ulciogenic drugs. Especially dangerous are long breaks in food intake, especially in individuals with increased secretion and acidity of gastric juice.

All etiological factors potentiate each other and lead to the formation of "aggression" factors. Ultimately, to be or not to be a peptic ulcer is determined by the ratio of the factors of "defense" and the factors of "aggression".

The factors of "aggression" include, first of all, HP infection and destruction of the mucous-bicarbonate barrier, as well as a high acid-peptic factor. The causes of hypersecretion of hydrochloric acid are hyperplasia of parietal cells, apparently, genetically conditioned vagotonia and hyperproduction of gastrin. It is known that the main stimulants of HCL secretion are histamine, gastrin, acetylcholine. In addition, it is known that inadequate production of glucagon and especially somatostatin also contributes to ulcer formation.

Pathogenetic factor in the realization of the disease, along with a high acid-peptic factor, is gastroduodenal dissotorics. If a healthy person has a rhythmic intake of gastric contents in the duodenum -3 contraction in 1 minute, then in patients with peptic ulcer in duodenum 15-minute periods of low pH are noted. High acidity can not maintain normal peristalsis, the "acidification" of the duodenum occurs. Prolonged contact of acidic contents with mucous leads to ulceration. "Oxidation" of duodenum is often associated with dyskinesia and a decrease in its alkalizing function due to a violation of the production of bicarbonates of pancreatic and biliary secret.

A definite value in the development of peptic ulcer is given to duodenogastral reflux (DGR) - casting of bile (bile acids) into the stomach. Bile, affecting the gastric mucosa, leads to a disruption of the mucous barrier and to an increase in the acid-peptic properties of gastric juice due to stimulation

of the endocrine apparatus of the stomach (first of all, the production of gastrin is enhanced). Dyskinesia duodenum, especially hypomotor type, lowering the tone of the antral part of the stomach promote DGR, make it long and intense. It is proved that DGR occurs much more often when a peptic ulcer is combined with diseases of the hepatobiliary system, especially with cholelithiasis.

The factors of "aggression" include the violation of the duodenal inhibitory mechanism (insufficient production of secretin, cholecystokinin, enterogastron) in duodenum, a disturbance in the exchange of biogenic amines - histamine and serotonin, which are released mainly from enterochromafin cells of the gastric mucosa. Histamine stimulates the secretion of HC1 through H2 receptors associated with cAMP. During the peptic ulcer exacerbation, histamine synthesis processes usually increase, which leads to the appearance of free histamine in the blood. According

to one hypothesis, histamine acts as a mediator of the parasympathetic nervous system. According to another widely held view, histamine is an intermediate link in the realization of gastrin action on secretory cells. The capillary circulation changes, the permeability of the vascular wall increases, the production of pepsin increases (histamine is a potent stimulant of the main cells). Histamine and serotonin, acting as activators of the kinin system (activate bradykinin), cause significant microcirculation disorders, blood circulation and trophism of the gastric mucosa suffer. Normally biogenic amines are rendered harmless by the amine oxidase of the intestinal wall.

The protective barrier of the gastric mucosa consists of three parts: 1) epineothelial (mucus, bicarbonates); 2) epithelial (epithelial cells and their repair, prostaglandins, growth hormones); 3) subepithelial (blood supply, microcirculation).

Mucous stomach is constantly exposed to hydrochloric acid, pepsin, and with duodenogastric reflux - and the effects of bile acids, pancreatic enzymes. In the protective barrier of the stomach, the first line of defense against damaging factors is the cells of the mucous membrane. These are surface cells and secretory additional, secreting mucus and bicarbonates. Due to these substances, a physicochemical barrier is created, which is a gel that maintains the pH of the neutral medium at the surface of the epithelium. All superficial epithelial cells lining the stomach and duodenum synthesize and secrete bicarbonates. The mucosa of the proximal part of the duodenum produces bicarbonates 2 times more than the entire gastric mucosa. An important role in maintaining the basal level of secretion of bicarbonates and mucus is also assigned to endogenous prostaglandins. Slime, its insoluble fraction, bicarbonates protect the gastric mucosa from the effects of hydrochloric acid and pepsin. The mucous barrier prevents the reverse diffusion of H + from the lumen of the stomach into the blood. Prolonged contact of the mucosa with acidic medium and changes in the composition of mucus (during the peptic ulcer exacerbation in the mucus the content of sialic acids and glycoproteins neutralizing hydrochloric acid decreases) lead to the breakthrough of the mucous barrier and the appearance of reverse diffusion of hydrogen ions. In response, histamine is released from the mast cells (tissue basophils of the stomach) and the cholinergic system is reflexively excited, venous stasis, capillary overflow, hydrochloric acid and pepsin production are enhanced - all this contributes to peptic ulcer formation.

In maintaining the stability of the mucous membrane of the stomach and the duodenum, the ability of cells to rapidly renew (repair), a good state of circulation and the secretion of chemical mediators of protection (prostaglandins, growth hormone) play an important role in the factors of aggression. It is known that the mucous membrane of the stomach and duodenum after the damage is

usually quickly restored (within 15-30 minutes). This process is not due to cell division, but as a result of their movement from the gastrointestinal epithelium of the stomach along the basal membrane and the closure of the defect in the area of the damaged epithelium. Prostaglandins, especially prostaglandin E2, contribute to improving the protective properties of the gastric mucosa, as they inhibit the activity of parietal cells, stimulate the secretion of mucus and bicarbonates and improve the blood supply to the mucous membrane, reducing the reverse diffusion of hydrogen ions and accelerating regeneration. Their secretion is carried out by the main, additional and parietal cells of the gastric mucosa.

The subepithelial part of the protective barrier of the gastric mucosa includes the optimal blood supply and microcirculation.

In addition, the factors of "protection" include the alkaline reaction of saliva, pancreatic juice, bile; Optimal motor and evacuation of the stomach; As well as the mechanism of duodenal inhibition of acid and pepsin formation (the production of cholecystokinin, secretin, enterogastrone duodenum).

When the factors of "aggression" outweigh the scales on the scales, an ulcer is formed, it becomes the focus of afferent impulsation in the central nervous system, where a pathological dominant arises. Other organs and systems of the body (liver, pancreas, etc.) are involved in the process, the disease becomes chronic.

The clinic of peptic ulcer includes pain syndrome, which is characterized by periodicity (depending on food intake, "hungry" pain), seasonality (exacerbation in spring and autumn),

rhythmicity (night, daytime - from daily rhythms of gastrointestinal juices). Pain syndrome is the leading subjective manifestation of the disease in the phase of exacerbation. The syndrome of dyspeptic disorders is characterized by heartburn, eructation, often regurgitation with salivation. Appetite remains good, with duodenal ulcers even increases (a painful feeling of hunger). Constipation occurs in 50% of patients, they worry even more than pain.

Complications of peptic ulcer include bleeding (small - up to 500 ml, average - up to 1000 ml, large - up to 1500 ml, massive - more than 1500 ml), posthemorrhagic anemia (mild, moderate, severe), penetration (into the small omentum, Pancreas, liver, gall bladder, etc.), perforation (into the free abdominal cavity, small gland cavity), stenosis (compensated, subcompensated, decompensated), malignancy (typical For peptic ulcer, I Duodenal ulcer is not malignant), reactive hepatitis, reactive pancreatitis, perivistseritis (perigastritis, periduodenitis).

Outcomes of peptic ulcer: scarring and healing; Stenosis of the pylorus and deformation of the stomach as a result of scarring; Lifelong existence of peptic ulcer; Malignization; A lethal outcome is usually a result of bleeding or perforation.

Experimental stomach ulcers. To reproduce the stomach ulcer in the experiment, the following methods are most often used:

1. Damage to the gastric mucosa by physical and chemical irritants (hot water, lapis, acids, croton oil, etc.). In the wall of the stomach develops acute inflammation and the formation of ulcerative defects, which usually quickly heal.

Disturbance of blood circulation in the wall of the stomach or duodenum (dressing, embolism, sclerosing of blood vessels). Blood flow is usually restored by anastomoses, and the resulting ulcers quickly heal.

Long-term administration of drugs that enhance gastric secretion (atofan, histamine, pentagastrin, pilocarpine, etc.), followed by the formation of a ulcerative defect.

Chronic irritation of vagus with increased gastric secretion and impaired microcirculation in the wall of the stomach.

Experimental neuroses with additional administration of gastric juice. In dogs, stomach ulcers arose when a burst of higher nervous activity was combined with a daily two-hour irrigation of the gastric mucosa with gastric juice.

Imposition of ligature on the gatekeeper with preservation of its patency (Shey's method). At the same time, erosions and sometimes ulcers appeared in the stomach of rats after 1-2 days as a result of vasodilation and the irritant effect of the ligature on n. Vagus, which caused a significant violation of blood circulation.

Introduction of gastro-cytotoxic serum obtained by immunizing animal donors with homogenate of gastric tissue.

For example, a rabbit is immunized with a dog's stomach tissue and the resulting serum containing anti-gastric antibodies is administered intravenously to an intact recipient dog. Antibodies interact with the stomach tissue of the recipient animal and cause damage to this tissue as a result of the antigen-antibody reaction.

The described methods of experimental modeling of ulcers cause mainly acute ulcerative defects. By the mechanism of origin and flow characteristics (usually quickly heal), they are fundamentally different from peptic ulcer, more reproducing the picture of symptomatic human ulcers. However, it is partially possible to model individual manifestations of this disease, which orientates in the developed antiulcer therapy.

Digestive disorders in the intestine

Digestion in the small intestine provides depolymerization of nutrients to the stage in which they are absorbed into the blood and lymph. Digestion in the small intestine first occurs in its cavity (cavity digestion), and then in the zone of the intestinal epithelium with the help of enzymes fixed on its microvilli and in the glycocalysis (parietal digestion). Cavity and parietal digestion is carried out by intestinal enzymes and enzymes of the pancreas.

An important role in the violation of digestion in the intestine is the violation of bile secretion, external secretion of the pancreas, as well as impaired secretory, absorption, motor, excretory functions of the intestine.

Violation of bile secretion

Bile is produced by hepatocytes and secreted into the intestine (in duodenum) in a volume of 500 ml per day. It contains bile acids, bile pigments, cholesterol and other lipids, as well as alkaline phosphatase.

Bile acids and their salts (sodium and potassium) are necessary for fat absorption. When bile acids enter through the duct and sphincter of Oddi in the duodenum, they are mixed with digestible lipids and fat-soluble vitamins, forming micelles (water-soluble complexes). Micelles are involved in the emulsification of fats, increase the surface area for hydrolysis and prepare fats for absorption. Hepatocytes produce cholic and chenodeoxycholic acids - primary bile acids. Under the influence of bacteria of the small intestine, they are modified into secondary bile acids (Deoxycholic, Methocholic and Ursocholic). The bile acids are reabsorbed in the small intestine and enter the portal vein system for recirculation. When entering the liver by the mechanism of negative feedback, they inhibit the synthesis of new bile acids, i.e. There is a process of intestinal-hepatic circulation of bile acids. Without this circulation, there is a violation of fat absorption, since the liver is not able to provide the synthesis of new bile acids necessary for the lipids entering the intestines. Changes in the composition of bile occur under the action of bile duct cells, which secrete bicarbonate and water (regulated by secretin) in bile. The final bile secreted in the duodenum has an alkaline reaction and is isosmolar to the blood plasma. This process is also regulated by cholecystokinin. These hormones also have a synergistic effect on the secretion of pancreatic juice.

Insufficient intake of bile in the intestine is called hypochole, and complete cessation of its admission is called achiolia. This is possible with plugging of the common bile duct with a stone, less often with worms, due to inflammation or compression of the tumor, enlarged lymph nodes, scar tissue of the liver gates. With hypocholism, especially acholia, digestion and absorption of fats are disrupted. Lipase pancreatic juice in the absence of bile is inactive, fats are not emulsified, and their contact with lipolytic enzymes is difficult. The process of absorption of fatty acids suffers, since for this, the formation of water-soluble complexes with bile acids is necessary. The absorption of cholesterol and fat-soluble vitamins is also disturbed, as they are absorbed, like food fats. Violation of the digestion of fats is manifested by steatoria (stear, atos - fat, fat, rhoe - flow) - excess fat in feces. With feces at the same time up to 70-80% of eaten fats. In the intestine, unsplit fats envelop the food chyme and hamper the action of amylolytic and proteolytic enzymes of duodenal juice, the activity of which decreases with insufficient intake of bile into the intestine. Sorption properties of the intestinal epithelium also suffer from a lack of bile acids, disturbed parietal digestion. This entails a violation of digestion and absorption of proteins and carbohydrates. Non-fat absorption promotes loss through the intestine of fat-soluble vitamins. Developing hypovitaminosis. Due to hypovitaminosis A, dermatitis occurs, growth slows down, vision is reduced until blindness (xerophthalmia). Lack of vitamin K leads to blood clotting and increased bleeding, vitamin D, which regulates the absorption of Ca2 + in the small intestine, to rickets and osteomalacia, and vitamin E deficiency to disorders of the nervous system (in the form of cerebellar disorders).

With hypocholia, peristaltic activity of the intestine weakens, which leads to increased flatulence, putrefaction, fermentation, as the bactericidal action of bile decreases.

Violation of the external secretion of the pancreas

The volume of the secretion of the pancreas is 1500 ml per day. It is secreted into the small intestine and contains enzymes, hydrolyzing proteins, fats and carbohydrates. Regulation of secretion is carried out by hormones - cholecystokinin (stimulates the secretion of enzymes) and

secretin (stimulates the secretion of bicarbonates). Regulation of pancreatic secretion is carried out through the vagus nerve.

The main causes of violations of external secretion of the pancreas are: 1) insufficient production of secretin in achlorhydria; 2) neurogenic inhibition of the pancreas function (with vagotomy, atropine poisoning); 3) development of allergic reactions; 4) exposure to various chemicals (poisoning with phosphorus, lead, mercury, cobalt); 5) injuries of the abdominal cavity;

6) toxicinfections (typhoid fever, paratyphus); 7) chronic infections (tuberculosis, malaria); 8) alimentary factors (excessive intake of food, animal fat, etc.); 9) destruction of the pancreas by the tumor process; 10) obstruction and compression of the duct with a tumor; 11) duodenitis - inflammatory processes in the DPC of any etiology (infectious, parasitic, etc.), leading to a decrease in secretin formation, followed by hypoxecretion of the pancreas; 12) exposure to alcohol, increasing the release of hydrochloric acid, which leads to stimulation of secretin secretion with excessive secretion of pancreatic secretions; 13) acute and chronic pancreatitis.

Etiology and pathogenesis of acute pancreatitis. The main etiological factors (in 70% of cases) of acute pancreatitis are cholelithiasis and alcohol intake. The emergence of acute alcoholic pancreatitis is due not only to the toxic effects of alcohol. Alcohol stimulates the release of hydrochloric acid, which, affecting the mucosa of the duodenum, increases the secretion of secretin. The latter is a potent stimulator of pancreatic secretion, the excess release of which leads to an increase in pressure in the ducts of the gland and the development of acute pancreatitis. In addition, strong alcoholic drinks contribute to the edema of the mucosa of the duodenum, which causes spasm of the faterov nipple with the subsequent increase in pressure in the pancreatic ducts. It is also known the direct effect of alcohol on the vessels of the pancreas, which causes their spasm. This leads to ischemia of the organ with death of the acinous cells and activation of enzymes in the gland tissue. Taking alcohol at a dose exceeding 100 g / day for several years can lead to the precipitation of pancreatic enzymes in small channels and the formation of protein caps. The more rare causes of acute pancreatitis are abdominal trauma, hyperlipidemia (especially type I and IV), the use of certain medications (nitropium, sulfasalazine, furosemide, corticosteroids, estrogens), infections (mumps, Botkin's disease, salmonellosis), surgical interventions, diagnostic Retrograde cholangiopancreatography, anatomical abnormalities of the pancreatic duct (strictures, tumors), hypercalcemia, uremia, vascular lesions, hereditary predisposition.

Three mechanisms of development of acute pancreatitis are considered. The most accepted theory of self-digestion of the gland tissue, according to which proteolytic enzymes - trypsinogen, chymotrypsinogen, proelastase and phospholipase A are activated inside the duct of the pancreas. It is believed that some factors (endo- and exotoxins, in particular alcohol, viral infections, ischemia and trauma) activate proenzymes, i.e. In conditions of pathology, trypsinogen can be activated in the gland under the influence of coenzyme cytokinase released from damaged parenchyma cells. An important role in the development of pancreatitis is played by the trypsin inhibitor, which is normally contained in a sufficient amount in the pancreas and prevents the conversion of trypsinogen to trypsin. With a high activity of trypsin, inhibitors of the anti- enzyme system are depleted, and their deficiency arises. This is used as a test in the diagnosis of acute pancreatitis: the higher the serum trypsinogen content, the less the trypsin inhibitor. When this factor is deficient, there is an active transition of

trypsinogen to trypsin. The increased activity of proteolytic enzymes, especially trypsin, leads to the digestion of pancreatic tissue and the activation of other enzymes - elastase and phospholipase. The active enzymes of cell membranes are digested, proteolysis, edema, interstitial inflammation, vascular damage, coagulation, fatty necrosis (steatoneecrosis) and necrosis of the parenchyma of the gland develop. Damage and destruction of cells lead to the release of activated enzymes. The digestive action of enzymes also affects the periphery. This is connected with the phenomenon of "enzyme evasion into the blood", which causes the development of necrotic processes in other organs. When lipase enters the blood, necrosis of distant organs with severe subsequent intoxication is possible. The process can be complicated by peritonitis and abscesses of the abdominal cavity. Trypsin activates pancreatic kallikrein, which causes the formation of callidin and bradykinin, which increase the damage to the gland tissue. There is a

further activation of the kinin system. Activation and release of bradykinin and histamine cause various hemodynamic disorders. Vessels are dilated, the permeability of their walls rises and the swelling of the gland develops. The release of fluid and protein into the tissue leads to a reduction in oncotic pressure and the development of pancreatic collapse, sometimes fatal. This collapse can be replicated in an experiment with intravenous administration of pancreatic juice to an animal. If the juice is pre-boiled, the collapse will not develop.

The second theory is the theory of the "common channel". Thanks to anatomical features, most people (80%) have a common biliary and pancreatic duct that facilitates reflux of bile into the pancreatic duct. However, normal pressure in the pancreatic duct is 2 times higher than in the common bile duct (200 mm of water). This prevents from casting bile and intestinal contents into the ducts of the pancreas. The casting of bile may be noted with hypertension of the sphincter of Oddi or hypermotor dyskinesia of the biliary tract. The frequent development of pancreatitis in cholelithiasis is due to the increased pressure in the biliary system. This ensures the transfer of infected bile under high pressure into the pancreatic duct, which causes chemical damage to the gland tissue, increases its enzymatic activity. The bile phospholipase activates trypsinogen. In cholelithiasis, attacks of acute pancreatitis may be associated with the transient obturation of the falcon nipple with gallstones. The casting of intestinal contents is possible with the festering nipple gaping or with hypertonic dyskinesia of duodenum arising from inflammation, the effects of nutritional and other factors. At the same time enteropeptidase, which enters the gland, activates trypsinogen. The resulting trypsin has an autocatalytic effect - it activates trypsinogen and other proteolytic enzymes. So, if in the experiment to introduce a small amount of trypsin into the pancreatic duct, then a pronounced necrosis of its tissue occurs, since active proteolytic enzymes are formed.

The third theory explains the development of pancreatitis by pancreatic duct obstruction and hypersecretion. Obstruction (spasm of the sphincter of Oddi, edema of the duodenum, etc.) causes a delay in the secretion of pancreatic secretions followed by activation of enzymes within the gland.

In pancreatitis, 3 stages develop: acute attack (edema, possibly pancreatic necrosis), incomplete cure with persistent chronic inflammation or destruction of the pancreatic duct, and then the stage of chronic inflammation with exocrine pancreatic insufficiency. With the development of fibrotic changes in the gland tissue associated with acute pancreatitis, an exocrine (exocrine) insufficiency of the pancreas occurs, characteristic of chronic pancreatitis. In iron, decreases, and then completely stops (with sclerosis, wrinkling of the body) the formation of digestive enzymes (pancreatic achilles). Violated cavity digestion (in the cavity of the small intestine) and absorption. First of all, the digestion

and absorption of fat sharply suffer. Fats up to 60-80% are not digested and in high amounts are excreted with feces (steatorrhea - excretion with feces more than 5 g per day or more than 5-6% of the introduced isotope - trioleate-glycerin). There is polyphecal, with coprologic examination in the feces of a lot of neutral fat (as broken fat splitting to fatty acids). Steatorrhea causes loss of calcium by the body, which is excreted together with fats in the form of insoluble soaps (in feces, in addition to neutral fat, there will be soaps). Along with calcium ions, magnesium and zinc ions are also lost, which also form soaps with unsweetened fats. Developed syndromes of hypocalcemia, hypomagnesemia. To a lesser extent and later digestion of protein is disrupted (not digested up to 30-40%). This is evidenced by the appearance of a large number of muscle fibers in the feces (creators), especially after eating meat. Digestion of carbohydrates is also impaired. There is a decrease in the volume of pancreatic secretion, bicarbonate in pancreatic juice (after stimulation with secretin of 1 mg / kg of weight) and enzymes - amylase, trypsin, lipase (after pancreosimine stimulation 1.5 mg / kg body weight). Digestive disorders are aggravated by a dyspeptic symptom complex. There is a syndrome of diarrhea, maldigestia syndrome develops, there is a progressive loss of body weight (in the absence of substitution therapy).

Violation of the secretory function of the small intestine

Disorders of the secretory function of the intestine may depend on a decrease in the amount of juice that is separated, reducing the content and activity of its enzymes and disturbances in the wall

digestion. They are often caused by intestinal enzymes-inadequate production of enzymes in the small intestine. Enzymopathy can be congenital and acquired.

More often there is a disaccharide deficiency (congenital deficiency of enzymes - disaccharidases) and especially a deficiency of lactase, sucrose and isomaltase. Significantly less frequent is the insufficiency of trehalase, an enzyme that breaks the disaccharide of trehalose found in fungi, algae and insects (in some Eastern peoples its share in food is considerable). With a deficiency of trehalase, mushrooms, especially young ones, are poorly tolerated. Rare forms of peptidase deficiency include congenital enterokinase deficiency (enteropeptidase). Enterokinase is the key enzyme of proteolytic processes in the intestine. It activates pancreatic trypsinogen, converting it into an active proteolytic enzyme called trypsin. In this case, children have severe disorders of protein metabolism, hypoproteinemia, edema, diarrhea, malabsorption syndrome. Patients are treated with pancreas extracts.

Congenital enteropathy includes gluten disease. When this disease develops, the splitting of gluten is broken (a gluten protein component gluing the constituents of some cereals: wheat, rye, barley, oats). There are two main theories of the pathogenesis of gluten disease. According to the first, intestinal epithelial cells involved in the process of digesting gluten are devoid of the corresponding peptidase or protease. In this regard, there is no splitting and subsequent absorption of gluten. The disease is considered as a metabolic defect, because of which undigested gluten and products of its incomplete cleavage have a toxic effect on the mucosa of the small intestine.

According to the second theory, the primary role is played by immunological reactions to gluten. Undivided gluten, interacting with mucosal immunocytes, leads to their sensitization, in particular to the sensitization of lymphocytes. As a result, various products of immunogenesis are formed - antibodies to gluten, immunized lymphocytes, lymphokines, causing damage to the intestinal

epithelium with a violation of its digestive and suction functions. There is evidence of the involvement of genetic factors in the pathogenesis of gluten disease. Its main diagnostic criteria are: malabsorption, subtotal or total atrophy of the small intestine mucosa, the clinical effect of the gluten-free diet.

Acquired enzymes can be associated with inadequate production of both (monoenzymopathy) and several (polyenzymopathy) enzymes of intestinal juice. They are accompanied by bloating (flatulence), diarrhea and lead to other manifestations of the syndrome of maldigestia.

Manifestations of intestinal enzimopathy - flatulence, diarrhea and the development of Maldigestia syndrome. Violation of predominantly cavitary digestion (Maldigestia syndrome) occurs due to many reasons: uncompensated reduction of the secretory function of the stomach, small intestine, pancreas, bile secretion. An important role in its occurrence is played by violations of the motor function of the gastrointestinal tract: congestion due to spasm, stenosis or compression of the intestine, acceleration of the passage of food chyme due to increased peristalsis.

In the clinical picture of maldigestia, signs of digestion disorders in various parts of the gastrointestinal tract may predominate. There are gastric, intestinal and pancreatic forms. The appearance of the gastric form is usually associated with atrophic gastritis, leading to secretory insufficiency. Perhaps the development of the gastric form and with decompensated stenosis of the pylorus, stomach cancer. Clinically, it is characterized by loss of appetite, a sense of heaviness, bursting and pressure in the epigastric area after eating, flatulence, diarrhea, belching, air, food with a rotten smell. In the study of gastric secretion reveal Achilia, achlorhydria.

When intestinal form associated with a chronic inflammatory process in the small intestine, with the development of intestinal enzymes, rumbling, intestinal transfusion, bloating, flatulence, unstable stool with prevalence of diarrhea are revealed. When intestinal cavity digestion is disturbed, intestinal steatorea is most often found, when fatty acids, soaps, amylorrhea, creators, and high content of ammonia predominate. The degree of impairment of the cavity digestion is judged by the level of enzymes (enterokinase and alkaline phosphatase) in intestinal contents and feces, as well as by the nature of the glycemic curve under starch loading and by the study of fat absorption by successive loading ith trioleate-glycerin and oleic acid labeled.

The emergence of the pancreatic form of maldigestia is associated with exocrine insufficiency of the pancreas. The clinic is dominated by anorexia, meteorism, colicky abdominal pains, abundant "pancreatogenic" diarrhea. When coprological analysis revealed steatorrhea pancreatic type (due to neutral fat), amylorea, creatorrhea. In diseases of the intestine, there is often a combination of all three forms of impaired cavitary digestion.

Disturbance of parietal (membrane) digestion in the intestine

In addition to the violation of the cavity digestion in the intestine (Maldigestia syndrome), there may be a disturbance of the parietal (membrane) digestion, which occurs in the zone of the intestinal epithelium with the help of enzymes fixed on its microvilli and in the glycocalysis. In the glycocalysis enzymes break down the products of cavity hydrolysis - oligomers, formed from large-molecule substances and adsorbed in the zone of striated border of enterocytes, to dimers. On the cytoplasmic

membrane of the microvilli, the cleavage proceeds to the final product - monomers that enter the enterocytes and then into the blood and lymph, i.e. Absorbed.

Microvilli of the apical membrane of enterocytes are the smallest cytoplasmic outgrowths, the length of which is 1 μm, the width is 0.1 μm. Thanks to this structure, the active digestive surface increases by 30 times. The distance between the villi varies from 10 to 20 nm, and therefore only small molecules penetrate the brush rim. Microbes, the size of which is several micrometers, are not able to penetrate it - it's a kind of bacterial filter. The processes of wall digestion are performed on a huge surface. The mucosa of the small intestine has folds, villi and microvilli, increasing its inner surface by 300-500 times.

Enzymes that consistently perform parietal digestion have a twofold origin. Some of them are adsorbed from the cavity of the small intestine (where they enter into the pancreatic and intestinal juices), and they bind to the glycocalysis of the microvilli. The other part is transferred from enterocytes (intestinal epithelium), fixing on cytoplasmic membranes of microvilli. The main intestinal enzymes involved in parietal hydrolysis of carbohydrates are D-glucosidases (maltase, trehalase, etc.), β-galactase (lactase), glucoamylase (γ-isoamylase), invertase, etc. Hydrolysis of oligo- and dipeptides is carried out by several pesticides of phosphorus Esters (for example, alkaline phosphatase), and lipids - lipases.

The causes of violation of parietal digestion can be:

1) violations of the structure of villi and microvilli, a decrease in their number per unit surface (AM Ugolev). This is a characteristic sign of chronic diseases of the small intestine, where the morphological substrate is inflammatory, dystrophic and sclerotic changes in the mucosa. The development of atrophic changes in the mucosa of the small intestine, predominantly villi, is noted in dysentery, cholera;

2) alteration of the enzymatic layer of the intestinal surface as a result of genetic or acquired deficiency of enzymes involved in parietal digestion. Primary insufficiency of parietal digestion, as a rule, develops in children at an early age with the expansion of the diet with the inclusion of new products containing the intolerant disaccharide. Acquired insufficiency is more often a consequence of diseases of the small intestine - chronic enteritis, as well as viral hepatitis and other infections;

3) disorders of intestinal peristalsis, which leads to disruption of the transfer of nutrients from the intestinal cavity to the surface of enterocytes, for example, chronic enteritis, Whipple's disease, Crohn's disease and other diseases of the small intestine;

4) Insufficiency of the cavitary digestion, when the little-split large molecules do not pass into the brush border of the villous epithelium.

The clinical picture of insufficiency of parietal digestion is similar to dyspepsia in the syndrome of insufficiency of absorption. There are persistent diarrhea, feces liquid, abundant, foamy. In order to clarify the diagnosis, the activity of enzymes (amylase, lipase) is determined upon their sequential disorption in homogenates of the biopsy of the small intestine mucosa obtained by inoscopy. Part of the biopsy specimen is examined morphologically, which allows detecting inflammatory, atrophic changes in the mucosa. Comparison of the activity of the enzymes in the desorbed fractions allows us to derive the activity curves of the enzymes, which characterize

the relationship between cavity and membrane digestion. The violation of parietal digestion in chronic enteritis is also determined by other methodical techniques.

Disturbance of absorption in the intestine

Disturbances of absorption are manifested in its slowing down or pathological enhancement. Slowing down the suction is the basis of the malabsorption syndrome (from the French mal - disease), caused by a violation of absorption in the small intestine of one or several nutrients. The range of clinical manifestations of malabsorption syndrome varies from the absence of its visible signs to the expressed loss of body weight. It combines the symptoms of diarrhea, steatorrhea, protein deficiency, hypovitaminosis. Malabsorption syndrome may be primary (congenital or hereditary) or secondary (acquired). Congenital malabsorption is rare in clinical practice. Most often this is the pathology of childhood, due, for example, to congenital disruption of transport (insufficiency of transporter vectors) of amino acids in the small intestine. So, this syndrome is associated with a violation of absorption of neutral amino acids (Hartnap's disease - pellagra skin changes, cerebellar ataxia); Syndrome of absorption disorders of cysteine and basic amino acids, syndrome of decreased absorption of many amino acids (Low syndrome - congenital cataract, glaucoma, hypertension, osteoporosis, mental retardation), decreased absorption of lysine (congenital lysinuria - protein intolerance, diarrhea, vomiting, retardation) and Other congenital malabsorption of glucose and galactose is possible. In the small intestine mucosa of such patients, the enzyme glucose-6-phosphatase is absent. With a congenital impairment of absorption of fructose in the mucosa, there is a deficiency of fructose-1-phosphataldolase, responsible for its transport. There is an isolated violation of absorption of these substances, there is diarrhea and abdominal pain. Primary malabsorption of vitamin B12 or folic acid leads to the development of megaloblastic anemia.

Secondary impairment of absorption is more common. It is associated with such diseases of the intestine, liver, pancreas and other organs as:

1) insufficient digestion of food in the stomach (due to achlorhydria, subtotal resection of the stomach, trunk vagotomy) or duodenum;
2) exocrine pancreatic insufficiency (chronic pancreatitis, cancer, cystic fibrosis, pancreas resection);
3) liver disease (chronic hepatitis, cirrhosis) and biliary tract obstruction (gall bladder stones or pancreatic head cancer), which is associated with insufficiency of bile acids entering the duodenum;

4) ischemic enteropathy with possible intestinal infarction (eg, lead poisoning, mesenteric atherosclerosis);
5) inflammation of the small intestine of various etiologies (acute and especially chronic enteritis with the development of changes in the small intestine mucosa down to atrophy, which reduces its suction surface), Crohn's disease (with duodenum or ileum injury);

6) dysbacteriosis, when absorption of fat and vitamin B12 is particularly affected, as microbes cause deconjugation of bile acids in the intestine and absorb vitamin B12;
7) radiation (radiation) enteropathy associated with irradiation of the intestine, for example, in the treatment of cancer, which causes swelling of the mucosa, later - atrophy of the villi and thinning of the mucous membrane. The defeat of the ileum leads to a deficiency of vitamin B12 and impaired intestinal hepatic exchange of bile acids;
8) resection of the small intestine (short bowel syndrome) associated with trauma, small intestinal obstruction, vascular thromboembolism, severe Crohn's disease, etc.;
9) intestinal obstruction in the upper parts of the intestine, when the food masses do not enter the distal parts of the gut;

10) movement disorders of the intestine, in particular with accelerated peristalsis, when the contact time of the chyme with the absorption surface of the small intestine decreases;

11) lymphatic obstruction (lymphangiectasia of the intestine, Whipple's disease, lymphoma);

12) cardiovascular diseases (pericarditis, congestive heart failure, vasculitis);

13) immunodeficiency, endocrine disorders (diabetes mellitus, hypo- and hyperparathyroidism, Zollinger-Ellison syndrome).

As a result of malabsorption, malabsorption syndrome develops, which, in addition to changes in the gastrointestinal tract, is characterized by pathological changes from other organs and systems.

Often there is bloating, usually after eating, associated with milk intake, increased gas production. Diarrhea is noted in connection with the accumulation of osmotically active substances in the intestinal cavity, acceleration of transit through the intestine and hyperexudation. There is polyphecal with the remnants of undigested food. There is a steatorrhea - a sign of a violation of fat absorption (fat loss with feces is more than 5 g / day, reaching 10 g / day or more).

An important clinical symptom of malabsorption is weight loss (at I degree of malabsorption - up to 5-10 kg, at grade II - over 10 kg, at grade III - over 20 kg). There are signs of hypoavitaminosis, trophic disorders. The skin becomes dry, with a decreased turgor, hair - dry, dull, hair loss is noted. There are changes in nail plates, their fragility, as well as gum disease, hyperemia of the tongue, smoothness of its papillae, which is explained by the deficiency of vitamins B2, B6, B12, nicotinic acid. There is bleeding gums associated with vitamin C deficiency. Polyneuritis, visual impairment caused by vitamin A deficiency is often developed. In severe malabsorption syndrome, the absorption of trace elements deteriorates. As a result of calcium deficiency, osteoporosis occurs, right up to osteomalacia. The violation of iron absorption leads to the development of iron deficiency anemia. Due to impaired absorption of proteins, hypoproteinemia develops with subsequent edematous syndrome. There may be abnormalities in the endocrine glands activity as a type of plurigandular insufficiency - the development of endocrinopathy with damage to the pituitary gland, adrenals, and gonads.

Pathogenesis of clinical manifestations of insufficiency of absorption

Pathogenesis	**Manifestations of insufficiency of absorption**
Infringement of absorption of fats, carbohydrates, proteins, decrease in receipt in an organism of calories	Weight loss
Impaired absorption of amino acids, hypoproteinemia	Peripheral edema

Vitamin D deficiency, osteoporosis and osteomalacia as a result of malabsorption of proteins and calcium.	Ossalgia (pain in the bones), myopathy
Deficiency of B vitamins	Peripheral neuritis
Impaired absorption of calcium and magnesium	Paresthesia, tetany
Reduction of absorption of proteins, vitamin B12, folic acid, iron	Anemia
Impaired absorption of vitamin K, vitamin A deficiency	Hemorrhages. Night blindness (Hemerallopia, xerophthalmia)
Deficiency of riboflavin (B2)	Heilit
Deficiency of vitamins B2, B6, B12, nicotinic acid	Glossitis
Deficiency of nicotinic acid	Dermatitis

Pathological increase in absorption can be associated with increased permeability of the intestinal wall (for example, with its arterial hyperemia or irritation of the intestinal epithelium). Intensification of absorption is easily developed in young children, when the permeability of the intestinal wall is quite high. At the same time, products of incomplete cleavage of nutrients are rapidly absorbed and intoxicated. Unchanged form can be absorbed protein cow's milk or chicken eggs, which causes sensitization of the body with the development of allergic reactions.

Violation of the motor function of the intestine

Motor activity of the small intestine provides mixing of food contents with digestive secretions, promotion of chyme and increased intestinal pressure, which facilitates the filtration of certain components into the blood and lymph.

Disorders of the motor function of the intestine are manifested in the acceleration or deceleration of peristalsis and the alternation of these processes, as well as in the disturbance of rhythmic segmentation, which occurs due to a predominantly circular layer of muscles and pendulum contractions that ensure the interaction of the longitudinal and circular layers of muscles. On the length of the intestine, several peristaltic waves are moving at the same time. In disorders of motor activity of the intestine, anti-peristaltic contractions are noted, when the wave of movement goes in the opposite (oral) direction. Tonic contractions can have a very small speed and sometimes do not spread, which causes the narrowing of the lumen of the gut on a large extent.

Motor activity of the intestine is excited through parasympathetic nerve fibers. An important role of the cerebral cortex in the regulation of motor activity is proved by the fact that motor activity is strengthened even at the thought of tasty food, and, in the negative attitude towards food, on the contrary, is inhibited. With fear, there is sometimes a turbulent peristalsis of the intestine ("nervous diarrhea"). The motor activity of the small intestine depends on the physical and chemical properties of the chyme. So, its activity is increased by rough food (black bread, vegetables) and fats. Intestinal motility is affected by a number of humoral substances, acting directly on the muscle fibers and through the receptors on neurons of intramural nervous ganglia. Thus, increased motility of the small intestine is observed with an increase in the level of vasopressin, bradykinin, serotonin, histamine, cholinomimetics, cholecystokinin - pancreosimin and peptides (motilin, gastrin). Usually the main empirical rhythm is constant - about 8 cuts per minute. However, in a number of cases it is more frequent, for example, with thyrotoxicosis.

The inhibition of motor activity of the intestine occurs under the influence of sympathetic fibers. Motor activity decreases with fasting. In a person after 24-36 h fasting, it is 34% of the initial.

The motor (motor) function of the small intestine plays an important role in the effectiveness of nutrient absorption from its lumen. Due to the contractile function of the intestine, the content is mixed and promoted in the intestinal cavity, which does not allow the formation of a high concentration of hydrolysis products in one wall layer, creating a diffusion barrier. Under experimental conditions, it has been proved that at a high rate of transit of chyme in the gut, its ability to absorb decreases. For example, this happens when including coarse-fiber products in the diet. The content of glucose in the blood becomes 2 times less than with a diet without coarse fibers.

Acceleration of peristalsis. As a result of the acceleration of peristalsis, the food gruel advances through the intestine more rapidly and develops diarrhea (diarrhoea).

Diarrhea can be acute (not exceeding 2-3 weeks) and chronic (lasts 4-6 weeks or more), infectious and non-infectious, inflammatory and non-inflammatory. By the mechanism of development, the following types of diarrhea are distinguished: hypersecretory (hyperexudative) and hyperosmolar, hypo - and hyperkinetic.

Hypersecretory type of diarrhea is characterized by increased secretion of water and electrolytes into the lumen of the intestine. This is due to the effect on the intestinal mucosa of bacterial endotoxins (with cholera, intestinal infections), bile and fatty acids, glucagon, prostaglandins and a whole series of laxatives (bisacodyl, castor oil, phenolphthalein). The pathogenesis of bacterial diarrhea is due to two mechanisms: invasion of bacteria in the mucosa and hypersecretion caused by enterotoxins. Hyper-secretory diarrhea is also observed with an increase in hydrostatic pressure due to damage to the lymphatic system of the intestine (with lymphoectasis, intestinal amyloidosis, lymphoma, Whipple's disease) and right ventricular heart failure. The stool is usually abundant in this type of diarrhea, watery.

Very severe diarrhea (the so-called aqueous diarrhea) can be caused by excessive production of the vasoactive intestinal polypeptide, which is normally contained in the gastrointestinal tract,

mainly in the wall of the small intestine. It suppresses the secretion of hydrochloric acid, stimulates intestinal and pancreatic secretions, increases the concentration of

cAMP in the small intestine mucosa. The vasoactive intestinal polypeptide (VIP) produces some tumors - ganglioneuroblastoma (more often in children) and adenoma of islet tissue (not α- and not β-cell) of the pancreas - WIPoma (Werner-Morrison syndrome - "pancreatic cholera"). By affecting specific receptors of the intestinal epithelium, the VIP activates adenylate cyclase and increases the level of cAMP. This causes an increase in the secretion of water and electrolytes, resulting in the development of profuse watery diarrhea (the osmotic density of the stool is close to the osmotic density of the plasma). There comes dehydration (more than 3 liters per day, sometimes up to 20 liters), hypokalemia (increased loss of potassium and stool), metabolic acidosis, cachexia (in the absence of steatorrhea) progresses. Due to the influence of VIP on the vascular tone, some of the patients experience hot flashes (a feeling of heat for 2-3 min) with a purple dyeing of the face and upper half of the trunk, while the other part develops diabetes mellitus. An elevated level of circulating VIP is defined, but this index has a high percentage of false positive and false negative results. Chronic diarrhea can also be a manifestation of other endocrine tumors that produce secretion stimulants. For example, in thyroid carcinoma diarrhea is caused by increased secretion of calcitonin and other peptides.

With excessive formation of cAMP, diarrhea is associated with cholera. The cholera vibrio toxin (cholerogen) in combination with the specific receptor with C1m1-ganglioside activates adenylcyclase catalyzing the formation of cAMP. Heavy watery diarrhea develops. It should be noted that with cholera, the intestinal mucosa remains normal and its absorption capacity is preserved. This creates a basis for oral rehydration with solutions containing simple sugars and sodium chloride "(the former stimulate the absorption of the latter).

With a hyperosmolar type of diarrhea, there is a decrease in the absorption of water and electrolytes. This type of diarrhea is noted in cases of absorption disorders, which is observed in cases of gluten, ischemic disease of the small intestine, congenital suction defects, chronic pancreatitis, pancreatic cancer, bile acid deficiency (eg, mechanical jaundice), insufficient contact time of the chyme with the intestinal wall With resection of the small intestine, enteroanastomoses), etc. There are polyphecal and steatorrhea. Thus, with resection of the ileum and some diseases of the small intestine (for example, with Crohn's disease) diarrhea can occur due to a violation of absorption of bile acids and free fatty acids that stimulate the secretion of fluid in the large intestine. In mild cases, the absorption of bile acids is inhibited. In particularly severe cases (resection of more than 100 cm of the terminal ileum), absorption of both bile acids and salts deteriorates, which in turn causes a violation of the digestion and absorption of fatty acids. The latter, getting into the large intestine, cause diarrhea. In other forms of steatorrhoea, for example in pancreatogenic insufficiency, unabsorbed triacylglycerols reach the colon, where they are hydrolyzed by microorganisms to fatty acids, which also causes diarrhea.

Hypo - and hyperkinetic types of diarrhea are caused by stimulation: neurogenic, for example, in irritable bowel syndrome, diabetic enteropathy; Hormonal (serotonin, secretin, pancreosimine); Pharmacological (laxatives isofenin, phenolphthalein). It is possible to slow the transit of intestinal contents in scleroderma, the syndrome of the cecum. The stool is usually liquid or mushy, ungrowth.

Slowing of peristalsis. When the peristalsis slows down, the food chyme moves along the intestine, and constipation (obstipatio) develops. With constipation, the intervals between acts of defecation increase in comparison with the individual physiological norm or the intestine is systematically insufficiently emptied. The frequency of the stool is very variable and can vary

depending on the habit of emptying the intestine after a certain time, the nature of nutrition, climatic and other factors. Most people have a chair once a day, a part - 2 times and a significantly smaller percentage (7%) - 3 times a day or more. As a rule, a chronic bowel evacuation delay of more than 48 hours is considered as constipation.

The terminal section of the food tract, carrying out the absorption of water and mineral salts, takes part in the regulation of water-salt metabolism. The main functions of the colon (formation, promotion, retention and release of stool) are realized by the interaction of the following

components of motility - the tone of the intestinal wall, different in strength and length of peristaltic waves, their coordination and discoordination. The motor activity of the large intestine is influenced by nervous, endocrine, physical and nutritional factors. In addition, it is characteristic to participate in the regulation of the motility of the microflora and the emotional-psychological sphere of man.

The etiology and pathogenetic factors are most fully taken into account by the classification of A.V. Frolkis, which produces constipation: 1) alimentary; 2) neurogenic (dyskinetic, reflex), due to suppression of urge to defecate, with organic diseases of the central nervous system; 3) hypodynamic; 4) due to inflammatory bowel diseases; 5) proctogenic; 6) mechanical; 7) due to anomalies in the development of the large intestine; 8) toxic; 9) medicamentous; 10) endocrine; 11) due to violations of water-electrolyte exchange.

Constipation may be a manifestation of mechanical obstruction in the intestine: sigmoid colon swelling, diverticulitis, invagination, hernia, swelling, scars, stools, etc. Isolate proctogenic constipation, i.e. Caused by pathological processes in the anal area of the rectum (hemorrhoids, anal fissures and perianal abscesses). They are associated with the suppression of urge to defecate because of severe pain and spasm of the anal sphincter, which mechanically prevents the release of stool. Possible so-called senile constipation associated with intestinal atony. Disorders of the motor activity of the intestine can also be associated with endocrine pathology. Constipations of endocrine origin include dyskinesia of the intestine in women during pregnancy, after childbirth, in the climacteric period. Thus, during pregnancy and after childbirth there is a relative hypotonia of the musculature of the intestine, caused by hormonal changes in the body of a woman. Chronic constipation develops in hypothyroidism, which is associated with a characteristic slowing of transit through the intestines. A similar situation occurs with hypercalcemia.

By the nature of motor disorders, hyper- and hypokinetic constipation is distinguished. Hyperkinetic constipation occurs with spasm of the intestinal wall, which hinders the progress of food chyme along the intestine. Spasm often develops in areas of the intestine, where there are strengthened contractions (sphincter of Bali, passage of the caecum into the ascending and colon, etc.). Hyperkinetic type of constipation is possible in case of poisoning with mercury, lead, sulemoy, when taking medications (iron, calcium, tranquilizers, ganglion blockers, etc.). Perhaps the development of this type of constipation under the influence of emotions and psychotic states (psychogenic constipation). They arise as a reaction to unfavorable conditions for evacuation of the intestine, i.e. Negative emotions, for example, when it is necessary to perform an act of defecation in unhygienic conditions, can lead to its involuntary suppression. With multiple "braking" defecation, desires disappear and habitual constipation develops. This type of constipation can occur under the influence of other psychogenic factors (mental overstrain, depression, schizophrenia, drug addiction), and also

can be associated with the influence of viscer-visceral reflexes from the stomach, pancreas, biliary tract, etc.

The change in the volume of intestinal contents, the composition of the intestinal microflora, and the breakdown of gastrointestinal reflux can lead to a weakening of propulsive motility, i.e. To the development of hypokinetic constipation. Quite often, constipation leads to a meager diet, the intake of easily digestible, fiber-poor food (mechanically and chemically sparing diets). The use of chemically purified, completely water-soluble products used in space flights, causes a reduction in stool frequency up to 1 time in 5-7 days, there are alimentary constipation. In the summer, when a lot of fruits and vegetables are consumed, the frequency of constipation decreases. The role of dietary fiber in the stimulation of bowel evacuation is proved. Bran increases the daily amount of feces, accelerates intestinal transit. Constipation aggravated dryness (drying of stool), a lack of calcium and potassium in the diet, excessive digestion of food masses in the stomach, for example, with hyperchlorhydria. In addition, inadequate, as well as untimely consumption of food leads to a violation of gastrointestinal reflux, which stimulates large peristaltic waves. Therefore, people neglecting breakfast, irregularly eating food, often suffer from constipation. Hypokinetic constipation occurs in the absence of physical exercises (with hypodynamia).

Primary motor disorders of the anorectal region and pelvic floor include congenital disorders of intestinal motility in Hirschsprung's disease, the mobile blind and sigmoid colon and congenital

splanchnoptosis. With Hirschsprung's disease, an anomaly of colon development is noted, characterized by chronic congestion of intestinal contents, expansion of the colon with hypertrophy of its wall. The essence of the disease is the complete absence or deficiency of intramural nerve ganglia. Thus, there are no ganglion cells of Auerbach's plexus completely absent in the internal anal sphincter, rectus and sigmoid colon. The affected area of the intestine is narrowed, not peristaltic, the intestinal contents over the site of the lesion stagnate, the overlying parts of the large intestine (megacolon) expand. The wall of the intestine is hypertrophic, since the peristalsis is enhanced by the need to overcome the narrowed non-irritating site. It is established that in this area the concentrations of VIP and substance P are sharply reduced, which normally stimulate intestinal motility. With a long zone of damage, the picture of intestinal obstruction grows. Stools usually do not happen 3-7 days, in rare cases it is independent, mostly - only after enema.

Intestinal obstruction (ileus) - impaired intestinal passability due to a violation of its functions or mechanical obstruction. Intestinal obstruction can be congenital, which is caused by abnormal development of the intestinal tube during the intrauterine period, and acquired. Acquired intestinal obstruction by pathogenesis is divided into mechanical, dynamic and thromboembolic.

Mechanical obstruction is associated with mechanical closure of the lumen of the intestine with a tumor, calic stones (coprostasis), helminths, foreign bodies, or due to compression of the gut from the outside by a tumor, scar. Mechanical obstruction develops when the intestine turns, intussusception, infringement of the intestinal loop in the hernial opening, with adhesive process in the abdominal cavity. Allocate its following reasons: 1) intestinal compression of the gut, for example, with adhesions of the abdominal cavity, hernia (external and internal); 2) internal compression of the intestine (diverticulosis, cancer, regional enteritis, or Crohn's disease); 3) Obturation, for example, gallstones or with intussusception.

Most often, the causes of the obstruction of the small intestine are adhesions of the abdominal cavity and external hernias, and the colon - a cancerous tumor, diverticulitis (sigmoid colon) and a curvature. Mechanical obstruction can be obturation and strangulation. With obstructive obstruction, the lumen of the intestine is closed, but the circulation in its wall is not initially disturbed, with strangulation, along with obstruction of the intestinal lumen, compression of the vessels and nerves of the mesentery occurs, which causes an extremely severe clinical picture. Rapid disruption of intestinal wall feeding leads to its necrosis. With mixed obstruction, along with the overlap of the lumen of the gut, there is a gradual compression of her mesentery with a violation of the blood supply to the intestinal wall.

Dynamic obstruction occurs with spasm (spasmodic), which can occur when heavy metals are poisoned by diseases, biliary tract and other abdominal organs, or paralysis of the intestinal musculature (paralytic), when the intestinal peristalsis sharply weakens until complete cessation. This occurs with severe long-term operations on the abdomen, trauma.

Thromboembolic (haemostatic) obstruction of the intestine develops as a result of circulatory disturbances in the intestinal wall with thrombosis (embolism) or paralysis of its vessels. Thrombosis or embolism of the intestinal arteries can be a manifestation of severe atherosclerosis, heart failure, may complicate atrial fibrillation, implantation of artificial heart valves or severe heart defects. Involvement in the process of large arterial vessels of the intestine is possible with systemic vasculitis.

The pathogenesis of intestinal obstruction is complicated. There is a stretching of the intestine with the accumulation of gases and liquid contents in it proximal to the septic segment. The accumulated fluid in the intestine consists of saliva, gastric juice, bile and pancreatic enzymes. In the first 12-24 hours of obstruction the motor activity of the intestine decreases, the transport of sodium and, consequently, the water from the lumen of the enlarged colon into the blood slows. After 24 hours, sodium and water accumulate in the gut lumen, which is accompanied by its stretching and loss of fluid. Intestinal pressure increases, vomiting occurs. There comes a strangulation (blood circulation is sharply disturbed) in connection with the expressed stretching of a gut proximal to a site of occlusion. Intramural blood flow is reduced to such an extent that bowel necrosis occurs. When the blood supply is disturbed, the pathogenic bacterial flora multiplies with

subsequent development of peritonitis. The high standing of the diaphragm due to swelling of the intestine causes a violation of pulmonary ventilation with the development of atelectasis in the lungs. The outflow of blood in the system of the inferior vena cava is disturbed. Loss of body tissues fluid and electrolytes can be pronounced. As a result, dehydration and thickening of blood quickly occur. In the blood, the chloride content decreases, which, together with water, passes into the abdominal cavity, the content of ammonia, urea and other rotting products that are formed in the intestine and is absorbed into the blood increases. Heavy intestinal toxicity develops. Increasing hypovolemia leads to the development of acute renal failure, shock and death of the patient. With complete obturation, gases and feces do not depart. Blood in the feces is rarely detected, only occasionally with an invagination form of occlusion. It is possible to vomit, more often with the obstruction of the small intestine than thick.

Isolate pseudo-obstruction of the intestine, which is based on pronounced motor disorders, which contributes to stretching of the intestine, the occurrence of abdominal pain, nausea and even vomiting. Pseudo-obstruction can be primary and secondary. In primary, or idiopathic, pseudo-obstruction, impaired motor activity of the intestine is caused by an anomaly of sympathetic innervation or its muscular layer, and the patient does not have any systemic disease. In secondary

pseudo-prolapse, the expansion of the thick and / or small intestine is associated with the involvement of the muscle layer in the process, for example, in autoimmune diseases (dermatomyositis, scleroderma, amyloidosis) or autonomic visceral nervous system in endocrine diseases - diabetes, myxedema. Secondary pseudo-obstruction may develop in chronic diseases of the nervous system (Parkinson's disease, cerebrovascular disease), and may also be associated with side effects of a number of drugs (calcium antagonists, cholinolytics, (5-adrenoblockers, psychotropic, etc.).

Violations of defecation. May occur in the following situations:

1) with strong mental shocks (fear, fright), the influence of the cerebral cortex on the spinal center of defecation falls, and at the same time defecation occurs involuntarily (reflexively);
2) with n damage. Pelvici, n. Hypogastrici defecation is disrupted, as the function of the muscles participating in this act is upset;
3) inflammatory processes in the rectum (with proctitis of any etiology) increase the sensitivity of its receptors, and there are false desires for defecation (tenesmus);
4) with injuries of the lumbosacral spinal cord due to the deenergizing of the center of defecation, incontinence occurs, or there is no urge to defecate. In addition, in connection with the abnormality of the muscles of the abdominal press, emptying the rectum may be incomplete, and constipation may occur;
5) with a decrease in muscle tone and physical activity in elderly, recumbent patients, the act of defecation is broken, there is a feeling of overflow of the rectum, the urge to defecate, constipation develops or paradoxical diarrhea (when liquid feces passes through the distal fecal stones).

Flatulence (accumulation of gases in the intestine, its swelling). A large number of gases pass through the digestive tract of healthy people every day. Gases enter the intestine along with the inhaled air and partially diffuse out of the blood. A certain amount of gases is formed in the intestine as a result of enzymatic processes and the vital activity of the intestinal microflora. On average, about 500 cm3 of gas is generated per day. However, this can be enhanced by aerophagia or increased formation of gases by intestinal bacteria. Gas formation increases with malabsorption syndrome, especially when eating foods such as beans, peas, cauliflower and cabbage, characterized by a high content of indigestible polysaccharides. When the gases in the intestine are held in a state of fermentation and decay, the amount of carbon dioxide, methane, and hydrogen sulphide increases. At the same time, blood circulation in the intestinal wall is disrupted, its mechano - and chemoreceptors are re-stimulated. There can be a happy reflex shifts: inhibition of diuresis, instability of arterial pressure. Due to the high standing of the diaphragm, breathing is disturbed. The secretion of digestive glands is inhibited, hypotension of the intestine is intensified, which further aggravates flatulence. A "vicious circle" is being created.

iolation of the excretory function of the intestine

The main mechanisms of excretion (sorption of substances by membranes, various types of membrane transport) underlie the interorganic exchange of nutrients, the leading role in which the digestive system plays. The term "nutrients" (nutrients) in this case is more accurate, since it comes from the word "nutrition" - nutrition. It is known that in the activity of the gastrointestinal tract, in addition to proper digestion, there is another side associated with the release into its cavity of a significant amount of endogenous substances which, together with the exogenous digest, are absorbed and promote assimilation of nutrients throughout the body. The body has developed a coordinated interaction between different bodies to obtain the necessary nutrients and supply them with each

other, which contributes to the normal course and good coordination of metabolism throughout the body. Some tissues, thanks to their specialized metabolism, are able to synthesize intensively certain substances and not only satisfy their own need, but also export them with blood for use by other tissues. For example, the muscles in fasting release into the blood amino acids with a branched carbohydrate chain, heavily used by the brain. The kidneys are intensively secreted into the blood of the series, which is then used by almost all the tissues of the body.

Participation of the digestive system in the interorgan exchange of nutrients is expressed: a) in the protein substance circulation between the blood and the digestive system; B) in the circulation of certain mineral substances, in particular zinc; C) in the export of phospholipids and other compounds by the liver for use by other, rapidly proliferating tissues; D) in the isolation of endogenous nutrients during the periodic activity of the gastrointestinal tract in conditions of famine.

The nutritional cycle is of clinical interest. Wherever there is a violation of their circulation (in places where endogenous substance is released, its transport or in the intestinal absorption zone), in all cases a secondary insufficiency of the substance in the body may occur.

The role of the intestine in the metabolism is determined not only by its absorbing activity, but also by the ability to secrete protein and other substances from the blood. The role of the digestive tract in the loss of endogenous protein is proved. For an objective assessment of the role of the gastrointestinal tract in the digestion and absorption of protein, it is necessary to know the rate of synthesis and decomposition of the protein in the body. The results of the study with labeled albumin indicate that in norm 10-20% of albumins can be excreted through the intestine. Isolation of protein from the bloodstream into the gastrointestinal tract is accomplished by simple diffusion. In this case, transudation occurs not through the cells of the mucosa, but through the intercellular space of its epithelium. The amount of protein passing into the intestine is proportional to the hydrostatic pressure and plasma protein concentration in the extravascular space. It is estimated that for a day in physiological conditions, 80 g of protein are excreted in the human cavity of the digestive tract. However, in a healthy person, its loss with feces is negligible. Most of the protein released into the gastrointestinal tract undergoes enzymatic digestion to amino acids that are absorbed along with the products of hydrolysis of exogenous nutrients. This process helps to ensure the consistency of amino acid homeostasis. Part of the protein enters the gastrointestinal tract with the secretions of the digestive glands, part is lost with the cells of the desquamated epithelium. In addition, in the lumen of the intestine, about 20 g of fat are released per day. Experimental studies have shown that cholesterol, triacylglycerols, a number of phospholipids are excreted only in the composition of the sloughing epithelial cells, and only free fatty acids can be released by transudation. In healthy people, lipids released into the intestine are almost completely reabsorbed, and their loss with feces is negligible. With depleted cells enter the lumen of the gastrointestinal tract and other substances - iron, folic acid, etc.

With an increase in the excretory function, the syndrome of "exudative enteropathy" can develop - protein-destroying enteropathy - protein loss due to increased release into the gastrointestinal tract. The main mechanism of increased protein loss with feces is an increase in its transudation into the lumen of the gastrointestinal tract, which occurs when the pressure in the lymphatic vessels of the intestine increases. In this regard, protein intussusception in the intestine is

nhanced in patients with obstruction or stasis of the intestinal lymphatic pathways (granulomatosis, neoplastic processes, lymphangiectasia in the intestine, constrictive pericarditis). It is possible to exudate the protein through the inflamed or ulcerated mucosa. Proteins are lost when the mucous membrane is destroyed (villous and superficial epithelium), which disturbs the regulation of their diffusion through the intercellular spaces.

As an independent disease, this syndrome is rare (primary exudative enteropathy - idiopathic intestinal lymphangiectasia). Secondary exudative enteropathies are quite common - about 90 diseases are accompanied by this syndrome. Symptomatic exudative enteropathies are observed in giant hypertrophic gastritis (Menetries disease), in conditions after gastrectomy, in a number of bowel diseases (tropical, nontropical spruce, acute gastroenteritis, Crohn's disease, ulcerative colitis), with cirrhosis, constrictive pericarditis, heart failure, with Generalized lymphosarcomas, nephrotic syndrome, radiation sickness, etc.

Due to the loss of protein with feces (proteinuria) in exudative enteropathy, pronounced hypoproteinemia with a significant decrease in albumin content in the blood and dysproteinemia takes place. The pronounced hypoproteinemia causes a decrease in the blood oncotic pressure followed by the transudation of liquid from the capillaries into the tissues, with the development of edema, secondary aldosteronism with a delay in the release of water and sodium ions from the body. With feces, a number of important biologically active substances of protein nature are lost, primarily immunoglobulins. This causes a decrease in the concentration of immunoglobulins of various classes, transferrin, ceruloplasmin, etc. Due to hypogammaglobulinemia, immunoglobulin deficiency, there are immunodeficiency states with a tendency to secondary infections. The content of lipoproteins and cholesterol in the blood also decreases. Along with proteinuria, a marked enzyme is noted. Patients lose digestive enzymes (enterokinase, etc.), a number of enzyme inhibitors (alpha-antitrypsin, etc.), calcium and other substances with feces.

The rate of synthesis and destruction of albumin is determined by the administration of radioactive albumin intravenously to study the level of radioactivity in serum. Exudative enteropathy is confirmed by a reduced amount of intravascular and total pool of albumin, its constant or accelerated synthesis, a markedly shortened period of "life" and an increase in protein losses with feces. A non-invasive method for diagnosing exudative enteropathy, which does not require the use of radioactive isotopes, was also developed. The method is based on the determination of the intestinal clearance of alpha1-antitrypsin. This antiferment, when it is determined in feces and blood, becomes an endogenous marker of protein loss with feces. Its content in healthy individuals is 0.4 mg / g dry weight of stool, with intensive lymphangiectasia - 16.2 mg/g, in patients with graft-versus-host disease with exudative enteropathy - 18.8 - 38.8 mg/g.

Intestinal Intoxication

Intestinal autointoxication develops with a decrease in intestinal secretion, intestinal obstruction, mechanical and toxic damage to the intestinal mucosa, etc. Gastrointestinal tract in humans and animals is a natural habitat for microorganisms. Especially rich in the microflora is the large intestine. In vertebrates, the number of microbes in it is 1010-1011 / g of intestinal contents. In the small intestine, their amount is much less due to the bactericidal properties of gastric juice and, probably, endogenous antimicrobial factors of the small intestine. For a day with feces, trillions of bacteria are excreted. The microflora of the intestine causes in it the processes of fermentation and

putrefaction, but in norm they are not expressed clearly. The resulting toxic substances are eliminated from the body or rendered harmless, and intoxication does not occur. The processes of fermentation and putrefaction intensify with a decrease in intestinal secretion and an increase in flatulence, which usually accompanies constipation. The most pronounced intoxication is with intestinal obstruction. Essential is the mechanical and toxic damage to the intestinal mucosa. In the pathological process, the nervous apparatus of the intestine is involved, which leads to disruption of its motor and secretory functions and aggravates trophic disorders in the intestinal wall. Develops dysbacteriosis, characterized by a decrease in the number of microorganisms that are constantly present in the intestine (bifidumbacterium, E. coli, lactobacilli). The ratio of bacteria in different

rts of the intestine with increased reproduction is conditional-pathogenic and the appearance of pathogenic flora. Secondary fermentopathy occurs. All this leads to an intensification of the processes of fermentation and decay. Amino acids turn into toxic substances: hydrogen sulphide, skatole, cresol, indole, phenol, etc. When decarboxylating amino acids, biogenic amines are formed: histamine, cadaverine, putrescine. Partially they are rendered harmless in the intestinal wall under the influence of aminoxidase. However, with an excess of these substances, they are absorbed into the blood and through the portal vein system enter the liver. In the liver, indole and scatol are rendered harmless by binding sulfuric and glucuronic acids (indoxylsulfur, skatoxylsulfur, indoxylglucuronic acid and skatoxyl glucuronic acid are formed). Other toxic substances in the liver are deaminated, oxidized, and also transformed into harmless compounds. Partly they are excreted by the kidneys. If a lot of toxic substances are formed and the processes of putrefaction in the intestine continue for a long time, then there is an overload of the detoxifying function of the liver. With the development of hepatic insufficiency, the main importance for the removal of toxins circulating in the blood is acquired by the kidneys. But if the functional state of the kidneys suffers, then the phenomena of intestinal intoxication are increasing. Being in the intestine, toxic substances reflexively influence various organs and systems. In addition to feelings of spreading in the abdomen, swelling, rumbling in the intestines, nausea, there is an unpleasant taste in the mouth, there are weakness, weakness, fatigue, headaches, decreased appetite, insomnia, depression. With chronic intestinal intoxication, dystrophic changes in organs, including the myocardium, can occur.

The toxic substances circulating in the blood act on the receptors of the vessels and the centers of the brain. This can lead to violations of the cardiovascular system in the form of lowering blood pressure, weakening heartbeats. Possible respiratory depression. Reducing glycogen stores in the liver and hypoglycemia can lead to a coma. Chronic intestinal intoxication leads to anorexia and severe digestive disturbances due to suppression of the glands of the digestive tract.

CONSEQUENCES OF DELETING VARIOUS DEPARTMENTS OF THE GASTROINTESTINAL TRACT

The first experiments to study this issue were carried out in the experimental laboratory of E.S. London, Removing the cardiac part of the stomach in dogs led to bulimia and polyphagia. Eating often ended with vomiting, which resembled an attack of suffocation and was accompanied by a contraction of the neck muscles. The peculiarities of vomiting were explained by the fact that it arose in the presence of food in the esophagus (esophageal vomiting).

Turning off the gatekeeper (imposing gastroenteroanastomosis) caused a violation of the evacuation of food chyme from the stomach, the more pronounced anastomosis was applied to the lower part of the small intestine. Removal of the bottom of the stomach led to a violation of its

reservoir and secretory functions. The disorders were more pronounced with complete removal of the stomach, but its functions were gradually taken over by the underlying parts of the digestive tract.

After surgical operations such as pyloroplasty, gastrectomy, anthrectomy leading to disruption of the functions of the antral part of the stomach or pylorus, a specific symptom complex known as "dumping syndrome" is observed due to rapid evacuation of stomach contents into the intestine. Early dumping syndrome develops within the first hour after eating, when there is a feeling of rapid saturation, loose stools, bloating and abdominal pain. There are also vegetative reactions in the form of facial flushing, sweating, and tachycardia. These symptoms are associated with the intake of a large amount of hypertonic chyme from the stomach or its stump into the proximal parts of the small intestine. In this case, there is a reflex stimulation of the motility, which causes diarrhea and a sudden increase in the fluid content in the small intestine, which leads to its extension. As a consequence, hypovolemia is possible. Symptomatics is enhanced by the release of intestinal hormones and vasoactive mediators (bradykinin, serotonin, etc.), which cause vegetative disorders. Late dumping syndrome includes dizziness, headaches, trembling, palpitations, sweating, hunger, confusion and sometimes fainting after 1.5-3 hours after eating. Symptoms can appear earlier, if food products contain a large number of simple carbohydrates, especially sucrose. This syndrome is

caused by hypoglycemia. Initially, there is a rapid increase in the amount of glucose in the blood (hyperglycemia) because of the sudden intake of sugar-containing food components from the stomach into the proximal parts of the small intestine, which is followed by hypoglycemia. Rapid absorption of carbohydrates stimulates the release of insulin, which circulates in the blood longer than glucose, and eventually develops hypoglycemia.

PATHOPHYSIOLOGY LIVER

The liver is a vital organ with a variety of functions aimed at maintaining homeostasis in the body. The liver is a "large chemical laboratory" (K. Ludwig), the central organ of the metabolism of proteins, carbohydrates, fats, and medicines. The structural and functional unit of the liver is the hepatic acinus. In the liver occur:

1. The formation of bile pigments, the synthesis of cholesterol, the synthesis and secretion of bile.

2. Neutralization of toxic products coming from the gastrointestinal tract.

3. Synthesis of proteins, including blood plasma proteins, their deposition, reamination and deamination of amino acids, urea formation and the synthesis of creatine.

4. Synthesis of glycogen from monosaccharides and non-carbohydrate products.

5. Oxidation of fatty acids, the formation of ketone bodies.

6. Depositing and exchanging many vitamins (A, PP, B, D, K), depositing ions of iron, copper, zinc, manganese, molybdenum, etc.

7. Synthesis of most enzymes that provide metabolic processes.

8. Regulation of the balance between coagulation and anticoagulation systems of blood, the formation of heparin.

9. Destruction of some microorganisms, bacterial and other toxins.

10. Depositing of blood plasma and shaped elements, regulation of the blood system.

11. Hood formation in the fetus.

LIVER INSUFFICIENCY

General etiology and pathogenesis of liver function disorders

Among the numerous etiological factors, the most important are:

1. Infectious agents, primarily hepatotropic viruses (A, B, C, D, E, F, G, TTV, etc.). Identification of these viruses became possible due to the method of enzyme immunoassay with determination of antigens and antibodies, polymerase chain reaction with the determination of RNA or DNA viruses. Epstein-Barr viruses, cytomegalovirus, herpes simplex virus, Coxsackie virus, etc. play a smaller role. Some infections (brucellosis, leptospirosis, salmonellosis, etc.) can also cause impaired liver function, but this is already seen as a secondary syndrome.
2. Acute or chronic alcohol intoxication.

3. Hepatotoxic substances-xenobiotics:

- industrial poisons (derivatives of benzene, lead, mercury, toluene, organophosphorus compounds, chloroform, carbon tetrachloride, acids, nitro-colors, alkalis, etc.);
- medicinal preparations (antibiotics, sulfonamides, narcotic, hypnotic and anti-inflammatory drugs

- brufen, indomethacin, paracetamol, etc.);

- mushroom poison - phalloidin, phalloin, contained in pale toadstool;

- aflatoxins (mold fungi);

- dyes, household chemical substances;

4. Parasitic, tumor lesions of the liver.

5. Disturbance of outflow of bile.

6. Disturbance of blood supply, prolonged venous congestion in the liver (hypoxia of hepatocytes).

7. Hereditary disorders of metabolism (with Wilson-Konovalov's disease, hemochromatosis, a1-antitrypsin deficiency).

Damage to the liver can be primary (for example, with viral hepatitis) or secondary (due to generalized diseases - tuberculosis, alcoholic illness, sepsis, etc.).

Pathogenesis of hepatocyte damage. Despite the constantly expanding volume of knowledge about the causes of liver diseases, many questions about the mechanism of the onset and progression of this pathology remain open.

Nevertheless, in the pathogenesis of viral liver damage, the following mechanisms can be distinguished:

1. damage, consisting of:

- n cytolytic action (due to the replication of viral particles within the cell and its complete destruction);

- in cytopathic action (damage to cellular organelles while maintaining the cell itself).

2. Immune mediated damage to hepatocytes:

- activation of resident liver macrophages (Kupffer cells, hepatic sinusoid endotheliocytes) and induction of a specific T- and / or B-immune response;
- activation of cytotoxic lymphocytes (CTL-CB8 +) and T-CD4 + lymphocytes, which results in the destruction of hepatocytes containing viral antigenic determinants;
- activation of the humoral immune response with the synthesis of specific antibodies (M- and G-classes) mediating complement-dependent lysis of immune complexes or antibody-dependent cellular cytotoxicity.

3. Induction of hepatocyte apoptosis:

- cytotoxic lymphocytes cause apoptosis of infected cells (via attachment to Fas-receptors of infected hepatocytes, which are expressed in a pre-infection);

- activation of apoptosis by viral proteins formed during viral replication (hepatitis B virus X-protein and co-protein of hepatitis C virus);
- Increased sensitivity of infected hepatocytes to cytokines (eg, TNF-α) secreted by immunocompetent cells during specific effector (CTL-CB8 +, T-CD4 +, normal killer) immune or autoimmune reactions.

4. Autoimmune mechanism: when exposed to pathogenic factors, the hepatocyte acquires new antigenic determinants and becomes an autoantigen. The virus, damaging the membrane of the hepatocyte, releases membrane lipoprotein, which is part of the structure of a specific hepatic antigen. In some cases, there may be a genetic defect in the immune system ("weakness" of T suppressors). The lack of suppressors increases the production of antibodies and the formation of immune complexes, which causes autoimmune lesions, accompanied by the death of hepatocytes and the involvement of other organs and systems in the pathological process (autoantibodies IgM and G markers of autoimmune hepatitis are formed). Perhaps in the development of autoimmune lesions, the existence of molecular mimicry between the AH of the virus and epitopes of host cells plays a significant role, which causes the lymphocytes to be sensitized to the lipoprotein of liver membranes, mitochondrial and other autoantigens.

In addition, in the pathogenesis of viral defeat, it is necessary to take into account the relationship between host and virus factors. The host factors (genetic, age, initial state of antiviral immunity) determine one or another response to infection, the possibility of elimination or persistence of the virus, the nature of the immune response.

Mechanism of damage to hepatocytes by toxic agents. Toxic agents can have a direct damaging effect on the liver, resulting in the development of dystrophic changes up to irreversible necrosis (poison pale toadstool). A number of xenobiotics do not themselves induce necrosis of hepatocytes, but in the body they can undergo biotransformation with the formation of metabolites that have a damaging effect (tetracycline, salicylates, ethanol). Thus, the main metabolite of ethanol

is acetaldehyde (85% of ethanol is converted to acetaldehyde under the influence of the cytosolic enzyme alcohol dehydrogenase).

Acetaldehyde is a chemically active molecule capable of binding to albumin, hemoglobin, tubulin, actin, etc., thus forming compounds that are capable of remaining in the liver tissue for a long period even after the completion of the metabolism of ethanol. The association of acetaldehyde with cytoskeleton proteins can lead to irreversible cell damage, disrupting the secretion of the protein and contributing to the formation of balloon dystrophy of hepatocytes (protein and water retention).

In addition, in the mechanism of damage to hepatocytes under the influence of ethanol, the following main effects are distinguished:

1. Enhancement of lipid peroxidation causes damage to cell membranes, leading to an increase in their permeability and, as a consequence, disruption of transmembrane transport, cellular receptors, membrane-bound enzymes.

2. Disturbance of mitochondrial functions (chronic alcohol consumption reduces the activity of mitochondrial enzymes, there is an uncoupling of oxidation and phosphorylation, which is accompanied by a decrease in the synthesis of ATP).

3. Suppression of DNA repair in cells and activation of apoptosis.

4. Activation of the complement system and stimulation of products superoxide by neutrophils, etc.

In a number of cases, immune mechanisms play a role, which are included when drugs or metabolites, acting as haptens, transform hepatocyte proteins into immunogens.

The main liver diseases are hepatitis and cirrhosis.

Hepatitis

Hepatitis is characterized by diffuse inflammation of the liver tissue. Among the hepatitis distinguish primary (independent nosological forms) and secondary (develop with other diseases).

Primary hepatitis for etiology are more often viral, alcoholic, medicinal, autoimmune.

Downstream they are divided into acute and chronic.

Acute hepatitis is characterized by dystrophic and necrobiotic changes in hepatocytes, reactive changes in interstitial tissue with the formation of inflammatory infiltrates in the stroma, as well as a vascular reaction characteristic of inflammation.

Viral hepatitis A and E are related to diseases with a fecal-oral mechanism of infection transmission and a reversible course. Carrier and transition to a chronic form, as a rule, are not noted. Infection with virus A is realized by water, food and contact-household transmission routes. Among the sick, about 80% are children under the age of 15. Viral hepatitis A (Botkin's disease) has a seasonal increase in morbidity in the summer-autumn period. After the transferred disease remains lifelong immunity, caused by antibodies antHAV-IgG.

Hepatitis B, C, D have a parenteral mechanism for the transmission of the pathogen. Viral hepatitis B can occur in the form of a mono-or mixed infection. According to WHO, hepatitis B affects more than 2 million people worldwide, the number of carriers - more than 350 million.

The transmission paths can be natural and artificial. Natural ways of transmission of infection:

1) sexual - during sexual intercourse, especially homo- and bisexual;
2) vertical - from the mother to the fetus;

3) household infection through shaving, manicure devices, toothbrushes, etc.

The artificial way of transmission is the penetration of the virus through the damaged skin, mucous membranes under various manipulations (operations, injections, endoscopic procedures, tattooing, etc.).

A group of people at risk for hepatitis B are drug addicts; Medical workers who have contact with the blood of patients (dentists, lab technicians, obstetrician-gynecologists, surgeons, etc.); People leading a promiscuous sex life, homosexuals, as well as persons who are addicted to tattooing, piercing, etc.

Sources of infection, the mechanism and ways of transmission of hepatitis C are largely similar to the hepatitis B virus. Most often, infection occurs when blood and its transfusions are transfused. The most numerous at risk are drug addicts with parenteral use of drugs. Transmission of the pathogen in everyday life with heterosexual and homosexual contacts, from an infected mother to a newborn can take place, but is less likely to be realized than in viral hepatitis B.

All viral hepatitis under the manifest course are four periods:

1. Incubation (from 2 to 26 weeks).
2. Prodromal (pre-jaundiced) - the detection of nonspecific symptoms.

3. Jaundice - the period of the unfolded clinical picture.

4. The period of convalescence.

The following clinical and morphological forms of acute viral hepatitis are distinguished:

1. Cyclic icteric (classical manifestation of viral hepatitis).

2. Without jaundice (80% of viral hepatitis C and 70% of viral hepatitis B).

3. Subclinical (inpatient).

Lightning or fulminant (with massive progressive necrosis of hepatocytes).

4. Cholestatic (involving small bile ducts in the process).

1. Complete recovery.

2. Recovering with residual effects (post-hepatitis syndrome, dyskinesia of the biliary tract, hepatophybrosis).

3. Transition to chronic hepatitis.

4. Development of cirrhosis of the liver.

5. Risk of hepatocellular carcinoma.

Chronic hepatitis. About chronic hepatitis speak in the event that acute hepatitis lasts more than 6 months without noticeable improvement. The duration of its flow - months, years, tens of years.

Chronic hepatitis - diffuse inflammatory-dystrophic chronic liver damage of various etiologies, morphologically characterized by dystrophy of hepatic cells, histiolymphoplasmocytic infiltration and moderate portal fibrosis, hyperplasia of stellate endotheliocytes while maintaining the lobular structure of the liver.

Chronic hepatitis is an independent nosological unit, but it can be part of some other disease, for example systemic lupus erythematosus (in this case it is considered a syndrome).

In addition, it is necessary to distinguish chronic hepatitis and nonspecific reactive hepatitis, which is a syndrome of various pathological processes, in particular diseases of the gastrointestinal tract (peptic ulcer of stomach and duodenum, stomach cancer, pancreatitis, etc.). The course of nonspecific reactive hepatitis depends on the underlying disease. The outlook is usually favorable.

The International Congress of Gastroenterologists, held in Los Angeles in 1994, proposed the classification of chronic hepatitis, taking into account the etiology, the degree of activity and the stage of chronicization of the process.

Taking into account the peculiarities of etiology, it is suggested to isolate 4 types of chronic hepatitis: viral, autoimmune, medicinal, cryptogenic (of unknown etiology, idiopathic). But, as can be seen from the cited classification, among the etiological forms of chronic hepatitis there are no such species as alcoholic, hereditary, mixed. The classification proposed in 1993 by S.D. Podymova, which distinguishes 8 types of chronic hepatitis:

1. Viral hepatitis (B, C, D).
2. Medicinal hepatitis.

3. Toxic hepatitis.

4. Alcoholic hepatitis.

5. Genetically determined or metabolic hepatitis (with Wilson-Konovalov disease, hemochromatosis).
6. Idiopathic (autoimmune, etc.).

7. Nonspecific reactive hepatitis.

8. Secondary biliary hepatitis with extrahepatic cholestasis.

The degree of activity of the process is established on the basis of laboratory enzyme tests and a morphological study of liver biopsy. Among the laboratory tests, the most informative is the determination of the activity of alanine aminotransferase (ALT) and aspartate aminotransferase (ASAT). In addition, the index of histological activity (IHA) is also known, known as the Knodell

index, which takes into account the morphological components of chronic hepatitis-necrosis intralobular or periportal, dystrophy, inflammatory infiltrates, fibrosis.

Proceeding from this, 4 levels of activity are distinguished: 1) minimal (IHA - 1-3 points); 2) weak (IHA - 4-8 points); 3) moderate (IHA - 9-12 points); 4) severe, severe degree (IHA - 13-18 points).

In determining the degree of activity of the process, extrahepatic manifestations must be considered. Patients may have glomerulonephritis, nodular periarteritis, arthralgia, etc. This can mask the presence of liver pathology.

The stage of chronicization is determined by the severity and nature of fibrosis:

0) without fibrosis;

1) mild portal and periportal fibrosis;

2) mild fibrosis with portoportal septa;

3) severe fibrosis with port-central septa;

4) cirrhosis of the liver (considered as an irreversible stage of chronic hepatitis): A) with manifestations of portal hypertension;
B) with signs of hepatic insufficiency.

Cirrhosis of the liver

Cirrhosis of the liver is a chronic, progressive polyhepatic disease of the liver characterized by a significant decrease in the number of functioning hepatocytes, increasing fibrosis, restructuring of the normal structure of the parenchyma and the vascular system of the liver, the appearance of regeneration sites and the subsequent development of hepatic insufficiency and portal hypertension.

Pathogenesis. As a result of the direct action of the etiological factor and the developing immune response, hepatocyte death occurs, massive parenchyma necrosis may occur. On the site of the dead cells the reticulin frame collapses and a scar forms. Vessels of the portal tract approach the central vein and conditions are created for the transfer of blood from the hepatic artery and portal vein into the central one, bypassing the sinusoids. The current of blood bypassing the sinusoid vessels of intact sites leads to their ischemia followed by necrosis. As a result of necrosis, substances that stimulate liver regeneration are released, regeneration nodes are formed, which compress the vessels and contribute to an even greater violation of blood flow. In addition, the decay products of hepatocytes stimulate the inflammatory response, the spread of inflammatory infiltrates, resulting in intense fibrosis. Vascular anastomoses are formed, due to which the blood, bypassing the parenchyma of the lobules, immediately enters the hepatic vein system, which leads to the development of ischemia and necrosis. This is also facilitated by compression of the venous vessels of the liver with a connective tissue.

Classification of cirrhosis of the liver. The first classification of liver cirrhosis was adopted by the V Pan American Congress of Gastroenterologists in 1956. According to this classification,

postnecrotic, portal, biliary (with or without extrahepatic biliary tract obstruction) and mixed cirrhosis were identified. In 1978, WHO recommended a morphological classification: small-node (micronodular), coarse nodular (macronodular), incomplete septal and mixed (macro-microiodular).

Depending on the role of the genetic factor, hereditary and acquired cirrhosis is distinguished. Among the acquired cirrhoses of the liver with established etiology, toxic (more often alcoholic cirrhosis of the liver), infectious (more often viral cirrhosis), biliary (with lesion of intra- and extrahepatic bile ducts), exchange-alimentary, dyscirculatory (with congestive heart failure) and mixed origin. Hereditary include cirrhosis in hemochromatosis, Wilson-Konovalov's disease, insufficiency of a1-antitrypsin.

Classification of cirrhosis of the liver (according to AS Loginov, Yu.E. Blok, 1987):

- On etiology: viral, alcoholic, autoimmune, toxic, genetically conditioned, cardiac, due to intrahepatic cholestasis, cryptogenic;
- by morphology: micronodular, macronodular, mixed, incomplete septal, biliary;
- depending on the stage of hepatic insufficiency: compensated, subcompensated, decompensated.

In addition, activity (minimal, moderate, severe) and phase (active and inactive) of the process are taken into account.

The main clinical and laboratory syndromes of cirrhosis:

1. Jaundice (jaundice forms can be diagnosed, but with biliary cirrhosis jaundice is always observed).

2. Portal hypertension. Syndrome of portal hypertension arises from the violation of blood flow in the portal vein.

There are 3 types of portal hypertension: subhepatic, intrahepatic, superhepatic.

Superhepatic portal hypertension occurs due to compression or thrombosis of the hepatic veins, right ventricular failure, pericarditis and is characterized by difficulty in venous outflow from the liver.

Intrahepatic portal hypertension develops with cirrhosis, tumors, echinococcosis and other liver lesions.

Sub-hepatic portal hypertension is associated with thrombosis or compression of the portal vein (scars, compression with ascitic fluid, tumor) or with abnormalities of its development.

The main link in the pathogenesis of portal hypertension is the stagnation of blood in the portal vein system.

Portal hypertension is accompanied by compensatory shunting of blood through portocaval anastomoses (the lower third of the esophagus and the cardiac part of the stomach, the anterior abdominal wall in the navel - the head of Medusa, the hemorrhoidal veins system) followed by

varicose vasodilation. This makes the walls of the vessels vulnerable to mechanical damage, the outcome of which can be gastrointestinal bleeding, often ending lethal.

As a result of portal hypertension, splenomegaly develops (enlarged spleen), hypersplenism (increased spleen function), resulting in pancytopenia (thrombocytopenia, anemia, leukopenia) and ascites (accumulation of fluid in the abdominal cavity).

In the mechanism of development of ascites, the following pathogenetic factors play a role:

- increased pressure in the portal vein;
- decrease in oncotic blood pressure due to a violation of the protein-synthesizing function of the liver;
- impaired lymph circulation;

- secondary aldosteronism (due to decreased metabolism in the liver), which is accompanied by hypernatremia, hypokalemia, hypervolemia.

3. Asthenovegetative syndrome (weakness, fatigue, mood lability, nervousness, emaciation).

4. Hemorrhagic syndrome - with hepatic diseases, deficiency of I, II, V, VII, IX, X and other factors of coagulation hemostasis due to impaired hepatic synthesis and inadequate absorption of vitamin K. In liver lesions, the activity of the fibrinolytic system increases (insufficient inhibition of hepatic Activators of plasmin), the DIC-syndrome can develop. Due to splenomegaly and hypersplenism, there is a disruption of vascular-platelet hemostasis (thrombocytopenia), which is accompanied by the formation of bruises and petechial hemorrhages in the skin, nasal and uterine

bleeding, patients have increased prothrombin time, clotting time and bleeding time. In clinical practice, a prothrombin ratio is determined that characterizes the total activity of clotting factors - prothrombin, proconvertin, acclerin, and the Stewart-Prower factor. A distinct decrease in prothrombin ratio is noted in acute and chronic liver diseases, when there is a significant necrosis of hepatocytes. A sudden and sharp decrease in prothrombin ratio in patients with liver disease always indicates a marked hepatic-cell insufficiency and an impending hepatic coma. If coagulopathy accrues in connection with cholestasis or intestinal dysfunction (due to the use of broad-spectrum antibiotics), then it is possible to improve the indices against intramuscular injection of vitamin K (10 mg). However, if hypoprothrombinemia is associated with hepatic insufficiency, then the coagulation with exogenous administration of vitamin K can not be corrected.

5. Skin itching is the earliest and permanent, and sometimes the only manifestation of cirrhosis. The nature of pruritus is not fully understood, but it has been established that the mediators of pruritus are proteases released in the skin under the action of bile acids.

Hepatocellular insufficiency

Hepatic-cell failure is a violation of one, several or many liver functions that result from damage to hepatocytes. Isolate acute and chronic hepatic insufficiency.

Acute liver failure is a syndrome that is associated with massive necrosis of hepatocytes, leading to severe severe impairment of liver function. The most frequent causes of acute hepatic

insufficiency are fulminant forms of acute viral or toxic hepatitis, more rare are cytomegalovirus, infectious mononucleosis virus, rickettsiosis, mycoplasmosis and mixed fungal infections leading to

severe liver necrosis. In addition, the causes of acute hepatic insufficiency can be acute fatty hepatosis in pregnant women, Reye's syndrome, postoperative state, as well as liver abscesses, purulent cholangitis, sepsis. Reye syndrome - acute encephalopathy with cerebral edema and fatty liver infiltration, occurs in newborns, children, adolescents (usually aged 4-12 years), is associated with a viral infection (chicken pox, influenza) and the intake of drugs containing acetylsalicylic acid. The most common cause of its occurrence is illiterate prescription of aspirin in acute viral infection, which is contraindicated, especially in children.

Chronic hepatic insufficiency develops in chronic liver diseases of infectious and non-infectious etiology, in the late stage of liver cirrhosis, and also after surgical interventions on portocaval shunting.

Isolate small hepatic insufficiency (hepatodepressive syndrome) and major hepatic insufficiency (hepatarga). In hepatarga, in contrast to small liver failure, there are signs of hepatic encephalopathy.

With true hepatic-cell insufficiency, the following syndromes develop:

1) the syndrome of impaired nutrition (worsening of appetite, nausea, abdominal pain, unstable stool, weight loss, the appearance of anemia). The basis of this syndrome is the violation of metabolic processes;

2) fever syndrome (up to 38 ° C and even up to 40 ° C) with a nuclear shift of the leukocyte formula to the left. This syndrome is associated with necrosis of hepatocytes, the intake of toxic products into the blood, bacteremia (possibly the entry of microorganisms into the blood from the intestine);

3) jaundice syndrome;

4) the syndrome of endocrine disorders. There is a decrease in libido, testicular atrophy, infertility, gynecomastia, mammary atrophy, uterus, menstrual cycle disorders. Possible development of diabetes mellitus and secondary aldosteronism;

5) syndrome of impaired hemodynamics - the accumulation of histamine-like and other vasoactive substances, leading to vasodilation (compensatory increase in cardiac output in combination with hypotension). Reduction of albumin synthesis and a decrease in oncotic pressure, as well as the development of secondary hyperaldosteronism, cause edematous-ascitic syndrome;

6) a specific hepatic odor (fetor hepatitis) is associated with the release of methyl mercaptan. This substance is formed from methionine, which accumulates in connection with a violation in the liver of the processes of demethylation and can be contained in the exhaled air;

7) "liver signs" - telangiectasia and palmar erythema;

8) syndrome of hemorrhagic diathesis - a decrease in the synthesis of clotting factors and frequent bleeding causes the possibility of developing DIC syndrome.

Hepatic insufficiency is characterized by the following laboratory parameters: in the blood serum, the albumin content (an extremely important indicator!) And clotting factors decreases, cholesterol level decreases, bilirubin content increases, phenol accumulation, ammonia accumulation and aminotransferase activity increase.

Hepatic insufficiency can lead to the development of hepatic encephalopathy and hepatic coma.

Hepatic encephalopathy (hepatocerebral syndrome) - a neuropsychic disorder with a violation of intelligence, consciousness, reflex activity and the functions of vital organs. Isolate acute and chronic hepatic encephalopathy (the latter can last for years with periodic episodes of precoma).

There are 4 stages of hepatic encephalopathy in accordance with the criteria adopted by the International Association for the Study of the liver.

Stage I - prodromal. There are initial changes in the psyche - slowing of thinking, behavior disorders, disorientation of the patient in the surrounding reality, sleep disorders (drowsiness during the day, sleeplessness at night), tearfulness, weak-willedness. Patients may fall into periods of stupor with a fixation of the glance. A characteristic and rather early symptom is a change in handwriting (dysgraphia). EEG, as a rule, is not changed.

Stage II - beginning coma. The symptoms of stage I are aggravated. Part of the patients have convulsions and psychomotor agitation, during which they try to escape from the ward. Stereotypic movements are formed, for example, clapping tremor of hands (asterixis), deafening. Patients can become untidy, familiar. Often the body temperature rises, liver odor from the mouth appears. On the EEG, minor initial changes are found.

Stage III - stupor. Patients are in a prolonged sleep, interrupted by rare awakenings. In the neurological status, the rigidity of the musculature, the masklike face, the slowing down of voluntary movements, gross speech disorders (dysarthria), hyperreflexia, the clonus of the patella, etc. are noted. EEGs reveal deep disturbances, the shape of the curve approaches the isoline.

Stage IV - coma. The consciousness is lost, there is no reaction to the pain stimulus, in the initial phase pathological reflexes are noted. In the future, the pupils dilate, reflexes fade, blood pressure drops, the breath of Kussmaul or Cheyne-Stokes may appear, and death occurs.

Consequently, the hepatic coma is the terminal stage of hepatic encephalopathy, characterized by loss of consciousness, lack of reflexes and a violation of the basic functions of the organs.

Factors that provoke the rapid development of coma: protein food, the intake of diuretics (not saving potassium), sedatives / Mortality of patients in stage IV, reaches 80-90%.

According to the etiology, 4 types of coma are distinguished: 1) endogenous; 2) exogenous; 3) mixed; 4) Electrolyte.

Endogenous (true) coma develops with massive necrosis of hepatocytes in cases of acute hepatic insufficiency, which is characterized by a disruption of many liver functions, marked bleeding, increased free bilirubin level in the blood, hepatic hyperaemiaemia, liver odor from the mouth. The treatment lends itself hardly.

Exogenous (shunt, by-pass) coma often occurs with cirrhosis in the case of the development of powerful collaterals between the portal and lower vena cava systems. It can also occur with artificial application of portocaval anastomoses, in which blood from the intestine, rich in biologically active substances (BAS - ammonia, cadaverine, putrescine, etc.), bypasses the liver, pours into the total bloodstream and has a toxic effect on the brain. This form is easier to treat (blood dialysis, intestinal cleansing, broad-spectrum antibiotics), has a more favorable prognosis.

Mixed coma is more common, which develops with far-reaching cirrhosis of the liver with the death of a large number of hepatocytes and the presence of portocaval anastomoses.

Electrolyte coma is associated with the development of hypokalemia. In the pathogenesis, secondary aldosteronism plays a role, the use of diuretic drugs that do not conserve potassium, frequent vomiting, diarrhea, which leads to a violation of the electrolyte balance (hypokalemia, alkalosis). Is manifested by severe weakness, decreased muscle tone, adynamia, convulsive twitching of the calf muscles, a violation of cardiac activity (tachycardia, the rhythm of the "woodpecker"), a violation of breathing. Treatment of electrolyte coma - the use of potassium preparations.

Pathogenesis of hepatic encephalopathy and coma. The mechanism of development of hepatic encephalopathy is not fully understood. There are three most common theories:

1. Theory of toxic effects of ammonia. Ammonia is formed in all tissues where proteins and amino acids are exchanged. However, the greatest amount of it enters the bloodstream from the gastrointestinal tract. The source of ammonia in the intestine is any substance that contains nitrogen: decaying food proteins, some polypeptides, amino acids and urea, which came from the blood. The release of ammonia occurs with the help of enzymes - urease and aminoacid oxidase of intestinal microflora and intestinal mucosa. 80% of ammonia coming from the intestine through the portal vein into the liver, is converted to urea (ornithine cycle). Ammonia not included in the ornithine cycle, as well as various amino and keto acids (glutamate, a-ketoglutarate, etc.) under the influence of glutamate synthetase, glutamine is formed. Both mechanisms prevent the entry of toxic ammonia into the total bloodstream. But with liver failure, an increase in the concentration of ammonia is observed not only in the blood, but also in the cerebral fluid. The entry of ammonium cations through the blood-brain barrier into the neurons of the brain causes their energy starvation (ammonia combines with a-ketoglutaric acid to form glutamine, as a result, an outflow of a-

ketoglutarate from the CTA is observed, which leads to a decrease in the synthesis of ATP) and, as a consequence, CNS.

Theory of false neurotransmitters (transmitto - transmit). Dysfunction of the liver helps to reduce the concentration of amino acids with branched chain - valine, leucine, isoleucine, which are used as a source of energy, and increase the level of aromatic amino acids - phenylalanine, tyrosine, tryptophan (their metabolism is normally carried out in the liver, with liver diseases, the concentration of these amino acids increases Not only in the blood, but also in the urine - aminoaciduria).

Normally the ratio between branched chain amino acids and aromatic amino acids is 3-3.5. With pathology, this indicator decreases. For these amino acids, there is a single transport system, and aromatic acids use a liberated transport system to penetrate the GEB into the brain, where the enzyme system involved in the synthesis of normal mediators is inhibited. The synthesis of dopamine and norepinephrine decreases and false neutrotransmiters (octopamine, β-phenylethylamine, etc.) are formed.

The theory of strengthened GABAergic transmission. The essence of this theory is that in pathology, the clearance of GABA in the liver is violated (GABA is formed in the reaction of decarboxylation of glutamic acid). GABA accumulates in brain tissue, exerting an inhibitory effect on neurons, disrupting their function, leading to the development of hepatic encephalopathy.

In addition, an important role in the mechanism of the development of hepatic encephalopathy and coma is played by other disorders: intoxication, acid-base, water-electrolyte (hypokalemia, hypernatremia) and hemodynamic disorders.

Violation of the detoxification and clearance functions of the liver

The liver is involved in the neutralization of toxic products endo - and exogenous origin. Detoxication is carried out by oxidative processes, reducing reactions, and also by hydrolysis. Oxidation is the most important reaction, which requires the presence of reduced NADP-2H and molecular oxygen. An important role is played by the transport system component - cytochrome P450. Some compounds are rendered harmless by including them in the synthesis of substances used in metabolism (for example, the inclusion of ammonia in the synthesis of urea).

The reaction of detoxification is conjugation, in which neutralization occurs due to a compound with glucuronic or sulfuric acids. So steroid hormones, bilirubin, bile acids, aromatic hydrocarbons, etc. are inactivated. Neutralization can also occur by binding with glycerol, taurine, cysteine, when binary compounds of bile, benzoic and nicotinic acids are formed. A number of substances are absorbed from the blood and excreted with bile in unchanged form.

In the liver, fixation and phagocytosis of various microbes occur due to the active activity of the cells of the reticuloendothelial system. Kupffer cells of the liver have not only pronounced phagocytic activity in relation to microbes, but also provide purification of blood from endotoxins of the intestinal microflora. The ability of the liver to metabolize foreign compounds can be enhanced by the introduction of inductor substances into the body. Some of them, for example phenobarbital, stimulate the metabolism of a number of xenobiotics in hepatocytes by inducing the synthesis of cytochrome P450 and NADP-2H-cytochrome C reductase and increase the activity of the enzyme glucuronyltransferase.

In a number of liver diseases, especially with cirrhosis, its detoxification function is usually inhibited. The function of the reticuloendothelial system ("blockade" of phagocytosis by the products of cell decay) falls out, hemodynamic changes appear (portocaval anastomoses, decreased blood supply to the liver). The results of these disorders are compared with the consequences of portocaval shunting, when the systemic blood flow is filled with products coming from the intestine through the portal vein. This leads to endotoxemia - fever, leukocytosis, erythrocyte hemolysis, renal failure, which is especially pronounced in hepatic coma.

The role of the liver in metabolic disorders

Violation of carbohydrate metabolism. The liver is involved in maintaining a normal level of glucose in the blood serum by glycogenogenesis, glycogenolysis and gluconeogenesis.

The homeostasis of glucose is often disturbed by cirrhosis of the liver. As a rule, at the same time, hyperglycemia and a decrease in glucose tolerance are determined. The level of insulin in the plasma or in the norm, or increased, which is associated with resistance to it. Insulin resistance is explained by the absolute decrease in the ability of the liver to metabolize glucose after a load due to a decrease in the mass of functioning hepatocytes. In patients with cirrhosis, a decrease in the response to insulin may be due to receptor and postreceptor anomalies in hepatocytes.

With cirrhosis of the liver, the level of lactate in the serum can also increase due to the reduced ability of the liver to utilize it for gluconeogenesis.

In severe acute hepatitis, as a rule, there is hypoglycemia, and with cirrhosis of the liver it occurs in the final stage - with hepatic insufficiency. In patients with liver cirrhosis, the role of carbohydrates as an energy source decreases (2% for cirrhosis and 38% for healthy ones) and the role of fats (respectively 86 and 45%) increases with fasting. This is accompanied by the mobilization of triacylglycerols as an energy source. In the final stage of cirrhosis, hypoglycaemia is due to a decrease in the ability of the liver (due to extensive damage to its parenchyma) to synthesize glycogen and a decrease in the production of insulinase (an enzyme that destroys insulin).

Normally, galactose, which enters the body as a part of milk sugar, turns into glucose, but in violation of the functional state of the liver (in acute and chronic diseases), the ability to use galactose is reduced.

Violation of protein and enzyme metabolism in liver diseases manifests itself in a change: the breakdown of proteins (up to amino acids), the synthesis of proteins, deamination, transamination, decarboxylation of amino acids, the formation of urea, uric acid, ammonia, creatine.

As a consequence, the following violations occur:

1. Hypoproteinemia - a decrease in protein level usually reflects a violation of the protein-synthetic function of the liver. Hepatocytes synthesize almost all albumin, up to 85% of globulins. In severe chronic liver diseases, albumin production decreases by more than 2-3 times, but its level decreases slowly due to a prolonged half-life. Therefore, in acute liver failure, the albumin concentration may turn out to be normal, and the violation of the albumin-synthesizing function of the liver will manifest itself only after two to three weeks.
2. Changes in the composition of globulins (high levels of α2 and especially β-globulins) can occur with biliary cirrhosis and serve as a differential sign of the difference between this type of cirrhosis and others. The α2 fraction includes ceruloplasmin proteins, α2-antithrombin, haptoglobin, and α2-macroglobulin. Ceruloplasmin is the main copper-containing plasma protein, which determines its antioxidant activity. A low concentration of this protein can be observed with Wilson-Konovalov's disease and with decompensated liver cirrhosis of any etiology. The level of haptoglobin decreases with chronic liver diseases, with haemolytic crisis. The content of transferrin (a part of β-globulin) decreases with hemochromatosis (a violation of iron metabolism) and with cirrhosis of the liver. In diffuse diseases of the liver, the content of γ-globulins increases significantly, which is associated with an increase in the antigenic stimulation of the immune system. So, with autoimmune hepatitis and cryptogenic cirrhosis, the level of IgG significantly increases. In a healthy person, α-fetoprotein is not detected, since after birth it disappears from the blood, but can appear in it in patients with primary liver cancer (hepatoma) and serves as a marker for this disease in the differential diagnosis of hepatomegaly.
3. Dysproteinemia develops in the synthesis of qualitatively altered globulins in the liver (paraproteins of macroglobulins, cryoglobulins).
4. Violation of the metabolism of amino acids occurs with severe liver damage and leads to an increase in the level of free amino acids in the blood and urine (aminoacidemia, aminoaciduria). In fulminant hepatitis, generalized aminoaciduria with predominant excretion of cystine and tyrosine is noted, which is a prognostically unfavorable feature.

5. Hemorrhagic syndrome develops due to a violation of the synthesis of coagulation factors and inhibitors of coagulation and fibrinolysis.

6. The increase in residual nitrogen and ammonia in the blood is detected when the synthesis of urea is violated (the index of severe hepatic insufficiency).

7. Increase in blood levels of a number of enzymes (aminotransferases, γ-glutamyltranspeptidase, etc.) The most important diagnostic value is the determination of the activity of aminotransferases - ALAT and ASAT in the blood serum. Their activity is the most reliable indicator of the cytolytic process in liver damage. The cytolysis syndrome is most pronounced in acute liver diseases of any genesis, but it acquires special significance for the diagnosis of acute viral hepatitis occurring in anicteric and latent forms. This test is informative even with small damage to the liver cells, which is of great importance for the early diagnosis of diseases. The cytolysis syndrome in liver pathology is characterized by a more pronounced increase in ALT activity compared to ASAT, and the de Ritis coefficient (the ratio of ASAT / ALAT) allows one to judge the severity of liver damage. Normally, this factor is 1.33; With acute viral hepatitis it becomes less than 1.

Of the markers of cholestasis (excretory enzymes) the greatest clinical significance is the determination of the activity of alkaline phosphatase in the blood. Sources of this enzyme, besides the liver, are bone tissue, intestine, placenta, but the main excretory organ is the liver. Therefore, an increase in the activity of alkaline phosphatase is an important indicator of violations of cholestatic (cholestasis). The highest hyperfermentemia is recorded with subhepatic jaundice and biliary cirrhosis. In acute viral hepatitis, the serum alkaline phosphatase level is usually either normal or increases to moderate levels. The diagnostic value of the determination of isoenzyme activity of this enzyme increases due to the fact that a high level of its activity may indicate the possibility of tumors of different localization.

Disturbance of fat metabolism. Fat metabolism in liver pathology is characterized by:

1) violation of the cleavage and absorption of food fats in the intestines, which is associated with a deficiency of bile acids in the pathology of bile formation and bile secretion;

2) a violation of the synthesis and oxidation of triacylglycerols, phospholipids, lipoproteins, cholesterol;

3) an increase in the formation of ketone bodies.

Damage to hepatocytes causes a decrease in the content of cholesterol, its esters and leads to a decrease in the production of bile acids. With a number of liver diseases, the synthesis of lipoproteins decreases, which leads to the accumulation of triacylglycerides followed by infiltration and fatty liver dystrophy. The causes of this condition, in particular, is the lack of food lipotropic substances (choline - an integral part of lecithin, methionine or participating in their synthesis of vitamin B12, folic acid). In the pathogenesis of fatty liver disease, the following main mechanisms can be distinguished: a) fat intake into the liver; B) reduced synthesis of phospholipids and increased production of triacylglycerols from fatty acids; C) reduction of oxidation of fatty acids and lipolysis;

4) a violation of the fat yield from the liver due to the decreased formation of very low density lipoproteins (VLDL is the main transport form of removing triacylglycerols from the liver) or the lack of lipocaine production by the pancreas.

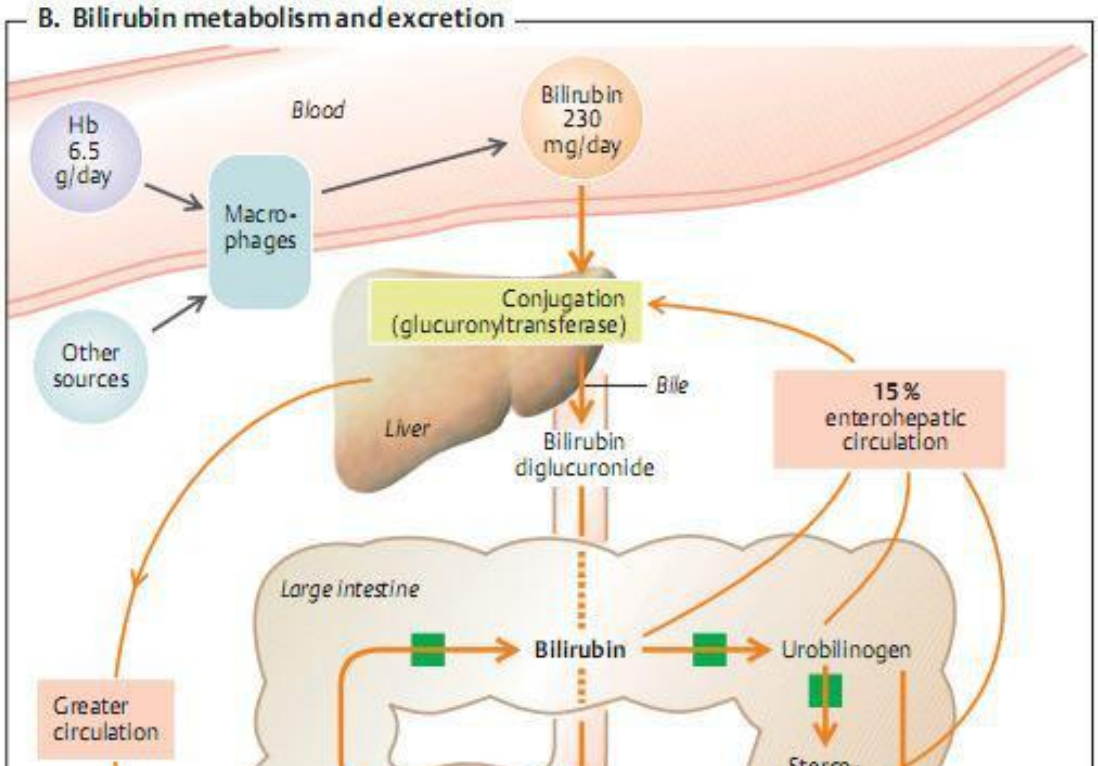
Hepatitis and cirrhosis are often accompanied by a decrease in the formation of esterified cholesterol or a decrease in its total amount in the blood, a violation of the synthesis and oxidation of cholesterol, its excretion with bile. Hypercholesterolemia with mechanical jaundice occurs as a result of cholesterol entering the bile into the bloodstream, and also due to a violation of the synthesis of bile acids from cholesterol.

Disturbance of hormone exchange. The violation of the metabolism of hormones and biologically active substances in liver pathology is manifested in a change in: a) the synthesis of hormones (tyrosine is the precursor of thyroxine, triiodothyronine, catecholamines), transport proteins (transcortin binding 90% glucocorticoids); B) inactivation of hormones (conjugation of steroid hormones with glucuronic and sulfuric acids, enzymatic oxidation of catecholamines under the influence of aminoxidases, insulin cleavage by insulinase); C) inactivation of biologically active substances (oxidative deamination of serotonin and histamine). The defeat of the liver and the violation of inactivation of hormones such as insulin, thyroxine, corticosteroids, androgens, estrogens leads to a change in their content in the blood and the development of the corresponding endocrine pathology. Reduction of deamination of BAS can aggravate the clinical manifestations of allergy in liver pathology.

Violation of the exchange of vitamins. Violation of vitamin metabolism in liver pathology is characterized by: a) a decrease in the absorption of fat-soluble vitamins (retinol, ergocalciferol, tocopherol, etc.) as a result of a violation of bile excretory liver function; B) a violation of the synthesis of vitamins and the formation of active forms (retinol from carotene, active forms of vitamin B6, etc.); C) violation of the deposition of vitamins (cyanocobalamin, folic, nicotinic acids, etc.) and their excretion. As a result of the violation of the exchange of vitamins, many pathological processes in the liver may be accompanied by hypovitaminosis.

VIOLATION OF LIVER-BORN AND SPECIFIED (EXCRETER) FUNCTION OF THE LIVER

Hepatocytes secrete bile, which includes bile acids, cholesterol, phospholipids, fatty acids, bile pigments, mucin, water and other substances.



The liver takes part in the synthesis, metabolism and excretion of bile pigments. In stellate endotheliocytes of the liver, macrophages of the bone marrow, spleen from the hem of the destroyed erythrocytes is formed under the influence of the enzyme biliverdin hemoxygenase, which, with the participation of the biliverdin reductase enzyme, turns into bilirubin (unconjugated, free, indirect), it binds to albumin in the blood, forming a water-insoluble complex, Which does not pass through the renal filter, is toxic, lipophilic. Indirect bilirubin with the participation of proteins (Y-ligandine and Z-glutathione transferase) is transferred to hepatocytes, where it is conjugated with uridine-diphospho-glucuronic acid under the influence of the microsomal enzyme UDP-glucuronyltransferase. A bilirubin that is bound or straight, which is soluble in water, is non-toxic, enters the intestine in the bile, where it is converted into urobilinogen (mesobilinogen) by the action of the enzymes of the intestinal microflora, while bilirubin cleaves glucuronic acid and restores it. From the small intestine, part of the urobilinogen is absorbed into the bloodstream and enters the liver via the portal vein, where it is split into dipyrrole compounds and does not penetrate into the general bloodstream. Unabsorbed in the blood urobilinogen in the large intestine is restored to sterocilinogen, and in the lower parts of the colon is oxidized, turning into stericilin. The main part of the sterocilin is excreted with feces, giving it a natural color. Only a very small amount of sterkobilinogen comes through the intestinal wall into the hemorrhoidal veins, and from there to the total blood flow and is excreted in the urine. Thus, normal urine contains traces of sterocilinogen.

Properties of direct and indirect bilirubin

Indirect bilirubin	Direct bilirubin
Toxic	Non-toxic
Gives an indirect reaction to Ehrlich's diazo reaction	Reacts directly with Ehrlich's diazo-reagent
Normally, the serum content does not exceed 3.4-22.2 μmol / l	It is found only in bile
Does not appear in the urine	Appears in the urine
Soluble in fats	Soluble in water
Not bound to glucuronic acid	Coupled with glucuronic acid

Etiology and pathogenesis of jaundice

Jaundice (icterus) is a symptom complex characterized by a yellow color of the skin, a sclera, more deeply located tissues and accompanied by an increased concentration of bile components in the blood serum and in some biological fluids.

Jaundice should be distinguished from the yellow pigmentation of the skin due to caroteneemia (when consuming a large amount of carrots), due to the presence of carotene pigments in the blood and the appearance of yellow staining in the palms, rather than the sclera. Jaundice is associated with diseases of the liver and biliary tract or with increased destruction (hemolysis) of erythrocytes. Visible

jaundice appears with hyperbilirubinemia more than 35 μmol / l. It is customary to distinguish between bilirubinophilic and bilirubinophobic tissues. Skin, mucous membranes and the inner wall of blood vessels are most dyed. The cornea of the eye, cartilage, nervous tissue usually stain little. Saliva, gastric juice, tear fluid, as a rule, are not yellow.

There are three types of jaundice: superhepatic, hepatic and subhepatic. Hyperbilirubinemia is noted in all cases.

Superhepatic (hemolytic) jaundice, not associated with liver damage, occurs due to increased hemolysis of erythrocytes and a violation of bilirubin metabolism. The causes of superhepatic jaundice are different. There are a number of hereditarily caused enzymes and hemoglobinopathies, accompanied by hemolytic jaundice, for example hereditary microspherocytic hemolytic and sickle-cell anemia. There are also autoimmune, infectious (for malaria, sepsis), toxic (poisoning with arsenic, lead, hydrogen sulphide, snake venom) and other acquired forms of hemolytic anemia.

With increased destruction of circulating erythrocytes, increased production of indirect bilirubin is noted.

Classification scheme of pathogenetic types of jaundice (according to AF Bluger)

Type of jaundice	Characteristics of the main pathological process	Leading mechanism of jaundice development	Nosological forms and syndromes
Superhepatic	Increased decay of erythrocytes	Increased formation of indirect bilirubin, insufficiency of the function of bilirubin capture by the liver	Hemolytic jaundice, hematomas, infarcts
		Violation of the capture and excretion of bilirubin, regurgitation of bilirubin	Hepatic-cell jaundice in acute and chronic hepatitis, hepatosis, cirrhosis
		Disturbance of excretion	Cholestatic jaundice with cholestatic hepatosis, primary

Hepatic	The defeat of hepatocytes (and cholangiol)	and regurgitation of bilirubin	biliary cirrhosis, with hepatic-cell lesions
		Disturbance of conjugation and capture of bilirubin by hepatocytes	Enzimopathic jaundice with Gilbert and Kriegler-Nayar syndromes, physiological jaundice of newborns
		Disturbance of bilirubin excretion	With the syndromes of Dabin-Johnson and Rotor
Posthepatic	Disturbance of conduction of bile ducts	Disturbance of excretion and regurgitation of bilirubin	Intracanalicular occlusion with stone, tumor, parasites, inflammatory exudate. Extracanalicular obstruction of the tumor, echinococcus, etc.

The liver is able to metabolize and release into bile the amount of bilirubin, 3-4 times higher than its normal physiological level. With the increased hemolysis of red blood cells, the liver can not cope with either the conjugation process or the transport of excess bilirubin, which can lead to at least a 4-fold increase in its concentration in the blood. With this variant of jaundice, bilirubin, it would seem, should only be unconjugated, since it is an accumulation of indirect bilirubin. However, it is necessary to take into account that an excess amount of bilirubin enters the hepatic cell, it is conjugated, and the transport system of removing it from the cell may be insufficient, and then in the blood, along with indirect bilirubin, the increased content of which will necessarily prevail, Bilirubin.

The main signs of this jaundice are an increase in the level of bilirubin mainly due to the unconjugated fraction, the absence of bilirubin in the urine. In addition, with hemolytic jaundice in the liver, bile ducts and intestines, excess amounts of bilirubin glucuronides, urobilinogen, strobobilinogen (hypercholia-increased secretion of bile in the intestine) are synthesized, which leads to an increase in the amount of urobilinogen and sterocilinogen in urine and feces in the absence of clinical and

Laboratory evidence of liver disease. The liver metabolizes more than normal, the amount of pigment, and therefore bilirubin is stronely secreted through the bile and

further into the intestine. Accumulation in the blood of bile acids and cholesterol does not occur, since the outflow of bile is free. In some cases (cirrhosis, tumors, infections) simultaneously can be defined as increased hemolysis of erythrocytes, as well as violations of the liver. As a rule, with uncomplicated hemolysis, serum bilirubin level increases only 2-3 times (40-60 μmol / l) and rarely reaches 100 μmol / l.

Unconjugated hyperbilirubinemia also occurs as a result of bilirubin conjugation disorders with a decrease in UDP-glucuronyl transferase activity. Almost every newborn on the 3-5th day of life has a slight, transient, unconjugated hyperbilirubinemia (up to 50 μmol / l), associated with immature during this period glucuronyl transferase. Within a few days (up to 2 weeks) of life, the activity of glucuronyltransferase increases and the level of bilirubin normalizes.

Hepatic jaundice (parenchymal or hepatocellular) develops in acute and chronic liver diseases of any etiology (viral, alcoholic, autoimmune), as well as in severe infections (typhus, malaria, acute pneumonia), sepsis, poisoning with fungi, phosphorus, chloroform and other poisons . As a result of the defeat of hepatocytes, lysosomes of liver cells secrete bile in the lymphatic and blood vessels. It is also possible to reverse the absorption of bile from the bile ducts into the blood. Hyperbilirubinemia is noted in the blood due to direct and indirect bilirubin, which is associated with a decrease in the activity of glucuronyltransferase in damaged cells and a violation of the formation of bilirubin glucuronides. Developed cholomic syndrome, which is due to the intake of bile acids in the blood. It is characterized by bradycardia and a decrease in blood pressure due to the influence of bile acids on the receptors and the center of the vagus nerve, the sinus node of the heart and blood vessels. The toxic effect of bile acids on the central nervous system is manifested in the form of asthenia, irritability, disturbance in the rhythm of sleep, headache and increased fatigue. Irritation of sensitive nerve endings of the skin with bile acids leads to skin itch. Urine has a dark color due to bilirubinuria (direct bilirubin) and urobilinuria (disrupted the transformation of urobilinogen, absorbed into the blood from the small intestine and entering the liver). In the urine, bile acids and traces of sterocilinogen are determined due to a decrease in its formation in the intestine, where little glucuronide bilirubin is supplied.

In the group of hepatic jaundice, hepatic-cellular, cholestatic and enzymatic jaundice are distinguished.

With hepatocellular jaundice, there is a complex disturbance of liver function, relating to both metabolism and transport of bilirubin. It is based on damage to the function and structure of hepatocytes - a cytolytic syndrome, leading to hepatic-cell failure.

Cholestatic jaundice (intrahepatic cholestasis) can be observed as an independent phenomenon or more often complicates the cytolytic syndrome. Cholestasis can occur both at the level of the hepatocyte, when the metabolism of bile components is disrupted, and at the level of the bile ducts, with bilirubinemia present, and the excretion of urobilin compounds with urine and feces is reduced.

Etymopathic jaundice is caused by a disturbance in the metabolism of bilirubin in hepatocytes. This is a partial form of liver failure, associated with a decrease or inability to synthesize enzymes involved in pigment metabolism. By origin these jaundices are, as a rule, hereditary.

Depending on the mechanism of development, the following forms of jaundice are distinguished:

Gilbert's syndrome is of a family nature and is characterized by benign chronically occurring unconjugated hyperbilirubinemia associated with a partial deficiency of UDP-glucuronyltransferase. Usually this syndrome manifests itself at the age not earlier than 20 years. As a rule, the level of bilirubin increases only to 30 μmol / l and rarely exceeds 50 μmol / l (only 20% of total bilirubin will be conjugated). Clinically, this pathology is often not manifested and is established in a laboratory study. The intensity of jaundice is transient, it disappears, then intensifies. The latter is observed after prolonged starvation or compliance with a low-calorie diet, after intercurrent infection, surgical interventions, alcohol intake. The intake of phenobarbital, increasing the activity of the enzyme, leads to a normalization of the level of bilirubin.

Syndrome Kriegler-Nayyar. Two forms of this disease are known: type I - a clinically severe form associated with complete absence of glucuronyl transferase, and type II, associated with partial deficiency. I type is rare. Characterized by the appearance of jaundice from the first days of life, a sharp increase in the content of indirect bilirubin in the blood, a lesion of the central nervous system. The level of unconjugated bilirubin in children reaches high figures - 200-450 μmol / l. The functional state of the liver does not suffer, but it does not contain a conjugating enzyme. In connection with the fact that the liver does not synthesize bound bilirubin, bile in such children is colorless. Treatment with phenobarbital is ineffectual. Sick children usually; Die in the first year of life due to brain damage (bilirubin encephalopathy). Patients with type II syndrome have only partial deficit of glucuronyltransferase, which is expressed in an increased level of unconjugated bilirubin up to 60-200 μmol / l. Treatment with phenobarbital gives a temporary effect. The disease refers to the proceeding relatively favorably in cases where the level of bilirubin does not exceed 200 μmol / l. The acquired glucuronyl transferase deficiency that occurs in newborns due to the inhibition of this enzyme by a number of drugs (levomycetin, novobiocin or vitamin K) is possible.

With Kriegler-Nayyar syndrome and hemolytic disease of newborns (Rh-incompatibility of erythrocytes of the mother and fetus), bilirubin encephalopathy can result from a so-called nuclear jaundice.

"Nuclear" jaundice is a severe form of jaundice of newborns, in which bile pigments and degenerative changes are found in the nuclei of the cerebral hemispheres and the brainstem (free bilirubin, not included in the bond with albumin, penetrates the blood-brain barrier and stains the nuclei of the brain - hence the term " Nuclear "jaundice). This jaundice is characterized by the following: in newborns on the 3rd-6th day of life spinal reflexes disappear, hypertone of the muscles of the trunk, sharp crying, drowsiness, restless limb movements, convulsions, respiratory failure, it may stop and die. If the child survives, then deafness, paralysis, mental retardation may develop.

Dabin-Johnson syndrome. This variant of jaundice arises from the defect of enzymes involved in the excretion of bilirubin-diglucuronide through the membrane of the hepatic cells into the bile capillaries. As a result, direct bilirubin enters not only the bile capillaries but also partially into the blood. Clinically, jaundice with a moderate increase in the blood content of direct bilirubin and its appearance in the urine. With liver biopsy in hepatocytes, a dark, brown-orange pigment (lipochrom) is detected.

Rotor Syndrome (conjugated hyperbilirubinemia). Clinically similar to the previous syndrome, but unlike it, in the syndrome of Rotor there is no accumulation of pathological pigment in the cells of the liver. The syndrome has a benign course, is inherited by an autosomal recessive type.

Subhepatic jaundice (mechanical or obstructive) develops when there is an obstruction to the flow of bile through the extrahepatic bile ducts. The causes are: a) obturation of the hepatic and common bile

duct with stone, parasites, tumor; B) compression of the bile ducts by a tumor of nearby organs, cysts; C) narrowing of the bile ducts with postoperative scars, spikes; D) dyskinesia of the gallbladder as a result of disturbance of innervation. With subhepatic jaundice, pain syndrome, nausea, vomiting, and upset of the stool are observed. Prolonged cholestasis is accompanied by an increase in the liver, which depends on the overflow of its stagnant bile and increase in the mass of the hepatic tissue. At the beginning of the development of mechanical jaundice, the hepatic cells still continue to produce bile, but the outflow of it in the usual ways is disturbed, and it pours out into the lymphatic fissures, getting from there into the blood. In the blood, the amount of bilirubin bound increases. Isolation of urobilin with urine is absent, the isolation of stercobilin with feces is reduced or insignificant. The blood contains all the components of bile, including bile acids, leading to the development of cholemia. In addition, this type of jaundice is characterized by achiolia, which is caused by a persistent violation of bile excretion through the bile capillaries (which leads to intrahepatic cholestasis), ducts and from the gallbladder.

Acholia syndrome is a condition characterized by a significant decrease or cessation of bile flow into the intestine, combined with a violation of cavitary and membrane digestion. In this

syndrome, there are: a) steatorrhea (loss of body fat with feces as a result of a violation of emulsification and assimilation of fat in the intestine due to a deficiency of bile); B) dysbacteriosis;

↓ intestinal autoinfection and intoxication due to loss of bactericidal action of bile, which promotes the activation of processes of putrefaction and fermentation in the intestine and the development of flatulence; D) deficiency of fat-soluble vitamins (A, D, E, K), leading to impairment of twilight vision, demineralization of bones with the development of osteomalacia and fractures, a decrease in the effectiveness of the antioxidant tissue protection system, development of hemorrhagic syndrome; E) decolorized feces due to a decrease or absence of bile in the intestine.

Cholelithiasis

Gallstone disease is one of the most common diseases, occupying the third place after cardiovascular pathology and diabetes. In Russia, the prevalence of this disease varies between 3-12%.

According to the chemical composition, three types of gallstones are distinguished: cholesterol (cholesterol content 79% and higher), black pigment and brown pigment. Cholesterol and black pigmented stones are formed mainly in the gall bladder, brown - in the bile ducts. In Russia, with cholelithiasis, cholesterol stones are more common (80-90%).

There are 4 main groups of factors that take part in the formation of cholesterol stones: 1) promoting the saturation of the bile with cholesterol; 2) contributing to precipitation of cholesterol;

↑ causing a violation of the gallbladder; 4) leading to disruption of enterohepatic circulation of bile acids.

Factors contributing to the saturation of bile with cholesterol:

age (with the increase in the content of cholesterol in bile);

Sex (women have cholelithiasis 3-4 times more often than men). Sexual differences are associated with the hormonal background. Chololithiasis is common in women who have repeatedly

given birth. During pregnancy, the evacuation function of the gallbladder suffers, which subsequently leads to the formation of gallstones;

heredity (risk of gallstones formation is 2-4 times higher in people whose relatives suffer from cholelithiasis);

obesity (increased synthesis and excretion of cholesterol);

food (high cholesterol foods, refined carbohydrates). It is believed that drinking coffee 2-3 cups a day reduces the risk of gallstones;

medicinal preparations (estrogens, oral contraceptives, etc.);

liver disease. It is suggested that people with HbsAg have the risk of gallstones.

↑ Bile proteins (the most important is mucinglicoprotein gel - N-aminopeptidase, immunoglobulins, phospholipase C, etc.);

Calcium bilirubinate. In the center of cholesterol stones is bilirubin, and, apparently, cholesterol crystals are deposited in the gall bladder on protein-pigment complexes.

Factors leading to a violation of the basic functions of the gallbladder (contraction, absorption, secretion). Disturbance of gallbladder emptying, which is observed with flatulence, pregnancy, decreased sensitivity and the number of receptors for cholecystokinin, methionine, etc., which are stimulants of motor activity. It is established that with age, the sensitivity of the gallbladder receptors to stimulants (cholecystokinin) decreases. The contractile function of the gallbladder is reduced by somatostatin, atropine, bile acids and other agents.

Factors leading to disruption of enterohepatic circulation of bile acids.

↑ diseases of the terminal section of the small intestine;

↑ resection of the ileum;

↑ diseases of the small intestine with severe impairment of absorption (eg, gluten enteropathy), as well as resection of the small intestine with violation of all major types of metabolism and absorption of bile acids;

↑ bile fistula (contribute to a massive loss of bile acids).

Pathogenesis of the formation of cholesterol stones

The main pathogenetic factors: a) glut of bile with cholesterol; B) violation of the colloidal properties of bile, increased mucus formation, precipitation of cholesterol crystals; C) a decrease in the evacuation function of the gallbladder.

Pathogenesis of formation of pigmented stones

Pigmented are stones containing less than 30% cholesterol. Isolate black and brown pigmented stones.

Black pigmented stones account for 20-30% of the total number of gallstones, more common in old age. They consist mainly of calcium bilirubinate, phosphate and calcium carbonate without an

admixture of cholesterol. The formation of such stones is characteristic for chronic hemolysis (hereditary spherocytic or sickle cell anemia), implantation of artificial heart valves, liver cirrhosis.

Brown stones are localized mainly in the bile ducts. These stones contain calcium bilirubin, palmitate and calcium stearate and cholesterol. Their formation is associated with infection (E. coli, opisthorchiasis, giardiasis, etc.). Under the influence of bacteria glucuronidase, deconjugation of direct bilirubin occurs, which leads to precipitation of insoluble unconjugated bilirubin. Brown pigmented stones are usually formed above the strictures or in the areas of dilatation of the biliary tract.

Gallstone disease, as a rule, does not have specific symptoms. The exception is biliary colic, which attacks are usually associated with an error in the diet and develop after a plentiful intake of fried, spicy food. The cause of the disease is mechanical irritation of the gallbladder wall and bile ducts with a stone, their hyperextension.

The main method of diagnosis of cholelithiasis is ultrasound.

Experimental modeling of liver pathology

A number of experimental methods used to study liver functions in physiological and pathological conditions are known.

The imposition of fistula Ecka is a method applied in 1877 by the Russian researcher Eck in the laboratory of N.V. Tarkhanov. It consists in the following: an anastomosis is created between the lower hollow and portal veins in dogs. The portal vein above the anastomosis is bandaged, and all blood flowing from the organs of the abdominal cavity enters directly into the lower vena cava, bypassing the liver. This experiment made it possible to study the detoxifying, as well as urea, formation of the liver.

After Eck's operation in animals, ataxia, maneuvers, periodically clonic and tonic convulsions appeared in animals 3-4 days later when feeding with meat food or 10-12 days after using the milk-plant diet. The blood increased ammonia, which is normally disinfected in the liver, protein synthesis was reduced, cholesterol metabolism and bile formation were disturbed.

Back fistula Ekka-Pavlova. In 1893, I.P. Pavlov proposed after dressing the anvil on the gates and in the lower vena cava to tie up the anus not the gates but the lower vena cava. In this case, the blood rushed blood not only from the digestive tract through the portal vein, but also from the posterior half of the trunk. Animals with such a fistula live for years. This experimental model is used to study the functional state of the liver under different conditions of the food load.

Complete removal of the liver. Produced in two stages. In the beginning, the back fistula Ekka-Pavlova is reproduced. The consequence of this operation is the development of collateral circulation. As a result, a part of the venous blood from the back of the body through v. Azygos and internal thoracic veins are diverted to the upper vena cava, bypassing the liver. 3-4 weeks after the first operation, the second is performed: the portal vein is bandaged and the liver is removed. In the next few hours after liver removal, the muscular weakness, adynamia, abruptly decreases the sugar content in the blood and at a decrease of less than 2.5 mmol / l, hypoglycemic coma may develop, followed by the death of the animal. The introduction of glucose can prolong the life of the animal. At the same time, the amount of ammonium compounds increases in the blood and the urea content decreases. Dogs after such surgery

live no more than 12-15 hours. Removal of the liver is, in fact, an experimental model of the hepatic coma. After partial removal of the liver (up to 3/4 of the

body), very severe disturbances of metabolism do not occur because the rest of the liver retains its functions and implements compensatory possibilities.

When studying the functional role of the liver in normal and pathological conditions, the angiostomian method of ES is also used. London, proposed in 1919. Metal cannulas (stainless or silver) are attached to the walls of large blood vessels (portal and hepatic veins), the free ends of which are removed through the covers of the abdominal wall to the outside. Cannulas make it possible to systematically draw blood from vessels and introduce various substances into them. The method of angiostomy has given much valuable in the study of the role of the liver in bilirubin formation, carbohydrate, protein, fat and salt metabolism.

An experimental model is the method of perfusion of an isolated liver. Liver donors are mainly laboratory animals: rats, rabbits, cats. Now for these purposes the liver of large animals is used: dogs, pigs and calves. This experimental model is applicable for studying the role of the liver in metabolic processes, as well as in solving organ transplant problems.

For the experimental reproduction of liver diseases, infectious and toxic agents are introduced into the body. A strong hepatotropic poison is CC14 (four-carbon chloride). Parenteral administration of 0.2 ml / 100 g of an 80% oily solution of this substance causes alteration and necrobiosis of hepatocytes in the central zones of the hepatic lobules. Chloroform, heliotrope seeds are also used for these purposes. Fat hepatitis is reproduced by the introduction of hydrazine sulphate and alcohol. The toxic effect of alcohol on the liver is expressed in vascular disorders and focal dystrophic-destructive changes in the parenchyma.

THE ENDOCRINE SYSTEM

The endocrine system is a system of glands, each of which secretes a type of hormone into the bloodstream to regulate the body. The endocrine system includes: specialised endocrine organ**s** (endocrine glands) and diffuse endocrine system - endocrine cells of the organs and **tissues**. The endocrine system together with the nervous system controls development of a body and its structure and functions. The endocrine system can perform a dual role in the development of the disease. If at the time of action of the pathogenic factors endocrine system is not broken, it carries out a **protective role.** If endocrine disorders are at the moment of action of pathogenic factors, the damage will be compounded. In addition, disturbances of the endocrine system are a source of disease. This is a **pathogenic role** of the endocrine system in the development of disease.

Organization of the endocrine system

There are two types of organization of the endocrine system: cerebropituitary type and pituitary-independent type.

Cerebropituitary type includes the brain cortex, hypothalamus, anterior pituitary, peripheral endocrine gland, and the target cells. The brain cortex exerts neurogenic influence on the hypothalamus which produces liberins or statins. The hypothalamic hormones are secreted into the pituitary portal system and affect trophocytes producing tropins (e.g. ACTH, gonadotropins). The latter are secreted into general circulation and reach the peripheral endocrine glands where they exert stimulating or inhibitory effect.

In pituitary-independent system the pituitary stage is omitted. For example, parathyroid gland or beta-cells of the pancreas are not regulated by pituitary trophins.

At the physiological conditions the endocrine system functions on the principle of negative feedback. The negative feedback - hormone affects its target organ, causing a response that usually reduces further hormone release and allows tight control over hormone levels. Violation of a negative feedback mechanism underlies some of endocrinopathies. The positive feedback is uncommon and occurs when the response by a target tissue to hormonal stimulation increases the further release of that hormone.

Endocrinopathy

The main pathogenetic chains in development of endocrine gland disorders:

- **centrogenous** - a violation of the central mechanisms of regulation of gland (at the level of the cerebral cortex, hypothalamus or pituitary);

↓ **glandular** - pathological processes in the gland itself;

↓ **postglandular** - peripheral mechanisms of violation hormones activity.

Endocrinopathy can result from hormone deficiency, hormone excess, resistance to hormone action, or production of abnormal hormones.

Deficiency states

With few exceptions (calcitonin), hormone deficiency results in pathologic manifestations. The destructive processes that cause failure of the endocrine organs include:

– infections,

– tissue death due to infarction or inflammation,

– tumors,

– autoimmune processesic hormones,

– dietary inadequacy,

– hereditary defects in hormone synthesis.

HORMONE EXCESS

With few exceptions (testosterone in men, progesterone in men and women) hormone excess causes pathologic effects. Hormone may be overproduced by the gland due to adenoma,

autoantibodies that mimic the action of tropins (as in the case of thyroid-stimulating immunoglobulins in hyperthyroidism), mutations in receptor-effector mechanisms that impair feedback. A second type of hormone excess results when a hormone is produced by a tissue (usually malignant) that does not synthesize it ordinarily (for example, ACTH production by carcinoma of the lungi). A third type of hormone excess involves the overproduction of hormones in peripheral tissues from circulating precursors.

Production of abnormal hormones

One form of diabetes mellitus is the result of a production of an abnormal insulin molecule that is ineffective because of defective binding to the insulin receptor. In other cases, hormone precursors, hormone subunits, or incompletely processed peptide hormones may be released into the circulation, as is common in so-called ectopic hormone production of neoplasia.

Hormone resistance

Hormone-resistance states frequently are due to mutations that impair hormone action, but they can be due to acquired defects in receptors and postreceptor effector mechanisms for hormones, to development of antibodies that block hormones or hormone receptors, or to the absence of target cells.

A common feature of hormone-resistance states is the presence of a normal or elevated level of the hormone in the circulation despite deficient hormone action. This feature is a consequence of the fact that hormones are normally under regulatory feedback control and that failure of hormone action leads to increased hormone production.

In general, disorders of the endocrine system can be classified as follows:

- Disorders of the central regulation associated with dysfunction of pituitary (secondary) or hypothalamus (tertiary).
- Disorders of the peripheral endocrine glands (primary).
- Extraglandular disorders (abnormal transport of hormones, resistance to the effects of hormones, abnormal metablism of hormones).

Typical forms of disease of the endocrine system

4) Violations of the hypothalamic-pituitary system.
5) Dysfunction of the adrenal glands.

6) Thyroid dysfunction.

7) Dysfunction of the parathyroid glands.

8) Dysfunction of the gonads.

9) Violations of endocrine function of the pancreas.

Pituitary gland

Anatomy. The pituitary gland or hypophysis in an adult weighs about 500 mg and is slightly heavier in females. It is situated at the base of the brain in a hollow called sella turcica formed out of the sphenoid bone. The gland is composed of 2 major anatomic divisions: anterior lobe (adenohypophysis) and posterior lobe (neurohypophysis).

- The ***anterior lobe or adenohypophysis*** is anectodermal derivative formed from Rathke's pouch which is an upward diverticulum fromthe primitive buccal cavity. The adenohypophysis has no direct neural connection but hasindirect connection through capillary portalcirculation by which the anterior pituitaryreceives the blood which has already passed through the hypothalamus.
- The ***posterior lobe or neurohypophysis*** is adown growth from the primitive neural tissue. The neurohypophysis, therefore, has direct neural connection superiorly with the hypothalamus.

Histology and functions. The histology and functions of the anterior and posterior lobes of the pituitary gland are quite distinct.

A. ***Anterior lobe (adenogypophysis)***. It is composed of round to polygonal epithelial cells arranged in cords and islands having fibrovascular stroma. These epithelial cells, depending upon their staining characteristics and functions, are divided into 3 types, each of which performs separate functions:

8. Chromophil cells with acidophilic granules: These cells comprise about 40% of the anterior lobe and are chiefly located in the lateral wings. The acidophils are further of 2 types:

i) *Sormtotrophs* (GH cells) which produce growth hormone (GH); and

ii) *Lactotrophs* (PRL cells) which produce prolactin (PRL).

Cell containing both GH and PRL, called mammosomatotrophs are also present.

9. Chromophil cells with basophilic granules: These cells constitute about 10% of the anterior lobe and are mainly found in the region of median wedge. The basophils include 3 types of cells:

i) *Gonadotrophs* (FSH-LH cells) which are the source of the FSH and LH or interstitial cell stimulating hormone (ICSH). ii) Thyrotrophs (TSH cells) are the cells producing TSH.

iii) *Corticotrophs* (ACTH-MSH cells) produce ACTH, melanocyte stimulating hormone. (MSH), β-lipoprotein and β-endorphin.

10. Chromophobe cells without visible granules: These cells comprise the remainder 50% of the adenohypophysis. These cells by light microscopy contain no visible granules, but on electron microcopy reveal sparsely granulatedcorticotrophs, thyrotrophs and gonadotrophs.

All these functions of the adenohypophysis are under the indirect control of the hypo-thalamus through stimulatory and inhibitory factors synthesized by the hypothalamus which reach the anterior lobe through capillary portal blood.

B. Posterior lobe (neurohypophysis). The neurohypophysis is composed mainly of interlacing nerve fibres in which are scattered specialised glial cells called pituicytes. These nerve fibres on electron microscpopy contain granules of neurosecretory material made up of 2 octapeptides - vasopressin or antidiuretic hormone (ADH), and oxytocin, both of which are produced by neurosecretory cells of the hypothalamus but are stored in the cells of posterior pituitary.

2) ADH causes reabsorption of water from the renal tubules and is essential for maintenance of osmolality of the plasma. Its deficiency results in diabetes insipidus characterised by uncontrolled diuresis and polydipsia.

3) Oxytocin causes contraction of mammary myoepithelial cells resulting in ejection of milk from the lactating breast and causes contraction of myometrium of the uterus at term.

It is obvious from the description above that pituitary, though a tiny organ, is concerned with a variety of diverse functions in the body. The pituitary gland and hypothalamus are so closely interlinked that diseases of the pituitary gland involve the hypothalamus, and dysfunctions of the hypothalamus cause secondary changes in the pituitary. The pituitary gland is involved in several diseases which include: non-neoplastic such as inflammations, haemorrhage, trauma, infarction and many other endocrine diseases; and neoplastic diseases. However, functionally and morphologically diseases of the pituitary can be classified as below, each of which includes diseases of anterior and posterior pituitary and hypothalamus, separately:

1) Hyperpituitarism

2) Hypopituitarism

3) Pituitary tumours

Hyperpituitarism

Hyperpituitarism is characterised by over-secretion of one or more of the pituitary hormones. Such hypersecretion may be due to diseases of the anterior pituitary, posterior pituitary or hypothalamus. For all practical purposes, however, hyperfunction of the anterior pituitary is due to the development of a hormone-secreting pituitary adenoma (discussed later), and rarely, a carcinoma. For each of the hormonal hyperfunction of the anterior pituitary, posterior pituitary and hypothalamus, a clinical syndrome is described. A few important syndromes are as follows:

A. Hyperfunction of Anterior Pituitary

Three common syndromes of adenohypophyseal hyperfunction are: gigantism and acromegaly, hyperprolactinaemia and Cushing's syndrome.

- **Gigantilism and acromegaly.** Both these clinical syndromes result from sustained excess of growth hormone (GH), most commonly by somatotroph (GH-secreting) adenoma.

Gigantism. When GH excess occurs prior to epiphyseal closure, gigantism is produced. Gigantism, therefore, occurs in prepubertal boys and girls and is much less frequent than acromegaly. The main clinical feature in gigantism is the excessive and proportionate growth of the child. There is enlargement as well as thickening of the bones resulting in considerable increase in height and enlarged thoracic cage.

Acromegaly. Acromegaly results when there is overproduction of GH in adults following cessation of bone growth and is more common than gigantism. The term 'acromegaly' means increased growth of extremities. There is enlargement of hands and feet, coarseness of facial features with increase in soft tissues, prominent supra-orbital ridges and a more prominent lower jaw which when clenched results in protrusion of the lower teeth in front of upper teeth (prognathism). Other features include enlargement of the tongue and lips, thickening of the skin and kyphosis. Sometimes, a few associated features such as TSH excess resulting in thyrotoxicosis, and gonadotropin insufficiency causing amenorrhea in the females and impotence in the male, are found.

- **Hyperprolactinaemia.** Hyperprolactinaemia is the excessive production of prolactin(PRL), most commonly by lactotroph (PRL-secreting) adenoma, also called prolactinoma. Occasionally, hyperprolactinaemia results from hypothalamic inhibition of PRL secretion by certain drugs (e.g. chlorpromazine, reserpineand methyldopa). In the female, hyperprolactinaemia causes amenorrhoea-galactorrhoeasyndrome characterised clinically by infertility and expression of a drop or two of milk from breast, not related to pregnancy or puerperium. In the male, it may cause impotence or reduced libido. These features result either from associated inhibition of gonadotropin secretion or interference in gonadotropin effects.
- **Cushing's syndrome.** Pituitary-dependent Cushing's syndrome results from ACTH excess. Most frequently, it is caused by corticotrdph (ACTH-secreting) adenoma.

B. Hyperfunction of Posterior Pituitary and Hypothalamus

Lesions of posterior pituitary and hypothalamus are uncommon. Two of the syndromes associated with hyperfunction of the posterior pituitary and hypothalamus are: inappropriate release of ADH and precocious puberty.

→ **Inapropriate release of ADH.** Inappropriate release of ADH results in its excessive secretion which manifests clinically by passage of concentrated urine due to increased reabsorption of water and loss of sodium in the urine, consequent hyponatraemia, haemodilution and expansion of intra- and extracellular fluid volume. Inappropriate release of ADH occurs most often in paraneoplastic syndrome e.g. in oat cell carcinoma of the lung, carcinoma of the pancreas, lymphoma and thymoma. Infrequently, lesions of the hypothalamus such as trauma, haemorrhage and meningitis may produce ADH hypersecretion. Rarely, pulmonary diseases such as tuberculosis, lung abscess, pneumoconiosis, empyema and pneumonia may cause overproduction of ADH.

→ **Precocious puberty.** A tumour in theregion of hypothalamus or the pineal gland may result in premature release of gonadotropinsca using the onset of pubertal changes prior to the age of 9 years. The features include premature development of genitalia both in the male and in the female, growth of pubic hair and axillary hair. In the female, there is breast growth and onset of menstruation.

Hypopituitarism

In hypopituitarism, there is usually deficiency of one or more of the pituitary hormones affecting either anterior, pituitary, or posterior pituitary and hypothalamus.

A. Hypofunction of Anterior Pituitary

Adenohypophyseal hypofunction is invariably due to destruction of the anterior lobe of more than 75% because the anterior pituitary possesses a large functional reserve. This may result from anterior pituitary lesions or pressure and destruction from adjacent lesions. Lesions of the anterior pituitary include nonsecretory (chromophobe) adenoma, metastatic carcinoma, craniopharyngioma, trauma, postpartum ischaemic necrosis (Sheehan's syndrome), empty-sella syndrome, and rarely, tuberculosis. Though a number of syndromes associated with deficiency of anterior pituitary hormones have been described, two important syndromes are: panhypopituitarism and dwarfism.

- **Panhypopituitarism.** The classical clinical condition of major anterior pituitary insufficiency is called panhypopituitarism. Three most common causes of panhypopituitarism are: nonsecretory (chromophobe) adenoma (discussed later), Sheehan's syndrome and Simmond's disease, and empty-sella syndrome.

Sheehan's syndrome and Simmond's disease. Pituitary insufficiency occurring due to postpartum pituitary (Sheehan's) necrosis is called Sheehan's syndrome, whereas occurrence of similar process without preceding pregnancy as well as its occurrence in males is termed Simmond's disease. The main pathogenetic mechanism underlying Sheehan's necrosis is the enlargement of the pituitary occurring during pregnancy which may be followed by hypotensive shock precipitating isthaemic necrosis of the pituitary. Other mechanisms hypothesised are: DIC following delivery, traumatic injury to vessels, and excessive haemorrhage. Patients with long-standing diabetes mellitus appear to be at greater risk of developing this complication.

The first clinical manifestation of Sheehan's syndrome is failure of lactation following delivery which is due to deficiency of prolactin.

Subsequently, other symptoms develop which include loss of axillary and pubic hair, amenorrhea, sterility and loss of libido. Concomitant deficiency of TSH and ACTH may result in hypothyroidism and adrenocortical insufficiency.

The pathologic changes in the anterior pituitary in Sheehan's syndrome during early stage are ischaemic necrosis and haemorrhage, while later necrotic tissue is replaced by fibrous tissue.

Empty-sella syndrome. Empty-sella syndrome is characterised by the appearance of an empty sella and features of parthypopituitarism. Most commonly, it results from herniation of subarachnoid space into the sella turcica due to an incomplete diaphragma sella creating an empty sella. Other less common causes are Sheehan's syndrome, infarction and scarring in an adenoma, irradiation damage, or surgical removal of the gland.

- **Pituitary dwarfism.** Severe deficiency of GH in children before growth is completed results in retarded growth and pituitary, dwarfism. Most commonly, isolated GH deficiency is the result of an inherited autosomal recessive disoder. Less often it may be due to a pituitary adenoma or craniopharyngioma, infarction and trauma to the pituitary. The clinical features of inherited cases of pituitary dwarfism appear after one year of age. These include proportionate retardation in growth of bones, normal mental state for age, poorly-developed genitalia, delayed puberty and episodes of hypoglycaemia. Pituitary dwarf must be distinguished from hypothyroid dwarf (cretinism) in which there is achondroplasia and mental retardation.

B. Hypofunction of Posterior Pituitary and Hypothalamus

Insufficiency of the posterior pituitary andhypothalamus is uncommon. The only significant clinical syndrome due to hypofunction of the neurohypophysis and hypothalamus is diabetes insipidus.

Diabetes insipipus. Deficient secretion of ADH causes diabetes insipidus. The causes of ADH deficiency are: inflammatory and neo-plastic lesions of the hypothalamo-hypophyseal axis, destruction of neurohypophysis due to surgery, radiation, head injury, and lastly, are those cases where no definite cause is known and are labelled as idiopathic. The main features of diabetes insipid us are excretion of a very large volume of dilute urine of low specific gravity, polyuria and polydipsia.

Adrenal gland

Anatomy. The adrenal glands lie at the upper pole of each kidney. Each gland weighs approximately 4 gm in the adult but in children the adrenals are proportionately larger. On sectioning, the adrenal is composed of 2 distinct parts: an outer yellow-brown cortex and an inner grey medulla. The anatomic and functional integrity of adrenal cortices are essential for life, while it does not hold true for adrenal medulla.

Histology and physiology. Microscopically and functionally, cortex and medulla are quite distinct.

Adrenal cortex. It is composed of 3 layers:

- **Zona glomerulosa** is the outer layer andcomprises about 10% of the cortex. It consists of cords or columns of polyhedral cells just under the capsule. This layer is responsible for the synthesis of mineralocorticoids, the most important of which is aldosterone, the salt and water regulating hormone.

- **Zona fasciculata** is the middle layer and constitutes approximately 70% of the cortex. It discomposed of columns of lipid-'rich cells which are precursors of various steroid hormones manufactured in the adrenal cortex such as glucocorticoids (e.g. cortisol) and sex steroids (e.g. testosterone).
- **Zona reticularis** is the inner layer which makes up the remainder of the adrenal cortex. It consists of cords of more compact cells than those of zona fasciculata but has similar functional characteristics of synthesis and secretion of glucocorticoids and androgens.

The synthesis of glucocorticoids arid adrenal androgens is under the control of ACTH from hypothalamus-anterior pituitary. In turn, ACTH release is under the control of a hypothalamic releasing factor called corticotropin-releasing factor. Release of aldosterone, on the other hand, is independent of ACTH control and is largely regulated by the serum levels of potassium and renin-angiotensin mechanism.

Adrenal medulla. The adrenal medulla is a component of the dispersed neuroendocrine system derived from primitive neuroectoderm; the other components of this system being paraganglia distributed in the vagi, paravertebral and visceral autonomic ganglia. The cells comprising this system are neuroendocrine cells, the major function of which is synthesis and secretion of catecholamines (epinephrine and nor-epihephrine). Various other peptides such as calcitonin, somatostatin and vasoactive intestinal polypeptide (VIP) are also secreted by these cells. The major metabolites of

catecholamine are metanephrine, normetanephrine, vanillyl mandelic acid (VMA) and homovanillic acid (HVA). In case of damage to the adrenal medulla, its function is taken over by other paraganglia.

Diseases affecting the two parts of adrenal glands are quite distinctive in view of distinct morphology, and function of the adrenal cortex and medulla. While the disorders of the adrenal cortex include adrenocortical hyperfunction (hyperadrenalism), adrenocortical insufficiency (hypoadrenalism) and adrenocortical tumours, the main lesions affecting the adrenal medulla are the medullary tumours.

Adrecortical hyperfunction (hyperadrenalism)

Hypersecretion of each of the three types of corticosteroids elaborated by the adrenal cortex causes distinct corresponding hyperadrenal clinical syndromes:

- Cushing's syndrome caused by excess of glucocorticoids (i.e. cortisol); also called chronic hypercortisolism.
- Conn's syndrome caused by oversecretion of mineralocorticoids (i.e. aldosterone); also called primary hyperaldosteronism.
- Adrenogenital syndrome characterised by excessive production of adrenal sex steroids (i.e. androgens); and also called adrenal virilism. Mixed forms of these clinical syndromes may also occur.

Cushing's Syndrome (Chronic Hypercortisolism).

Cushing's syndrome is caused by excessive production of cortisol of whatever cause. The full clinical expression of the syndrome, however, includes contribution of the secondary derangements.

Etiopathogenesis. There are 4 major etiologic types of Cushing's syndrome which should be distinguished for effective treatment.

- ***Pituitary Cushing's syndrome.*** About 60-70% cases of Cushing's syndrome are caused by excessive secretion of ACTH due to a lesion in the pituitary gland, most commonly a corticotroph adenoma or multiple corticotrophmicroadenomas. This group of cases was the first to be described by Harvey Cushing, an American neurosurgeon, who termed the condition as Cushing's disease. Also included in this group are cases with hypothalamic origin of excessive ACTH levels without apparent pituitary lesion. All cases with pituitary Cushing's syndrome are characterised by bilateral adrenalcortical hyperplasia and elevated ACTH levels. These cases show therapeutic response on administration of high doses of dexamethasone which suppresses ACTH secretion and causes fall in plasma cortical level.

- ***Adrenal Cushing's syndrome.*** Approximately 20-25% cases of Cushing's syndrome are caused by disease in one or both the adrenal glands. These include adrenal cortical adenoma, carcinoma, and less often, cortical hyperplasia. This group of cases is characterised by low serum ACTH levels and absence of therapeutic response to administration of high doses of glucocorticoid.
- ***Ectopic Cushing's syndrome.*** About 10-15% cases of Cushing's syndrome have an origin in ectopic ACTH elaboration by nonendocrine tumours. Most often, the tumour is an oat cell carcinoma of the lung but other lung cancers, malignant thymoma and pancreatic tumour shave also been implicated. The plasma ACTH level is high in these cases and cortisol secretionis not suppressed by dexamethasone administration.

- ***Iatrogenic Cushing's syndrome.*** Prolonged therapeutic administration of high doses of glucocorticoids or ACTH may result in Cushing'ssyndrome e.g. in organ transplant recipients and in autoimmune diseases. These cases are generally associated with bilateral adrenocortical insufficiency.

Clinical features. Cushing's syndrome occurs more often in patients between the ages of 20-40 years with three time's higher frequency in women than in men. The severity of the syndrome varies considerably, but in general the following features characterise a case of Cushing's syndrome:

- Central or truncal obesity contrasted with relatively thin arms and legs, buffalo hump dueto prominence of fat over the shoulders, and rounded oedematous moon-face.
- Increased protein breakdown resulting in wasting and thinning of the skeletal muscles, atrophy of the skin and subcutaneous tissue with formation of purple striae on the abdominal wall, osteoporosis and easy of the thin skin to minor trauma.

3. Systemic hypertension is present in 80% of cases because of associated retention of sodium and water.

4. Impaired glucose tolerance and diabetes mellitus are found in about 20% cases.

5. Amenorrhea, hirsutism and infertility in many women.

6. Insomnia, depression, confusion and psychosis.

Conn's Syndrome (Primary Hyperaldosteronism)

This is an uncommon syndrome occurring due to overproduction of aldosterone, the potent salt-retaining hormone.

Etiopathogenesis. The condition results primarily due to adrenocortical diseases such as:

- Adrenocortical adenoma, producing aldosterone.

- Bilateral adrenal hyperplasia, especially inchildren (congenital hyperaldosteronism).

- Rarely, adrenal carcinoma.

Primary hyperaldosteronism from any of the above causes is associated with low plasma renin levels. Secondary hyperaldosteronism, on the contrary, occurs in response to high plasma renin level due to overproduction of renin by the kidneys such as in renal ischaemia, reninoma or oedema.

Clinical features. Conn's syndrome is more frequent in adult females. Its principal features are as under:

- Hypertension, usually mild to moderate diastolic hypertension.
- Hypokalaemia and associated muscular weakness, peripheral neuropathy and cardiacarrhythmias.
- Retention of sodium and water.

- Polyuria and polydipsia due to reduced concentrating power of the renal tubules.

Adrenogenital Syndrome (Adrenal Virilism)

Adrenal cortex secretes a smaller amount of sex steroids than the gonads. However, adrenocortical hyperfunction may occasionally cause sexual disturbances.

Etiopathogenesis. Hypersecretion of sex steroids, mainly androgens, may occur in children or in adults:

3. In children, it is due to congenital adrenal hyperplasia in which there is congenital deficiency of a specific enzyme.
4. In adults, it is caused by an adrenocortical adenoma or a carcinoma. Cushing's syndrome is often present as well.

Clinical features. The clinical features depend upon the age and sex of the patient.

In children, there is distortion of the external genitalia in girls, and precocious puberty in boys. In adults, the features in females show virili-sation (e.g. hirsutism, oligomenorroea, deepening

of voice, hypertrophy of the clitoris); and in males may rarely cause feminisation.

There is generally increased excretion of 17-ketosteroids in the urine.

Adrenocortical insufficiency (hypoadrenalism)

Adrenocortical insufficiency may result from deficient synthesis of cortical steroids from the adrenal cortex or may be secondary to ACTH deficiency. Three types of adrenocortical hypofunction are distinguished:

- Primary adrenocortical insufficiency caused primarily by the disease of the adrenal glands. Two forms are described: acute or 'adrenal crisis', and chronic or Addison's disease.
- Secondary adrenocortical insufficiency resulting from diminished secretion of ACTH.
- Hypoaldosteronism characterised by deficient secretion of aldosterone.

Primary adrenocortical insufficiency

Primary adrenal hypofunction occurs due to defect in the adrenal glands and normal pituitary function. It may develop in 2 ways:

A. Acute primary adrenocortical insufficiency or 'adrenal crisis'.

B. Chronic primary adrenocortical insufficiency or Addison's disease.

Primary Acute Adrenocortical Insufficiency (Adrenal Crisis)

Sudden loss of adrenocortical function may result in an acute condition called adrenal crisis.

Etiopathogenesis. Causes of acute insufficiency are :

- Bilateral adrenalectomy e.g. in the treatment of cortical hyperfunction, hypertension and in selected cases of breast cancer.

- Septicaemia e.g. in end toxic shock and meningococcal infection producing grossly haemorrhagic and necrotic adrenal cortex termed adrenal apoplexy. The acute condition so produced is called Waterhouse-Friderichsen's syndrome.

- Rapid withdrawal of steroids.

- Any form of acute stress in a case of chronic insufficiency i.e. in Addison's disease. **Clinical features.** Clinical features of acute adrenocortical insufficiency are due to deficiency of mineralocorticoids and glucocorticoids. These are as follows:

I. Deficiency of mineral corticoids (i.e. aldosterone deficiency) results in salt deficiency, hyperkalaemia and dehydration.

Deficiency of glucocorticoids (i.e. cortisol deficiency) leads to hypoglycaemia, increased insulin sensitivity and vomitings.

Primary Chronic Adrenocortical Insufficiency (Addison's disease)

Progressive chronic destruction of more than 90% of adrenal cortex on both sides' results in an uncommon clinical condition called Addison's disease.

Etiopathogenesis. Any condition which causes marked chronic adrenal destruction may produce Addison's disease. These include: tuberculosis, autoimmune or idiopathic adrenalin's, histoplasmosis, amyloidosis, metastatic cancer, sarcoidosis and haemochromatosis. However, currently the first two causes - tuberculosis and autoimmune chronic destruction of adrenal glands, are implicated in majority of cases of Addison's disease. Irrespective of the cause, the adrenal glands are bilaterally small and irregularly shrunken. Histologic changes, depending upon the cause, may reveal specific features as in tuberculosis and histoplasmosis, or the changes may be in the form of nonspecific lymphocytic infiltrate as in idiopathic (autoimmune) adrenalins.

Clinical features. Clinical manifestations develop slowly and insidiously. The usual features are:

- Asthenia i.e. progressive weakness, weight loss and lethargy as the cardinal symptoms.
- Hyperpigmentation, initially most marked on exposed areas, but later involves unexposed parts and mucous membranes as well.
- Arterial hypotension.

- Vague upper gastrointestinal symptoms such as mild loss of appetite, nausea, vomiting and upper abdominal pain.
- Lack of androgen causing loss of hair in women.

- Episodes of hyperglycaemia.

- Biochemical changes include reduced GFR, acidosis, hyperkalaemia and low levels of serum sodium, chloride and bicarbonate.

Secondary adrenocortical insufficiency

Adrenocortical insufficiency resulting from deficiency of ACTH is called secondary adrenocortical insufficiency.

Etiopathogenesis. ACTH deficiency may appear in 2 settings:

3. Selective ACTH deficiency due to prolonged administration of high doses of glucocorticoids. This leads to suppression of ACTH release from the pituitary gland and selective deficiency.

4. Panhypopituitarism due to hypothalamus-pituitary diseases is associated with deficiency of multiple tropic hormones.

Clinical features. The clinical features of secondary adrenocortical insufficiency are like those of Addison's disease except the following:

b) These cases lack hyperpigmentation because of suppressed production of melanocytestimulating hormone (MSH) from the pituitary.

c) Plasma ACTH levels are low-to-absent insecondary insufficiency but are elevated in Addison's disease.

d) Aldosterone levels are normal due to stimulation by renin.

Hypoaldosteronism

Isolated deficiency of aldosterone with normal cortisol level may occur in association with reduced renin secretion.

Etiopathogenesis. The causes of such hyporeninism are:

- Congenital defect due to deficiency of an enzyme required for its synthesis.
- Prolonged administration of heparin
- Certain diseases of the brain.
- Excision of an aldosteronesecreting tumour.

linical features. The patients of isolated hypoaldosteronism are adults with mild renal failure and diabetes mellitus. The predominant features are hyperkalaemia and metabolic acidosis.

Thyroid gland

Anatomy. Embryologically, the thyroid gland arises from a midline invagination at the root of the tongue and grows downwards in front of trachea and thyroid cartilage to reach its normal position. Failure to descent may produce anomalous lingual thyroid. The thyroglossal duct that connects the gland to the pharyngeal floor normally disappears by 6th week of embryonic life. In adults, its proximal end is represented by foramen caecum at the base of the tongue and distal end by the pyramidal lobe of the thyroid. Persistence of the remnants of thyroglossal duct in the adults may develop into thyroglossal cyst. The C-cells of the thyroid originate from the neuroectoderm.

The thyroid gland in an adult weighs 15-40 gm and is composed of two lateral lobes connected in the midline by a broad isthmus which may have a pyramidal lobe extending upwards. Cut section of normal thyroid is yellowish and translucent.

Histology. The thyroid is composed of lobules of colloid-filled spherical follicles or acini. The lobules are enclosed by fibrovascular septa. The follicles are the main functional units of the thyroid. They are lined by cuboidal epithelium with numerous fine microvilli extending into the f ollicular colloid that contains the glycoprotein, thyroglobulin. The follicles are separated from each other by delicate fibrous tissue that contains blood vessels, lymphatics and nerves. Calcitonin-secreting C-cells or parafollicular cells are dispersed within the. follicles and can only be identified by silver, stains and immunohistochemical methods.

Functions. The major function of the thyroid gland is to maintain a high rate of metabolism which is done by means of iodine-containing thyroid hormones, thyroxine (T4) and triiodothyronine (T3).

The thyroid is one of the most labile organs in the body and responds to numerous stimuli such as puberty, pregnancy, physiologic stress and various pathologic states. This functional lability of the thyroid is responsible for transient hyperplasia of the thyroidal epithelium. Under normal conditions, the epithelial lining of the follicles may show changes in various phases of function as under:

- **Resting phase** characterised by large follicles lined by flattened cells and filled with deeply staining homogeneous colloid e.g. in colloid goitre and iodine-treated hyperthyroidism.
- **Secretory phase** in which the follicles are lined by cuboidal epithelium and the colloid is moderately dark pink e.g. in normal thyroid,
- **Resorptive phase** is characterised by follicleslined by columnar epithelium and containing lightly stained vacuolated and scalloped colloid e.g. in hyperthyroidism.

The synthesis and release of the two main circulating thyroid hormones, T3 and T4 are regulated by hypophyseal thyroid-stimulating hormone (TSH) and involves the following steps:

Iodine trapping by thyroidal cells involves absorbing of iodine from the blood and concentrating it more than twenty-fold.

Oxidation of the iodide takes place within the cells by a thyroid peroxidase.

Iodination occurs next, at the microvilli level between the oxidised iodine and the tyrosine residues of thyroglobulin so as to form mono-iodotyrosine (MIT) and di-iodotyrosine (DIT).

Coupling of MIT and DIT in the presence of thyroid peroxidase forms tri-iodothyronine (T3) and thyroxine (T4).

The thyroid hormones so formed are released by endocytosis of colloid and proteolysis of thyroglobulin within the follicular cells resulting, in discharge of T3 and T4 into circulation where they are bound to thyroxinebinding globulin.

A number of thyroid function tests are currently available. These include:

6. Determination by radioimmunoassay (RIA) of serum levels of T3, T4-TSH and TRH;

7. Assessment of thyroid activity by its ability to uptake radioactive iodine (RAIU); and

8.To assess whether thyroid lesion is a non-functioning cold nodule') or hyperactive mass ('hot nodule').

Diseases of the thyroid include: functional disorders (hyperthyroidism and hypothyroi-dism), thyroiditis, Graves' disease, goitre and tumours. The relative frequency of some

of these diseases varies in different geographic regions according to the iodine content of the diet consumed.

Functional disorders

Two significant functional disorders characterised by distinct clinical syndromes are described. These are: hyperthyroidism (thyrotoxicosis) and hypothyroidism.

Hyperthyroidism (thyrotoxicosis)

Hyperthyroidism, also called thyrotoxicosis, is a hypermetabolic clinical and biochemical state caused by excess production of thyroid hormones. The condition is more frequent in females and is associated with rise in both T3 and T4 levels is blood, though the increase in T3 is generally greater than that of T4.

Etiopathogenesis. Hyperthyroidism may be caused by many diseases but three most common causes are: Graves' disease (diffuse toxic goitre), toxic multinodular goitre and a toxic adenoma. Less frequent causes are hyper-secretion of pituitary TSH by a pituitary tumour, hypersecretion of TRH, thyroid if is, metastatic tumours of the thyroid, struma ovarii, congenital hyperthyroidism in the newborn of mother With Graves' disease, HCG-secreting tumours due to mild thyrotropic effects of HCG (e.g. hydatidiform mole, choriocarcinoma and testicular tumours), and lastly, by excessive doses of thyroid hormones or iodine called Basedow disease.

Clinical features. Patients with hyperthyroidism have a slow and insidious- onset, varying in severity from case to case. The usual symptoms are emotional instability, nervousness, palpitation, fatigue, weight loss in spite of good appetite, heat intolerance, perspiration, menstrual disturbances and fine tremors of the outstretched hands (Fig. 24.4,A). Cardiac manifestations in the form of tachycardia, palpitations and cardiomegaly are invariably present in hyperthyroidism. The skin of these patients is warm, moist and flushed. Weakness of skeletal muscles and osteoporosis are common. Typical eye changes in the form of exophthalmos are a common feature in Graves' disease. The serum T3 and T4 levels are elevated but TSH secretion is usually inhibited.

A sudden spurt in the severity of hyperthyroidism termed 'thyroid storm' or 'thyroid crisis' may occur in patients who have undergone subtotal thyroidectomy before adequate control of hyperthyroid state, or in a hyper-thyroid patient under acute stress, trauma and with severe infection. These patients develop high grade fever, tachycardia, cardiac arrhythmias and coma and may die of congestive heart failure or hyperpyrexia.

Hypothyroidism

Hypothyroidism is a hypometabolic clinical state resulting from inadequate production of thyroid hormones for prolonged periods, or rarely, from resistance of the peripheral tissues tithe effects of thyroid hormones. The clinical manifestations of hypothyroidism, depending upon the age at onset of disorder, are divided into 2 forms:

- Cretinism or congenital hypothyroidism is the development of severe hypothyroidism during infancy and childhood.
- Myxoedema is the adulthood hypothyroidism.

Cretinism

A cretin is a child with severe hypothyroidism present at birth or developing within first two years of postnatal life. This is the period when brain development is taking place so that in the absence of treatment the child is both physically and mentally retarded. The word 'Cretini' is derived from the French, meaning Christ-like because these children are so mentally retarded that they are incapable of committing sins.

Etiopathogenesis. The causes of congenital hypothyroidism are as follows:

1. Developmental anomalies e.g. thyroid agenesis and ectopic thyroid.

3. Genetic defect in thyroid hormone synthesise, defect in iodine trapping, oxidation, iodination, coupling and thyroglobulin synthesis.

4. Foetal exposure to iodides and antithyroid drugs.

5. Endemic cretinism in regions with endemic goitre due to dietary lack of iodine (sporadic cretinism, on the other hand, is due to developmental anomalies and genetic defects in thyroid hormone synthesis described above).

Clinical features. The clinical manifestations usually become evident within a few weeks to months of birth. The presenting features of a cretin are: slow to thrive, poor feeding, constipation, dry scaly skin, hoarse cry and bradycardia. As the child ages, clinical picture of fully-developed cretinism emerges characterised by impaired skeletal growth and consequent dwarfism, round face, narrow forehead, widely-set eyes, flat and broad nose, big protuberant tongue and protuberant abdomen. Neurological features such as deaf-mutism, spasticity and mental deficiency are more evident in sporadic cretinism due to developmental anomalies and dyshormonogenetic defects. Characteristic laboratory findings include a rise in TSH level and fall in T3 and T4 levels.

Myxoedema

The adult-onset severe hypothyroidism causes myxoedema. The term myxoedema connotes non-pitting oedema due to accumulation of hydrophilic mucopolysaccharides in the ground substance of dermis and other tissues.

Etiopathogenesis. There are several causes of myxoedema listed below but the first two are the most common causes:

- Ablation of the thyroid by surgery or radiation.
- Autoimmune (lymphocytic) thyroiditis (termed primary idiopathic myxoedema).
- Endemic or sporadic goitre.

- Hypothalamic-piruitary lesions.
- Thyroid cancer.
- Prolonged administration of antithyroid drugs.
- Mild developmental anomalies and dyshormonogenesis.

Clinical features. The onset of myxoedema is slow and a fully-developed clinical syndrome may appear after several years of hypothyroidism. The striking features are cold intolerance, mental and physical lethargy, constipation, slowing of speech and intellectual function, puffiness of face, loss of hair and altered texture of the skin.

The laboratory diagnosis in myxoedema is made by low serum T3 and T4 levels and markedly elevated TSH levels as in the case of cretinism but cases with suprathyroid lesions (hypothalamic-pituitary disease) have low TSH levels.

Thyroiditis

Thyroiditis is classified into the following types:

I. Autoimmune or lymphocytic thyroiditis (includes Hashimoto's thyroiditis, atrophic thyroiditis and focal lymphocytic thyroiditis).

II. Infectious thyroiditis.

3. Granulomatous thyroiditis (de Quervain's thyroiditis, giant cell thyroiditis: or subacute thyroiditis).

IV. Riedel's thyroiditis (or invasive fibrous thyroiditis).

However, except the first group i.e. autoimmune thyroiditis, other varieties of thyroiditis are less common. Accordingly, this group is discussed in detail below, while the other forms are briefly outlined.

AUTOIMMUNE (LYMPHOCYTIC) THYROIDITIS

This is a group of thyroiditis having, in common, infiltration of the thyroid by lymphocytes and plasma cells, and occurrence of thyroid specific autoantibodies in the serum. Autoimmune thyroiditis includes the following 3 entities:

A. Hashimoto's thyroiditis

B. Atrophic thyroiditis

C. Focal lymphocytic thyroiditis

Hashimoto's Thyroiditis.

Hashimoto's thyroiditis, also called diffuse lymphocytic thyroiditis, struma lymphomatosa or goitrous autoimmune thyroiditis, is characterised by 3 principal features:

- diffuse goitrous enlargement of the thyroid;
- lymphocytic infiltration of the thyroid gland; and
- occurrence of thyroid autoantibodies.

Hashimoto's thyroiditis occurs more frequently between the age of 30 and 50 years and shows an approximately ten-fold preponderance among females.

Etiopathogenesis. Hashimoto's thyroiditis is an autoimmune disease is well established. Described by Hashimoto, a Japanese surgeon in 1912, it was the first autoimmune disease of any organ. In order to explain the autoimmune pathogenesis of Hashimoto's thyroiditis, two mutually interlinked observations are worth noting:

- HLA association. Hashimoto's thyroidit ishas some genetic predisposition as evidenced by familial occurrence of the disease and association with HLA-DR5.
- Autoimmune disease association. Hashimoto's disease has been found in association with other autoimmune diseases such as Graves' disease, SLE, Sjogren's syndrome, rheumatoid arthritic, pernicious anaemia and Type I (juvenile-onset) diabetes.

Hashimoto's thyroiditis is immunologically closely linked to Graves' disease but the latter condition is more often associated with HLA-DR3 (page 955). The particular HLA type associated with Hashimoto's thyroiditis, HLA-DR5, causes a genetic defect in the immune system resulting in destruction of the thyroid parenchyma by release of several cytotoxic autoantibodies and by cell-mediated immune mechanisms. The basic immunologic abnormality is activation of CD4 + T cells which induce CD8 + cytotoxic T cells and form autoantibodies. The follow in gautoantibodies against different thyroid cell antigens are detectable in the sera of most patients with Hashimoto's thyroiditis:

- Thyroid microsomal autoantibodies (against the microsomes of the follicular cells).
- Thyroglobulin autoantibodies.
- Less frequently, TSH receptor autoantibodies.
- Less constantly found are thyroid autoantibodies against follicular cell membranes, thyroid hormones themselves, and colloid component other than thyroglobulin.

Pathologic changes. Pathologically, two varieties of Hashimoto's thyroiditis are seen: classic form, the usual and more common, and fibrosing variant found in only 10% cases of Hashimoto's thyroiditis. Grossly, the classic form is characterised by diffuse, symmetric, firm and rubbery enlargement of the thyroid which may weigh 100-300 gm. Sectioned surface of the thyroid is fleshly with accentuation of normal lobulations but with retained normal shape of the gland. The fibrosing variant has a firm, enlarged thyroid with compression of the surrounding tissues.

Histologically, the classic form shows the following features:

- There is extensive infiltration of the gland by lymphocytes, plasma cells, immunoblasts and macrophages, with formation of lymphoid follicles having germinal centres.
- There is decreased number of thyroid follicles which are generally atrophic and areoften devoid of colloid.

- The follicular epithelial cells are transformed into their degenerated state termed Hurthle cells (also called Askanazy cells, or oxyphil cells, or oncocytes). These cells have abundant oxyphilic or eosinophilic and granular cytoplasm due to large number of mitochondria and contain large bizarre nuclei.
- There is slight fibrous thickening of the septa separating the thyroid lobules.

The less common fibrosing variant of Hashimoto's thyroiditis shows considerable fibrous replacement of thyroid parenchyma and a less prominent lymphoid infiltrate.

Clinical features. The presenting feature of Hashimoto's thyroiditis is a painless, firm and moderate goitrous enlargement of the thyroid gland, usually associated with hypothyroidism, in an elderly woman. At this stage, serum T3 and T4 levels are decreased and RAIU is also reduced. A few cases, however, develop hyperthyroidism, termed hashitoxicosis, further substantiating the similarities in the autoimmune phenomena between Hashimoto's thyroiditis and Graves' thyrotoxicosis. There is no increased risk of developing thyroid carcinoma in Hashimoto's thyroiditis but there is increased frequency of malignant lymphoma in these cases.

Atrophic Thyroiditis

Atrophic thyroiditis is another form of autoimmune thyroiditis in which the gland is decreased in size and manifests clinically as spontaneous hypothyroidism. The condition is closely related to Hashimoto's thyroiditis in having lymphocytic infiltration, atrophy of the thyroid follicles and fibrosis but differs from it in lacking the regeneration of thyroid follicles which is responsible for thyroid enlargement in cases with Hashimoto's thyroiditis. The lack of regeneration in atrophic thyroiditis is thought to be due to the presence of blocking antibodies against thyroid growth.

Focal Lymphocytic Thyroiditis

A clinically less important variant of autoimmune origin is focal lymphocytic thyroiditis which may be present in association with other thyroid diseases such as goitre, adenoma or carcinoma. As the name suggests, the condition is characterised by focal aggregates of lymphoid cells with germinal centres without significant epithelial alterations.

INFECTIOUS THYROIDITIS

Acute thyroiditis by microbial infection with bacteria, viruses and fungi is uncommon and is generally a complication of infection elsewhere in the body. The inflammatory involvement in all such cases is generally transient and responds to specific therapy without seriously impairing the thyroid unction.

GRANULOMATOUS THYROIDITIS

Granulomatous thyroiditis, also called de Quervain's or subacute, or giant cell thyroiditis, is a distinctive form of self-limited inflammation of the thyroid gland. Etiology of the condition is not known but clinical features of a prodromal phase and preceding respiratory infection suggest a possbile viral etiology. The disease is more common in young and middle-aged women and may present clinically with painful moderate thyroid enlargement with fever, features of hyperthyroidism in the early

phase of the disease, and hypothyroidism if the damage to the thyroid gland is extensive. The condition is self-limiting and shows complete recovery of thyroid function in about 6 months.

Pathologic changes. Grossly, there is moderate enlargement of the gland which is often asymmetric or focal. The cut surface of the involved area is firm and yellowish-white. Microscopically, the features vary according to the stage of the disease:

2 Initially, there is acute inflammatory destruction of the thyroid parenchyma and formation of microabscesses.

3 Later, the more characteristic feature of granulomatous appearance is produced. These granulomas consist of central colloid material surrounded by histiocytes and scattered multinucleate giant cells.

4 More advanced cases may show fibroblasticproliferation.

Morphologically similar appearance may be produced in cases where vigorous thyroid palpation may initiate mechanical trauma to follicles, so-called palpation thyroiditis.

RIEDEL'S THYROIDITIS

Riedel's thyroiditis, also called Riedel's struma or invasive fibrous thyroiditis, is a rare chronic disease characterised by stony-hard thyroid that is densely adherent to the adjacent structures in the neck. The condition is clinically significant due to compressive clinical features (e.g. dysphagia, dyspnoea, recurrent laryngeal nerve paralysis and stridor) and resemblance with thyroid cancer. Riedel's struma is seen more commonly in females in 4th to 7th decades of life.

The etiology is unknown but possibly Riedel's thyroiditis is a part of multifocal idiopathic fibrosclerosis. This group of disorders includes: idiopathic retroperitoneal, mediastinal and retro-orbital fibrosis and sclerosing cholangitis, all of which may occur simultaneously with Riedel's thyroiditis.

Pathologic changes. Grossly, the thyroid gland is usually contracted, stony-hard, asymmetric and firmly adherent to the adjacent structures. Cut section is hard and devoid of lobulations.

Microscopically, there is extensive fibro-collagenous replacement, marked atrophy of the thyroid parenchyma, focally scattered lymphocytic infiltration and invasion of the adjacent muscle tissue by the process.

GRAVES' DISEASE (DIFFUSE TOXIC GOITRE)

Graves' disease, also known as Basedow's disease, primary hyperplasia, exophthalmic goitre, and diffuse toxic goitre, is characterised by a triad of features:

5. hyperthyroidism (thyrotoxicosis);
6. diffuse thyroid enlargement; and
7. ophthalmopathy.

The disease is begin frequent between the age of 30 and 40 years and has five-fold increased prevalence among females.

Etiopathogenesis. Graves' disease is an autoimmune disease and, as already stated, there are many immunologic similarities between this condition and Hashimoto's thyroiditis. These are as follows:

4. HLA association. Like in Hashimoto's thyroiditis, Graves' disease too has genetic predisposition. A familial occurrence has been observed and (Graves' disease is associated with HLA-DR 3).

5. Autoimmune disease association. Graves' disease may be found in association with other organ-specific autoimmune diseases. Hashimoto's thyroiditis and Grave's disease are frequently present in the same families and the two diseases may coexist in the same patient.

As in Hashimoto's thyroiditis, the basic immunologic abnormality in Graves' disease responsible for autoimmune phenomena is genetically-induced organ-specific defect in suppressor T-lymphocytes. Autoantibodies against thyroid antigens are detectable in the serum of patients with Graves' disease but frequency of their occurrence is somewhat different from that of Hashimoto's thyroiditis. These autoantibodies are:

- Most consistently, TSH receptor autoantibodies.
- Low levels of thyroid microsomal autoantibodies.
- Less often, other circulating autoantibodies. The pathogenesis of Graves' ophthalmopathy is also of autoimmune origin. The evidence in support is the intense lymphocytic infiltrate around the ocular muscles and detection of circulating autoantibodie against muscle antigen that cross-react with thyroid microsomes.

Pathologic changes. Grossly, the thyroid is moderately, diffusely and symmetrically enlarged and may weigh up to 70-90 gm. On cut section, the thyroid parenchyma is typically homogeneous, red-brown and meaty and lacks the normal translucency.

Histologically, the following features are found:

- There is considerable epithelial hyperplasia as seen by increased height of thefollicular lining cells and formation of papillary enfolding of piled up epithelium into the lumina of follicles which are small.
- The colloid is markedly diminished and slightly staining, watery land finely vacuolated.
- The stroma shows increased vascularity and accumulation of lymphoid cells.

However, the pathologic changes in gross specimen as well as on histologic examination are considerably altered if preoperative medication has been administered. Iodine administration results in accumulation of colloid in the follicles and decrease in vascularity and height of follicular cells, while anti-thyroid drugs such as thiouracil cause marked hyperplasia.

Clinical features. Graves' disease generally develops slowly and insidiously. The patients are usually young women who present with symmetric, moderate enlargement of the thyroid gland with features of thyrotoxicosis, ophthalmopathy and dermatopathy. The ocular abnormalities are lid lag, upper lid retraction, stare, weakness of eye muscles and proptosis. In extreme cases, the lids can no longer close and may produce corneal injuries and ulcerations. Dermatopathy in Graves' disease most

often consists of pretibial (localised) myxoedema in the form of firm plaques. Like in Hashimoto's thyroiditis, there is no increased risk of development of thyroid cancer in Graves' disease.

GOITRE

The term goitre is defined as thyroid enlargement caused by compensatory hyperplasia and hypertrophy of the follicular epithelium in response to thyroid hormone deficiency. The end-result of this hyperplasia is generally a euthyroid state (in contrast to thyrotoxicosis occurring in diffuse toxic goitre or Graves' disease) though at some stages there may be hypo- or hyperthyroidism. Two morphologic forms of goitre are distinguished:

A. Simple goitre (diffuse nontoxic goitre or colloid goitre).

B. Nodular goitre (multinodular goitre or adenomatous goitre).

Pathogenesis of Goitre

The pathogenetic mechanisms of both forms of goitre can be considered together since nodular goitre is generally regarded as the end-stage of long-standing simple goitre. The fundamental defect is deficient production of thyroid hormones due to various etiologic factors described below, but most common is dietary lack of iodine. Deficient thyroid hormone production causes excessive TSH stimulation which leads to hyperplasia of follicular epithelium as well as formation of new thyroid follicles. The hyperplastic stage followed by involution stage completes the picture of simple goitre. Repeated and prolonged cyclic changes of hyperplasia and involution result in nodular goitre.

Simple Goitre (Diffuse Nontoxic Goitre, Colloid Goitre)

Diffuse nontoxic simple or colloid goitre is the name given to diffuse nodular enlargement of the thyroid gland, unaccompanied by hyperthyroidism. Most cases are in a state of euthyroid though they may have passed through preceding stage of hypothyroidism due to inadequate supply of iodine. TSH levels are invariably elevated. In general, goitre is more common in females. Simple goitre often appears at puberty or in adolescence, following which it may either regress or may progress to nodular goitre.

Etiology. Epidemiologically, goitre occurs in 2 forms: endemic, and non-endemic or sporadic.

Endemic goitre. Prevalence of goitre in a geographic area in more than 10% of the population is termed endemic goitre. Such endemic areas are several high mountainous regions far from the sea where iodine content of drinking water and food is low such as in the regions of the Himalayas, the Alps and the Andes. Of late, however, the prevalence in these areas has declined due to prophylactic use of iodised salt. Though most endemic goitres are caused by dietary lack of iodine, some cases occur due to goitrogens and genetic factors. Goitrogens are substances which interfere with the synthesis of thyroid hormones. These substances are drugs used in the treatment of hyperthyroidism and certain items of food such as cabbage, cauliflower, turnips and cassava roots.

• Sporadic goitre. Non-endemic or sporadic simple goitre is less common than the endemic variety. In most cases, the etiology of sporadic goitre is unknown. A number of causal influences have been attributed. These include:

• Suboptimal iodine intake in conditions of increased demand as in puberty and pregnancy.

• Genetic factors.

• Dietary goitrogenes.

Hereditary defect in thyroid hormone synthesis and transport (dyshormonogenesis).

• Inborn errors of iodine metabolism.

Pathologic changes. Grossly, the enlargement of the thyroid gland in simple goitre is moderate (weighing up to 100-150 gm), symmetric and diffuse. Cut surface is gelatinous and translucent brown.

Histologically, two stages are distinguished:

- Hyperplastic stage is the early stage and is characterised by tall columnar follicular epithelium showing papillary in foldings and formation of small new follicles.
- Involution stage generally follows hyperplastic stage after variable period of time. This stage is characterised by large follicles distended by colloid and lined by flattened follicular epithelium.

Nodular Goitre (Multinodular Goitre, Adenomatous Goitre)

As already stated, nodular goitre is regarded as the end-stage of long-standing simple goitre. It is characterised by most extreme degree of tumourlike enlargement of the thyroid gland and characteristic nodularity. The enlargement of the gland may be sufficient to cause not only cosmetic disfigurement, but in many cases may cause dsyphagia and choking due to compression of oesophagus and trachea. Most cases are in a euthyroid state but about 10% cases may develop thyrotoxicosis resulting in toxic nodular goitre or Plummer's disease. However, thyrotoxicosis of Plummer's disease (toxic nodular goitre) differs from that of Graves' disease (diffuse toxic goitre) in lacking features of ophthalmopathy and dermatopathy. Such 'hot nodules' may be picked up by scintiscan or by RAIU studies. Since nodular goitre is derived from simple goitre, it has the same female preponderance but affects older individuals because it is a late complication of simple goitre.

Etiology. Etiologic factors implicated in endemic and non-endemic or sporadic variety of simple goitre are involved in the etiology of nodular goitre too. However, how nodular pattern is produced is not clearly understood. Possibly, epithelial hyperplasia, generation of new follicles, and irregular accumulation of colloid in the follicles - all contribute to produce increased tension and stress in the thyroid gland causing rupture of follicles and vessels. This is followed by haemorrhages, scarring and sometimes calcification, resulting in development of nodular pattern.

Pathologic changes. Grossly, the thyroid m nodular goitre shows asymmetric and extreme enlargement, weighing 100-500 girt or even more. The five cardinal macroscopic features are:

- nodular it with poor encapsulation;

- fibrous scarring;
- haemorrhages:
- focal calcification; and
- Cystic degeneration.

Cut surface generally shows multinodularity but occasionally there may be only one or two nodules which are poorly-circumscribed (unlike complete encapsulation of thyroid adenoma, described below). Histologically, the same heterogeneity as seen on macroscopic structure is seen. These features are:

- Partial or incomplete encapsulation of nodules.
- The follicles varying from small to large and lined by flat to high epithelium. A few may show macropapillary formation.
- Areas of haemorrhages, haemosiderin-laden macrophages and cholesterol crystals.
- Fibrous starring with foci of calcification.
- Microcyst formation.

2. Age	Middle to old age	All ages	Middle to old-age; familial too	Old age
3.Female/male ratio	2.5:1	3:1	1:1	1.5:1
4. Cell of origin	Follicular	Follicular	Parafollicular	Follicular
5. Regional metastases	Rare	Common	Common	Common
6. Distant metastases	Common	Rare	Rare	Common
7. 10-year survival	50-70%	80-95%	60-70%	5-10% (median survival about 2 months)

Parathyroid glands

Anatomy. The parathyroid glands are usually 4 in number: the superior pair derived from the 3rd branchial pouch and inferior pair from the 4th branchial pouch of primitive foregut. Both pairs are usually embedded in the posterior aspect of the thyroid substance but separated from it by a connective tissue capsule. In the adults, each gland is an oval, yellowish-brown, flattened body, weighing 35-45 mg. There may, however, be variation in the number, location and size of parathyoid glands.

Histology and functions. Microscopically, parathyroid glands are composed of solid sheets and cords of parenchymal cells and variable amount of stromal fat. The parenchymal cells are of 3 types: chief cells, oxyphil cells and water-clear cells. The chief cells are most numerous and are the major source of parathyroid hormone. The latter two types of cells appear to be derived from the chief cells and have sparse secretory granules but are potentially capable of secreting parathyroid hormone. The major function of the parathyroid hormone, in conjunction with calcitonin and vitamin D, is to regulate serum calcium levels and metabolism of bone. Parathyroid hormone tends to elevate serum calcium level and reduce serum phosphate level. Secretion of parathyroid hormone takes place in response to serum levels of calcium by a feedback mechanism—lowered serum calcium stimulates secretion of parathyroid hormone, while elevated serum calcium causes decreased secretion of the hormone. The role of parathyroid hormone in regulating calcium metabolism in the body is at the following 3 levels:

 Parathyroid hormone stimulates osteoclasticactivity and results in resorption of bone and release of calcium. Calcitonin released by C-cells, on the other hand, opposes parathyroid hormone by preventing resorption of bone and lowering serum calcium level.

 Parathyroid hormone acts directly on renaltubular epithelial cells and increases renal reabsorption of calcium and inhibits reabsorption of phosphate; calcitonin enhances renal excretion of phosphate.

 Parathyroid hormone increases renal production of the most active metabolite of vitamin D, 1, 25-dihydrocholecalciferol, which in turn increases calcium absorption from the small intestine.

The major parathyroid disorders are its functional disorders (hyper-and hypopara-thyroidism) and neoplasms.

HYPERPARATHYROIDISM

Hyperfunction of the parathyroid glands occurs due to excessive production of parathyroid hormone. It is classified into 3 types - primary, secondary and tertiary.

Primary hyperparathyroidism occurs from oversecretion of parathyroid hormone due to disease of the parathyroid glands.
Secondary hyperparathyroidism is caused by diseases in other parts of the body.

Tertiary hyperparathyroidism develops from secondary hyperplasia after removal of the cause of secondary hyperplasia.

Primary Hyperparathyroidism

Primary hyperparathyroidism is not uncommon and occurs more commonly with increasing age. It is especially likely to occur in women near the time of menopause.

Etiology. Common causes of primary hyperparathyroidism are as follows:

 Most commonly, parathyroid adenomas in approximately 80% cases.
 Carcinoma of the parathyroid glands in 2-3%patients.

 Primary hyperplasia in about 15% cases (usually chief cell hyperplasia).

Also included above are the familial cases of multiple endocrine neoplasia (MEN) syndromes where parathyroid adenoma or primary hyperplasia is one of the components.

Clinical features. The patients with primary hyperparathyroidism have the following characteristic biochemical abnormalities:

1.Elevated levels of parathyroid hormone

2.Hypercalcaemia

3.Hypophosphataemia

4.Hypercalciuria

Clinical presentation of individuals with primary hyperparathyroidism may be in a variety of ways:

- Most commonly, nephrolithiasis and or/nephrocalcinosis. These dysfunctions result from excessive excretion of calcium in the urine due to hypercalcaemia induced by increased parathyroid hormone level.

- Metastatic calcification, especially in the blood vessels, kidneys, lungs, stomach, eyes and other tissues.
- Generalised osteitis fibrosa cystica due to osteoclastic resorption of bone and its replacement by connective tissue.
- Neuropsychiatric disturbances such as depression, anxiety, psychosis and coma.

- Hypertension is found in about half the cases.

- Other changes such as pancreatitis, cholelithiasis and peptic ulcers due to hypercalcaemia and high parathyroid hormone level are less constant features.

Secondary Hyperparathyroidism

Secondary hyperparathyroidism occurs due to increased parathyroid hormone elabortion secondary to a disease elsewhere in the body. Hypocalcaemia stimulates compensatory hyperplasia of the parathyroid glands and causes secondary hyperparathyroidism.

Etiology. Though any condition that causes hypocalcaemia stimulates excessive secretion of parathyroid hormone, the important causes of secondary hyperparathyroidism are as under:

- Chronic renal insufficiency resulting in retention of phosphate and impaired intestinal absorption of calcium.
- Vitamin D deficiency and consequent rickets and osteomalacia may cause parathyroidhyperfunction.
- Intestinal malabsorption syndromes causing deficiency of calcium and vitamin D.

Clinical features. The main biochemical abnormality in secondary hyperparathyroidism is mild hypocaleaemia, in striking contrast to hypercalcaemia in primary hyperparathyroidism. The patients with secondary hyperparathyroidism have signs and symptoms of the disease which caused it. Usually, secondary hyperparathyroidism is a beneficial compensatory mechanism, but more severe cases may be associated with renal osteodystrophy (i.e. features of varying degree of osteitis fibrosa, osteomalacia, osteoporosis and osteosclerosis in cases of chronic renal insufficiency) and soft tissue calcification.

Tertiary Hyperparathyroidism

Tertiary hyperparathyroidism is a complication of secondary hyperparathyroidism in which the hyperfunction persists in spite of removal of the cause of secondary hyperplasia. Possibly, a hyperplastic nodule in the parathyroid gland develops which becomes partially autonomous and

continues to secrete large quantities of parathyroid hormone without regard to the needs of the body.

HYPOPARATHYROIDISM

Deficiency or absence of parathyroid hormone secretion causes hypoparathyroidism. Hypoparathyroidism is of 3 types - primary, pseudo-and pseudopseudohypoparathyroidism.

Primary Hypoparathyroidism

Primary hypoparathyroidism is caused by disease of the parathyroid glands. Most common caused of primary hypoparathyroidism are: surgical procedures involving thyroid, parathyroid, or radical neck dissection for cancer. Other causes are uncommon and include idiopathic hypoparathyroidism of autoimmune origin in children and may occur as sporadic or familial cases. These cases are generally associated with other autoimmune diseases.

Clinical features. The main biochemical dysfunctions in primary hypoparathyroidism are hypocalcaemia, hyperphosphataemia and hypocalciuria. The clinical manifestations of these abnormalities are:

- Increased neuromuscular irritability and tetany.
- Calcification of the lens and cataract formation.
- Abnormalities in cardiac conduction.
- Disorders of the CNS due to intracranialcalcification.
- Abnormalities of the teeth.

Pseudo-hypoparathyroidism

In pseudo-hypoparathyroidism, the tissues fail to respond to parathyroid hormone though parathyroid glands are usually normal. It is a rare inherited condition with an autosomal dominant character. The patients are generally females and are characterised by signs and symptoms of hypoparathyroidism and other clinical features like short stature, short metacarpals and metatarsals, flat nose, round face and multiple exostoses. Since renal tubules cannot adequately respond to parathyroid hormone, there is hypercalciuria, hypocalcaemia and hyperphosphataemia.

Pseudopseudo-hypoparathyroidism.

Pseudopseudo-hypoparathyroidism is another rare familial disorder in which all the clinical features of pseudo-hypoparathyroidism are present except that these patients have no hypocalcaemia or hyperphosphataemia and the tissues respond normally to parathyroid hormone.

Pseudopseudohypoparathyroidsm has been considered an incomplete form of pseudo-hypoparathyroidism.

Endocrine pancreas

The human pancreas histologically and functionally has 2 distinct parts - the exocrine and endocrine. The discussion here deals with the endocrine pancreas and its two main disorders: diabetes mellitus and islet cell tumours.

The endocrine pancreas consists of microscopic collections of cells called islets of Langerhans found scattered within the pancreatic lobules, as well as individual endocrine cells found in duct epithelium and among the acini. The total weight of endocrine pancreas in the adult, however, does not exceed 1-1.5 gm (total weight of pancreas 60-100 gm). The islet cell tissue is greatly concentrated in the tail than in the head or body of the pancreas. Islets possess no ductal system and they drain their secretory products directly into the circulation. Ultrastructurally and immunohistochemically, 4 major and 2 minor types of islet cells are distinguished, each type having its distinct secretory product and function. These are as follows:

A. Major cell types:

4. Beta (B) cells comprise about 70% of islet cells and secrete insulin, the defective response or deficient synthesis of which causes diabetes mellitus.

Alpha (A) cells comprise 20% of islet cells and secrete glucagons which induce hyperglycemia.

a Delta (D) cells comprise 5-10% of islet cells and secrete somatostatin which suppresses both insulin and glucagon release.

a Pancreatic polypeptide (PP) cells or F cells comprise 1-2% of islet cells and secrete pancreatic polypeptide having some gastrointestinal effects.

B. Minor cell type:

a Dl cells elaborate vasoactive intestinalpeptide (VIP) which induces glycogenolysis and hyperglycaemia and causes secretary diarrhoea by stimulation of gastrointestinal fluid secretion.

a Enterochromaffin cells synthesise serotonin which in pancreatic tumours may induce cardioid syndrome.

DIABETES MELLITUS

Diabetes mellitus is a chronic clinical syndrome characterised by hyperglycaemia due to deficiency or defective response of insulin. It is estimated that approximately 1% of population suffers from diabetes mellitus.

Classification of Diabetes Mellitus

Generally speaking, if not specified, diabetes mellitus means primary or idiopathic diabetes mellitus. Secorufary4iabete$ mellitus is occurrence of hyperglycaemia associated with some identifiable causes such as due to chronic pancreatitis, postpancreatectomy, hormone-producing tumours, certain drugs, haemochromatosis and genetic endocrinologic disorders.

Primary or idiopathic diabetes mellitus, the common form, is currently divided into 2 major categories:

5) Type I diabetes, previously termed juvenile-onset diabetes, or insulin-dependent diabetes mellitus (IDDM).
6)Type II diabetes, previously called maturity-onset diabetes, or noninsulin dependent diabetes mellitus (NIDDM). It is further of 2 types - obese and nonobese type II diabetes.

Primary (idiopathic)	Secondary
Typt I (autoimmune) diabetes mellitus Insulin-dependent (IDDM) Type II (non-autoimmune) diabetes mellitus Non insulin-dependent (NIDPM) Maturity-onset diabetes of the young (MODY)	1. Pancreatic disease (chronic pancreatitis, post- pancreatectomy) 2. Hormonal abnormalities 3. Drugs and chemicals-induced diabetes 4. Insulin receptor abnormalities 5. Genetic disorders 6. Haemochromatosis

Etiology and Pathogenesis

Etiology and pathogenesis of the two types of diabetes mellitus ate discussed separately below, but before that, an understanding of the normal insulin synthesis and secretion is considered essential.

Normal insulin metabolism. The major stimulus for both synthesis and release of insulin is glucose. The steps involved in biosynthesis and release of insulin from B-cells are as follows:

4. Glucose stimulation initiates production of proinsulinin the endoplasmic reticulum. Proinsulin is a single chain of 86 aminoacids consisting of A and B chains of insulin, linked together by connecting segment called C-peptide.

Contrasting Features of Two Types of Diabetes Mellitus

Feature	Type I (IDDM, JOD)	Type II (NIDDM, MOD)
1. Frequency	10-20%	80-90%
2. Age at onset	Early (below 40 years)	Late (after 40 years)
3. Type of onset	Abrupt and severe	Gradual and insidious
4. Weight	Normal	Obese
5. HLA	HLA-Dlinked	No HLA association
6. Family history	< 20%	About 60%
7. Genetic locus	Unknown	Chromosome 6
8. Identical twins	50% chance in identical	60-80% chance in
9. Pathogenesis	Autoimmune	Insulin resistance
10. Islet cell	Yes	No
11. Blood insulin	Decreased insulin	Normal or increased
12. Islet cell	Insulitis, beta cell	No insulitis, mild beta
13. Clinical	Insulin and diet	Diet and drugs
14. Acute	Ketoacidosis	Hyperosmolar coma

Proinsulin is transferred to the Golgi complex where C-peptide is split off by a proteolytic enzyme. Both insulin and C-peptide are then stored in secretory granules in the Golgi complex from where they are released in membranous sacs acquired from the Golgi membranes into the cytoplasm where insulin is converted into zinc-insulin crystals.

Glucose stimulation of B cells causes insulin release as a biphasic process. First phase is the immediate release of insulin in response to risein blood glucose level, followed by slow second phase which continues till the blood glucose level •returns to normal limits.

After glucose stimulation, the membranous sacs containing zinc-insulin crystals and C-peptide in the cytoplasm of B cells are brought to the surface of plasma membrane by microtubule-microfilament system which requires intra-cellular calcium.

The final step is the release of B granules containing insulin and C-peptide by emiocytosis into the extracellular space from where insulin and C-peptide are transported into the capillary system of islets and thence into the systemic circulation.

A defect in any one step in the biosynthesis or release may lead to deficiency or defective release of insulin. Insulin is a major anabolic hormone and its main metabolic function is to increase the

transmembranous transport of glucose into certain cells of the body. In addition, insulin is required for glycogen formation in the liver and skeletal muscles, conversion of glucose to triglycerides, and for synthesis of nucleic acids and proteins. Insulin acts on its target cells by binding to the insulin receptors present on insulin responsive cells.

Etiopathogenesis of type – I diabetes. Type I diabetes mellitus, or juvenile-onset diabetes or insulin-dependent diabetes mellitus (IDDM) is caused by absolute deficiency of insulin resulting from reduction in B cell mass. These patients, therefore, respond to exogenously administered insulin. Currently, the pathogenesis of type I diabetes is explained on the basis of 3 mutually-interlinked mechanisms, each with sufficient evidences in support. These are: genetic susceptibility, autoimmunity, and certain environmental factors.

I. Genetic susceptibility. Diabetes mellitus runs in families has been known for years.

5. More recently, however, it has been shown in identical twins that if one twin has type I diabetes, there is a 50% chance of the second twin developing diabetes.
6. Secondly, a higher frequency (80%) of type I diabetes has been observed in HLA-DR 3 and HLA-DR 4 individuals.
7. Thirdly, different mutations have been identified with predisposition to the disease.

II. Autoimmunity. Type I diabetes is believed to be an autoimmune disease that results inspecific immunologic destruction of B cells of islet of Langerhans. The evidences in support areas follow:

1. Presence of islet cell antibodies in patients with type I diabetes.

2. Occurrence of lymphocytic infiltration in and around the islets (insulin's).

3. Association of type I diabetes with other autoimmune diseases. j

4. Remission of type I diabetes in response to immunosuppressive therapy such as administration of

cyclosporin A.

5. About 10% cases of type I diabetes has other organ-specific autoimmune disease such as Graves' disease, Addison's disease or autoimmune thyroiditis.

III. Environmental factors. Epidemiologic studies in type I diabetes have revealed involvement of certain environmental factors in its pathogenesis. These factors are certain viruses, chemicals and common environmental toxins.

1. Certain viral infections may precede the onset of type I diabetes e.g. mumps, measles, coxsackie B virus, cytomegalovirus and infectious mononucleosis.

2. Experimental induction of type I diabetes with certain chemicals has been possible e.g. alloxan, streptozotocin and pentamidine.

3. Geographic variations in the incidence of type I diabetes suggest some common environmental factors.

4. It can thus be summarised by interlinking the three mechanisms described above that in type I diabetes, some 'environmental factor'' initiates the 'autoimmune destruction' of B cells in 'genetically susceptible' individuals.

Etiopathogenesis of type II diabetes. Type II diabetes, or maturity-onset diabetes, or noninsulindependent diabetes mellitus (NIDDM); is more common and constitutes 80 - 90% cases of diabetes. Type II diabetes is further of 2 subtypes - obese and non-obese. The basic metabolic defect in this type of diabetes is either a delayed insulin secretion relative to glucose load (deranged insulin secretion), or the peripheral tissues are unable to respond to insulin (insulin resistance).

Though much less is known about the mechanisms involved in the pathogenesis of type II diabetes, a number of factors have been implicated. HLA association and autoimmune phenomena are, however, not involved. These factors are as under:

I. Genetic factors. Genetic susceptibility has a greater role in the pathogenesis of type II diabetes than in type I diabetes. For instance:

1. There is approximately 60-80% chance of developing diabetes in the other identical twin if one twin has diabetes.

2. Matvuiiy-onset diabetes of the young (MODY) has autosomal dominant inheritance but nothing is known about the inheritence of other cases of type II diabetes.

II. Obesity (Obese type II diabetes). Obesity is a common finding in type II diabetes. There is impaired insulin sensitivity of peripheral tissues such as muscle and fat cells to the action of insulin in obese individual’s insulin resistance).Weight reduction in such Obese patients produces improvement in the diabetic state.

III. Insulin receptor defect (Non-obese type II diabetes). It has been observed that insulinresistance is a factor not only in obese type II diabetes but also in non-obese type Π diabetes. In such individuals, the increased insulinresistance of peripheral tissues is due to either decrease in the number of insulin receptors or there is post-receptor defect.

Thus; type II diabetes is a complex multi-factorial disease involving 'deranged insulin secretion' and 'insulin resistance', with possible genetic defects, obesity and fault in the insulin receptors.

Pathologic Changes in Islets.

Pathologic changes in islets have been demonstrated in both types of diabetes, though the changes are more distinctive in type I diabetes. These changes are as under:

1. Insulitis. Lymphocytic infiltration in some but not all islets is a feature of type I diabetes.

2. Islet cell mass. There is reduction in the size and number of islets in type I diabetes, But in type II diabetes, B cell mass is either normal or mildly reduced. Infants of diabetic mothers, however, have hyperplasia and hypertrophy of islets as a compensatory response to maternal hyperglycaemia.

3. B-cell degranulation and glycogenosis. Type I diabetes is associated with B cell degranulation and subsequent deposition of glycogen in these cells.

4. Amyloidosis. Amyloid deposited around the capillaries of the islets causing compression and atrophy of islets cells is the characteristic lesion found in 'chronic long-standing type II diabetes, and infrequently in type I diabetes.

5. Fibrosis of islets. Fibrocollagenous replacement of the islets is found in type II and less often in type I diabetes.

Clinical Features

Diabetes mellitus is not a single disease but numerous diseases and symptoms are associated with hyperglycaemia.

Type I diabetes. Type I diabetes, previously called juvenile-onset diabetes or insulin-dependent diabetes mellitus (IDDM), comprises about 10-20% cases of diabetes. Type I diabetes usually manifests at early age, generally below the age of 40. Characteristically, the plasma insulin levels are low and patients respond to exogenous insulin therapy. The onset of symptoms is generally abrupt with polyuria, polydipsia and polyphagia. The patients are not obese but have generally progressive loss of weight. These patients are prone to develop metabolic complications such as ketoacidosis and hypoglycaemic episodes.

Type II diabetes. Type II diabetes, formerly termed maturity-onset diabetes or noninsulindependent diabetes mellitus (NIDDM), is more common and comprises 80-90% cases of diabetes. This form of diabetes generally manifests in middle life or beyond, usually above the age of 40. The onset of symptoms in type II diabetes is slow and insidious. Generally, the patient is asymptomatic when the diagnosis is made on the basis of glucosuria or hyperglycaemia during physical examination. The patients are frequently obese and may present with polyuria, polydipsia, unexplained weakness and loss of weight, In contrast to type I diabetes, plasma insulin levels in type II diabetes are normal-to-high, though they are lower relative to the plasma glucose level i.e. there is relative insulin deficiency. Metabolic complications such as ketoacidosis are infrequent.

Complications of Diabetes

As a consequence of hyperglycaemia of diabetes, every tissue and organ of the body undergoes biochemical and structural alterations which account for the major complications in diabetics. Possibly, these complications are related to the severity of hyperglycaemia since control of blood glucose from clinical point of view is associated with minimising the development of complications. However, the following two biochemical mechanisms have been implicated in the development of most complications of diabetes:

1) Non-enzymatic glycosylation: The free amino group of any body proteins binds reversibly to glucose by non-enzymatic mechanism and causes chemical alterations in the involved tissue proteins. An example of this mechanism is the measurement of glycosylated haemoglobin (HbAxC) as a test for monitoring control in a diabetic patient. Accumulation of glycosylation products on

collagen and other tissues of the blood vessel wall forms irreversible advanced glycosylation end-products (AGE). The AGE's bind to receptors on different cells and produce variety of biologic and chemical changes.

2) Polyol pathway mechanism: This mechanism is responsible for producing lesions in the aorta, lens of the eye, kidney and peripheral nerves. These tissues have an enzyme, aldose reductase, that reacts with glucose to form sorbitol and fructose in the cells of the hyperglycaemic patient as under:

$$\text{Glucose} + \text{NADPH} + H^{++} \xrightarrow{\text{aldose reductase}} \text{Sorbitol} + \text{NADP}^{++}$$

$$\text{Sorbitol} + \text{NAD} \xrightarrow[\text{dehydrogenase}]{\text{sorbitol}} \text{Fructose} + \text{NADH} + H^{++}$$

ntracellular accumulation of sorbital and fructose so produced results in entry of water inside the cell and consequent cellular swelling and cell damage. Also, intracellular accumulation of sorbitol causes intracellular deficiency of myoinositol which is essential for polyol energy

metabolism. This, in turn, results in disturbed polyol metabolism and consequent complications of diabetes.

Both types of diabetes mellitus may develop complications which are broadly divided into 2 major groups:

I. Acute metabolic complications: These include diabetic ketoacidosis, hyperosmolar nonketoticcoma, and hypogiycaemia.

II. Late systemic complications: These are atherosclerosis, diabetic microangiopathy, diabeticnephropathy, diabetic neuropathy, diabeticretinopathy and infections.

ACUTE METABOLIC COMPLICATIONS

Metabolic complications develop acutely. While ketoacidosis and hypoglycaemic episodes are primarily complications of type I diabetes, hyperosmolar nonketoic coma is chiefly a complication of type II diabetes

I. Diabetic ketoacidosis. Ketoacidosis is almost exclusively a complication of type I diabetes. It can develop in patients with severe insulin deficiency combined with glucagon excess. Failure to take insulin and exposure to stress are the usual precipitating causes. Severe lack of insulin causes lipolysis in the adipose tissues, resulting in release of free fatty acids into the plasma. These free fatty acids are taken up by the liver where they are oxidised through acetyl coenzyme-A to ketone bodies, principally acetoacetic acid and P-hydroxy-butyric acid. Such free fatty acid oxidation to ketone bodies is accelerated in the presence of elevated level of glucagon. Once the rate of ketogenesis exceeds the rate at which the ketone bodies can be utilised by the muscles and other tissues, ketonaemia and ketonuria occur. If urinary excretion of ketone bodies is prevented due to dehydration, systemic metabolic ketoacidosis occurs. Clinically, the condition is characterised by anorexia, nausea,

vomitings, deep and fast breathing, mental confusion and coma. Most patients of ketoacidosis recover.

II. Hyperosmolar nonketotic coma. Hyperosmolar nonketotic coma is usually a complication of type II diabetes. It is caused by severe dehydration resulting from sustained hyperglycaemic diuresis. The loss of glucose in urine is so intense that the patient is unable to drink sufficient water to maintain urinary fluid loss. The usual clinical features of ketoacidosis are absent but prominent central nervous signs represent. Blood sugar is extremely high and plasma osmolality is high. Thrombotic and bleeding complications are frequent due to high viscosity of blood. The mortality rate in hyperosmolar nonketotic coma is high.

III. Hypoglycaemia. Hypoglycaemic episode may develop in patients of type I diabetes. It may result from excessive administration of insulin, missing a meal, or due to stress. Hypoglycaemic episodes are harmful as they produce permanent brain damage, or may result in worsening of diabetic control and rebound hyperglycaemia, so called Somogyi's effect.

LATE SYSTEMIC COMPLICATIONS

A number of systemic complications may develop after a period of 15-20 years in either type of diabetes. These late complications are largely responsible for morbidity and premature mortality in diabetes mellitus. These complications are briefly outlined below as they are discussed in detail in relevant chapters.

1. Atherosclerosis. Diabetes mellitus of both type I and type II accelerates the development of atherosclerosis so that consequent atherosclerotic lesions appear earlier than in the general population, are more extensive, and are more often associated with complicated plaques such as ulceration, calcification and thrombosis. The cause for this accelerated atherosclerotic process is not known but possible contributory factors are hyperlipidaemia, reduced HDL levels, nonenzymatic glycosylation, increased platelet adhesiveness, obesity and associated hypertension in diabetes.

The possible ill-effects of accelerated atherosclerosis in diabetes are early onset of coronary artery disease, silent myocardial infarction, cerebral stroke and gangrene of the toes and feet. Gangrene of the lower extremities is 100 times more common in diabetics than in non-diabetics.

2. Diabetic microangiopathy. Microangiopathy of diabetes is characterised by basement membrane thickening of small blood vessels and capillaries of different organs and tissues such as the skin, skeletal muscle, eye and kidney. Similar type of basement membrane-like material is also deposited in nonvascular tissues such as peripheral nerves, renal tubules and Bowman's capsule. The pathogenesis of diabetic microangiopathy as well as of peripheral neuropathy in diabetics is believed to be due to recurrent hyperglycaemia that causes increased glycosylation of haemoglobin and other proteins (e.g. collagen and basementmembrane material) resulting in thickening of basement membrane.

3. Diabetic nephropathy. Renal involvementis a common complication and a leading cause of death in diabetes. Four types of lesions are described in diabetic nephropathy:

i) Diabetic glomerulosclerosis which includes diffuse and nodular lesions of glomerulosclerosis.

ii) Vascular lesions that include hyaline arteriolosclerosis of afferent and efferent arterioles and atheromas of renal arteries,

iii) Diabetic pyelonephritis and necrotising renal papillitis.

iv) Tubular lesions or Armanni-Ebstein lesion.

4. Diabetic neuropathy. Diabetic neuropathy may affect all parts of the nervous system but symmetric peripheral neuropathy is most characteristic. The basic pathologic changes are segmental demyelination, Schwann cell injury and axonal damage. The pathogenesis of neuropathy is not clear but it may be related to diffuse microangiopathy as already explained, or may be due to accumulation of sorbitol and fructose as a result of hyperglycaemia.

5. Diabetic retinopathy. Diabetic retinopathy is a leading cause of blindness. There are 2 types of lesions involving retinal vessels: background and proliferative. Besides retinopathy, diabetes also predisposes the patients to early development of cataract and glaucoma.

6. Infections. Diabetics have enhanced susceptibility to various infections such as tuberculosis, pneumonias, pyelonephritis, otitis, carbuncles and diabetic ulcers. This could be due to various factors such as impaired leucocyte functions, reduced cellular immunity, poor blood supply due to vascular involvement and hyperglycaemia per se.

Diagnosis of Diabetes

Hyperglycaemia remains the fundamental basis for the diagnosis of diabetes mellitus. In symptomatic cases, the diagnosis is not a problem and can be confirmed by finding glucosuria and a random plasma glucose concentration above 250 mg/dl. The severity of clinical symptoms of polyuria and polydipsia is directly related to the degree of hyperglycaemia. In asymptomatic cases, when there is persistently elevated fasting plasma glucose level, diagnosis again poses no difficulty. The problem arises in asymptomatic patients who have normal fasting glucose level in the plasma but are suspected to have diabetes on other grounds and are thus subjected to oral glucose tolerance test (GTT). If abnormal GTT values are found, these subjects are said to have 'chemical diabetes'. The WHO has suggested definite diagnostic criteria for early diagnosis of diabetes mellitus.

The following investigations are helpful in establishing the diagnosis of diabetes mellitus:

I. URINE TESTING. Urine tests are cheap and convenient but the diagnosis of diabetes cannot be based on urine testing alone since there may be false-positives and false-negatives. They can be used in population screening surveys. Urine is tested for the presence of glucose and ketones.

1. Glucosuria. Benedict's qualitative test detects any reducing substance in the urine and is not specific for glucose. More sensitive and glucose specific test is dipstick method based on enzyme-coated paper strip which turns purple when hipped in urine containing glucose.

The main disadvantage of relying on urinary glucose test alone is the individual variation in renal threshold. Thus, a diabetic patient may have a negative urinary glucose test and a nondiabetic individual with low renal threshold may have a positive urine test.

Besides diabetes mellitus, glucosuria may also occur in certain other conditions such as: renal glycosuria, alimentary (lag storage) glucosuria, many metabolic disorders which cause secondary diabetes, starvation and intracranial lesions (e.g. cerebral tumour, haemorrhage and head injury).

However, two of these conditions - renal glucosuria and alimentary glucosuria, require further elaboration here.

Renal glucosuria: After diabetes, the next most common cause of glucosuria is the impaired renal threshold for glucose. In such cases, the blood glucose level is below 180 mg/dl (i.e. below normal renal threshold for glucose) but glucose appears regularly and consistently in the urine.

Renal glucosuria is a benign condition unrelated to diabetes and runs in families and may occur temporarily in pregnancy without symptoms of diabetes.

Alimentary (lag storage) glucosuria: A rapid and transitory rise in blood glucose level above the normal renal threshold may occur in some individuals after a meal. During this period, glucosuria is present. This type of response to meal is called 'lag. storage curve' or more appropriately 'alimentary glucosuria.' A characteristic feature is that unusually high blood glucose level returns to normal 2 hours after meal.

2. Ketonuria. Tests for ketone bodies in the urine are required for assessing the severity of diabetes and not for diagnosis of diabetes. However, if both glucosuria and ketonuria are present, diagnosis of diabetes is almost certain. Rothera's test (nitroprusside reaction) and strip test are conveniently performed for detection of ketonuria.

Besides uncontrolled diabetes, ketonuria may appear in individuals with prolonged vomitings, fasting state or exercising for long periods.

II. SINGLE BLOOD SUGAR ESTIMATION

For diagnosis of diabetes, blood sugar determinations are absolutely necessary. Folin-Wu method of measurement of all reducing substances in the blood including glucose is now obsolete. Currently used are O-toluidine, Somogyi-Nelson and glucose oxidase methods. Whole blood or plasma may be used but whole blood values are 15% lower than plasma values.

A grossly elevated single determination of plasma glucose may be sufficient to make the diagnosis of diabetes. A fasting plasma glucose value above 250 mg/dl is certainly indicative of diabetes. In other cases, oral GTT is performed.

III. ORAL GLUCOSE TOLERANCE TEST

The patient who is scheduled for oral GTT is instructed to eat a high carbohydrate diet for at least 3 days prior to the test and comes after an overnight fast on the day of the test. A fasting blood sugar sample is first drawn. Then 75 gm of glucose dissolved in 300 ml of water is given. Blood and

urine specimen are collected at half-hourly intervals for at least 2 hours. Blood or plasma glucose content is measured and urine is tested for glucosuria to determine the approximate renal threshold for glucose. Venous whole blood concentrations are 15% lower than plasma glucose values.

The previous criteria suggested by Fajans and Conn (1960) employing 4-5 test glucose determinations have been revised upwards by the WHO in 1985, placing higher reliance on two test glucose determinations. Individuals with fasting value of plasma glucose higher than 140 mg/dl and 2-hour value after 75 gm oral glucose higher than 200 mg/dl are labelled as diabetics, whereas those with fasting and 2-hour plasma glucose value between 140 and 200 mg/dl are considered to have 'impaired glucose tolerance (IGT)' and are kept under observation for repeating the test later. During pregnancy, however, a case of IGT is treated as a diabetic.

IV. OTHER TESTS. A few other tests are sometimes performed in specific conditions in diabetics and for research purposes:

1. Glycosylated haemoglobin (HbAlc).

Measurement of blood glucose level in diabetics suffers from variation due to dietary intake of the previous day. Long-term objective assessment of degree of diabetic control is better done by measurement of glycosylated haemoglobin (HbAlc), a minor haemoglobin component present in normal persons. This is because the non-enzymatic glycosylation of haemoglobin takes place over 120 days, life span of red blood cells. Hb A1C assay, therefore, gives an estimate of diabetic control for the preceding 6-10 weeks.

2. Extended GTT.

The oral GTT is extended to 3-4 hours for appearance of symptoms of hyperglycaemia. It is a useful test in cases of reactive hyperglycaemia of early diabetes.

3. Intravenous GTT.

This test is performed in persons who have intestinal malabsorption or inpostgastrectomy cases.

4. Cortisone-primed GTT.

This provocative testis a useful investigative aid in cases of potential diabetics.

5. Insulin assay.

Plasma insulin levels can be measured by radioimmunoassay and ELISA techniques.

6. C-peptide assay.

This test is even more sensitive than insulin assay because its levels are not affected by insulin therapy.

HISTORY OF THE TEACHINGS ABOUT STRESS

Holistic teaching of stress was formed by the Canadian scientist H. Selye (1936). American researcher U.Kennon at the beginning of the XX century, before the works of H. Selye studied the role of the autonomic nervous system in non-specific reactions, the protection of the whole organism. He showed that the basis of these reactions is a reflex excitation of splanchnic nerves, which leads to an increased release of adrenaline in the blood of the adrenal medulla, ie the activation of sympathetic-adrenal system (SAS). Under the action of norepinephrine, released in the endings of the postganglionic sympathetic nerve fibers, and the adrenaline flowing in the blood, there is a range of fast, emergency responses, the biological significance of which is to mobilize all vital forces in the fight against threatening him danger (the reaction of the "fight" or "flight ").

At present, we can highlight the following activation effects SAS on various organs and systems:

1. Metabolic:

- An increase in blood glucose levels by enhancing glycogenolysis in the liver (the action of catecholamines on the β2-adrenergic receptors of hepatocytes);

- Entry into the blood free fatty acids by activation of lipolysis in adipose tissue (the action of catecholamines on the β2-adrenergic receptors of the adipocytes);

2. The effects on the heart and blood vessels:

- An increase in strength and frequency of contractions of the heart (the action of catecholamines on the myocardium β1-receptors), leading to increased stroke and minute blood volume and increase in blood pressure;

- Increase the intensity of metabolic processes and the consumption of oxygen by the myocardium and skeletal muscle - calorie-gene effect, leading to an increase in strength of muscle contractions (the action of catecholamines on β-adrenergic receptors of muscle cells);

- Centralization of circulation - the redistribution of blood flow to the brain and heart (where arteriolar smooth muscle β2-adrenergic receptors predominate) due to spasm of blood vessels of the internal organs and skin (where smooth muscle cells of arterioles dominated α1-adrenergic receptors);
- Spasm of the renal arteries and decrease in urine output with fluid retention in the body (the action of catecholamines on α1-adrenergic receptors and renal arteries);

3. Effects on the respiratory system:

- Increase ventilation (respiratory minute volume) due to activation of the respiratory center central adrenergic structures;

- Bronchiectasis, facilitating an increase in ventilation (the action of adrenaline and noradrenaline in the β2-adrenergic receptors of bronchial smooth muscle cells);

4. Effects on the blood system:

- Reduction of trabecular muscle and spleen capsule (the action of catecholamines on α1-adrenergic receptors of the smooth muscle cells of the spleen) and the blood flow in an additional amount of red blood cells;

- An increase in the blood concentration of mature neutrophils through the redistribution of their marginal pool of circulating;
- Increasing the velocity of blood coagulation, platelet adhesion and aggregation by activation of Hageman factor and adrenaline platelets;

5. Effects on CNS and the senses:

- Activation of the functions of the cerebral cortex, increasing the rate of formation of conditioned reflexes, decrease response time, increase mental alertness;

- Dilated pupils (the action of catecholamines on α1-adrenergic receptors of the muscles, dilates the pupil).

Thus, the sympathetic response of the body increases the capacity of functioning in extreme situations. The main task, which is solved by activating sympathetic-adrenal system - vital to

mobilize all resources for a response in the form of the "fight" or "flight", as well as to prepare for a possible injury and bleeding.

Despite the great importance Cannon work, he has not shown the critical role of the hypothalamic-pituitary-adrenal axis in the development of non-specific adaptation reactions. And by the time the first works H.Selye about the physiological role of the adrenal cortex, and it produced glucocorticoids was not yet known.

It H.Selye (1936) formed an integral doctrine of the stress and found essential in the body to adapt to various extreme factors activation of the hypothalamic-pituitary-adrenal system, in general, and the role of glucocorticoid hormones in particular. He called stress "the nonspecific response of the body to any demand that it shall be presented, or a non-specific reaction of the organism to any stimulus."

Today, we can somewhat clarify the concept of stress, defining it as a non-specific component of the response of the whole organism to any stimulus, implemented with the participation of the neuroendocrine system (A.M. Hare, 2001).

The effects of glucocorticoid hormones

Glucocorticoid effects of carbohydrate metabolism is to strengthen the formation of glycogen in the liver (glycogenetic effect); increasing concentrations of glucose (hyperglycemic effect) due to the blood:

1) amplification of gluconeogenesis in the liver from the amino acids (glycogenetic effect);

2) inhibition of glucose utilization by peripheral tissues.

Glucocorticoids enhance protein catabolism (proteocatabolic effect) in the cells of most organs and tissues (muscles, lymphoid tissue, epithelia, and other than the liver.) And increase the concentration of free amino acids in the blood due to:

1) inhibition of transport of amino acids into cells and subsequent proteosyntesis;
2) hydrolysis of proteins;

3) amplification deamination of amino acids in the liver.

Glucocorticoid effects on fat metabolism is to enhance lipolysis in adipose tissue (lipolytic effect), causing blood to enter the free fatty acids. Simultaneously, liver glucocorticoid activated fatty acid in the conversion of ketone bodies (ketogenesis activation).

Impact on water and electrolyte metabolism of glucocorticoids is provided in their interaction with the same receptors in the renal tubule cells, which bind to mineralocorticoid hormones. Evolving with the effect (mineralocorticoid) is similar to that of aldosterone and e is a delay in the body of Na + and water, as well as strengthening the excretion of K + ions and hydrogen. This increases the content of Na + in the extracellular fluid, there is an increase in extracellular fluid volume.

Ensuring the effects of other hormones. Glucocorticoids are required for the manifestation of biological effects of catecholamines, and glucagon. This is achieved by enhancing the expression and increase the sensitivity of the receptors, such as receptors for catecholamines on the cell surface of various organs and tissues (bronchi, blood vessels, liver, etc.).

The effect on the central nervous system and sense organs (the optimal concentration of glucocorticoids provide adequate mental activity, as well as the ability to properly distinguish the taste, smell and sound sensations).

Should be high to distinguish the effects of so-called pharmacological doses of glucocorticoids (i.e., those that are used for the treatment of various inflammatory allergic and autoimmune diseases), the effects of glucocorticoid concentrations, which correspond to their normal levels in the body. High concentrations of glucocorticoids (10 or more times higher than physiological) occur in the body in the adrenal cortex hyperfunction and application of exogenous glucocorticoids. In addition to the above, for higher concentrations glucocorticoids are characterized following effects:

- Fixation inhibition and stimulation of bone resorption;

Lympholitic (downsizing lymphoid tissue as a result of violations of lymphocyte proliferation and death);

- Immunosuppressant;

- An anti-inflammatory and anti-allergic.

Immunosuppressive, anti-inflammatory and anti-allergic effects of high concentrations of glucocorticoids are due, first and foremost, the suppression of the production of interleukin macrophages, lymphocytes and other cells. In the development of immunosuppressive action of glucocorticoids significant role also belongs inhibition of protein synthesis in lymphoid tissue.

H. Selye tried to find new ovarian hormone in extracts of cattle. He introduced these drugs to rats, hoping to find new reactions bodies that could not be explained by the action of any of the known hormones. Already after a few daily injections of crude extracts of H. Selye discovered in the study of the internal organs of experimental animals slaughtered characteristic triad of symptoms, later named after him (Selye triad):

- Hypertrophy and hyperplasia of the cells of the adrenal cortex;

- Hypoplasia of the thymus and lymph nodes (the mass of these structures and the number of lymphoid cells in them is reduced);
- The emergence of erosion and ulceration of the mucous membrane of the stomach and duodenum.

Intensity of these phenomena directly dependent on the amount of injected extract.

First, the researchers attributed these changes effect the new hormone, "was present in

extracts" but soon he found that injection of crude extracts of various animals - extracts from the kidneys, spleen, and various toxins and even ordinary formalin cause the same effects.

Further experiments showed "that the" triad Selye "occurred in the case when the animals were exposed to a wide variety, nothing inherently having no factors:

- Mechanical trauma (eg, fractures)

- The impact of pain (eg, electric current shocks)

- Heavy physical exertion (eg, long voyage for a few days)

- Repeated hypothermia,

- Repeated overheating,

- Infection by pathogenic bacteria,

- Bloodletting,

- Prolonged deprivation of food (fasting)

- Immobilization (immobilization)

- Being in the vicinity of the previously known animal source of danger (predators, fire, etc.) and others.

The only thing that was common in all of these factors - their "extreme", that they are sharply violated customary, the natural conditions of animal existence, violated its homeostasis applicable to the adaptive capacity of animals increased demands, threatened the very existence of the animal, could cause death.

Naturally, the question arose of what to call this general nonspecific adaptation syndrome and how to call the general properties of pathogenic factors. And Selye advantage has already been applied in biology the term "stress". General properties of pathogenic factors that can give rise to stress in the body, they are called stressors (stress factors they are the same).

Later H. Selye established and proved that they initially described the triad of symptoms (Selye triad) - a consequence of the activation of the hypothalamic-pituitary-adrenal axis (HPA axis) and an increase in blood levels of ACTH and cortisol. Various stressors acting on the body's receptors. Signals are transmitted from receptors in the hypothalamus, which increases the release of CRH, which activates the pituitary gland to ACTH production. ACTH acts on the adrenal cortex, causing it to hypertrophy, hyperplasia and increased production by cells of the beam area of the cortex of the adrenal cortisol. Cortisol acts on the spleen and lymph node lymphocytes, causing them to migrate, diffuse clusters of lymphoid tissue (which is most likely encounter with the antigen) and red bone marrow. As a result, the mass of the lymph nodes and spleen decreased. Furthermore, in the elevated cortisol concentration gives prostaglandin synthesis by inhibiting

phospholipase A2 in the mucosa of the stomach and duodenum. Prostaglandins are required for proper secretion of mucus that protects the mucosa from injury by proteolytic enzymes and hydrochloric acid. Reducing the formation of prostaglandins cause mucosal damage aggressive factors of gastric and intestinal juices. The result is a stress ulcer. Their education also promotes arteriolar spasm lining of the digestive tract, resulting from the activation under stress sympathetic-adrenal system.

CURRENT UNDERSTANDING OF STRESS

Thus, stress - a set of common, whole organism nonspecific reactions in response to the damaging factors that mobilize the body in order to adapt and maintain homeostasis. In other words, we call stress occurring in the body of the general non-specific adaptation reactions in response to the extreme effects - that is, one which is currently a living organism is not able to adapt and which requires the mobilization of all its vital resources.

Currently, we have every reason to be attributed to the stress typical pathological processes characteristic of the organism as a whole (as opposed to inflammation, manifested at the tissue level, and hypoxia, which manifests itself at the cellular). Stress evolutionarily developed and is found in animals of various kinds, classes and types. Stress induced by the action on the body of a plurality of etiological factors. Stress is an integral component of any non-specific disease ("disease generally syndrome").

Stress causes a reorganization of the metabolism and physiological functions, which greatly increases the body's resistance to death from acute hypoxia.

This is demonstrated by a simple classic experiments on mice. Preliminary swim in cold water for a few minutes, causing a strong stress in rodents leads to a significant increase in animals resistance to acute hypobaric hypoxia. As a result of stressed animals remain alive at the time, when not subjected to the animals die of stressing (A.M. bunny, L.P.Churilov, 2001).

Hypoxia (energy deficiency in neurons) of the brain - the most important life-threatening factor which is anyway present at the violent death of almost any external influence and from any serious illness. It is therefore absolutely logical that the process of evolution there was a non-specific mechanism of protection given away the phenomenon and its prevention. Such a mechanism is stress.

The main task, which is solved as a result of the activation of the stress-realizing system - for a short time to prevent possible energy deficit in the brain cells, which are the non-insulin dependent, and the most sensitive to oxygen deficiency and glucose.

Furthermore, stress-activated system realizing processes in an organism, directed to the preparation:

- The possibility of obtaining a mechanical injury (increase in blood clotting);

- A possible meeting with the infectious agent - access to the blood granulocytes (adrenaline effect), and the redistribution of lymphocytes in diffuse clusters of lymphoid tissue and bone marrow (the effect of glucocorticoids).

The role of glucocorticoid hormones in the adaptive changes in metabolism during stress. Increased levels of cortisol during stress has important metabolic consequences, needed to improve the body's resistance to acute hypoxia and prolonged adverse conditions of existence, especially after mechanical trauma (injury, broken bones, surgery), during infection, when fasting.

With continued action of the stressor (pain after injury, increased levels of cytokines in infectious process, fasting hypoglycemia, and others.) Under the influence of glucocorticoids is a redistribution of energy resources for the benefit of the brain. Glucocorticoids cells make insulin-dependent tissues insensitive to insulin and cause contrainsular metabolic effects.

Glucocorticoids potentiate the effects of adrenaline and noradrenaline, preventing depletion of their reserves. Thanks to the mineralocorticoid effect of glucocorticoids contribute to a delay in the body of sodium and water.

Activated proteolysis in muscles. The blood comes amino acids, which are captured by hepatocytes. The cells in the liver gluconeogenesis reactions (activated glucocorticoid) is formed

rom amino acids, glucose and intensively enters the bloodstream. There is stress hyperglycemia. From the blood glucose in these conditions only effectively penetrates tissue insulin dependent neurons of the brain and spinal marrow, retinal cells of the eye, adrenal and gonads. Thus, it is delivered to the vital organs substrate oxidation, which, combined with the centralization of blood circulation increases the resistance of the whole organism to hypoxia.

Muscle proteolysis is essential for the creation of so-called free amino acid pool in the blood. The fact that is very common stressor mechanical trauma to tissue destruction which makes animal unable to get food efficiently. The pool of free amino acids originating from the muscles, can be used in place of tissue breakdown and protein synthesis for repair.

Lipolysis activated in fat tissue. Fatty acids enter the bloodstream, where the captured cardiac myocytes and skeletal muscle, who use them as a substrate for oxidation under glucose limitation. In the liver of free fatty acids under conditions of excess cortisol heavily synthesized ketone bodies. Ketone bodies, along with glucose, using brain neurons and cardiomyocytes.

Stress as a result of the activation of the hypothalamic neuronal circuits

The basis of stress are reflex reactions that activate specific neural circuit of the brain stem (mainly the hypothalamus). They are sympathetic centers of the brain stem (sympathetic-adrenal system) and hypothalamic neuronal groups that control production of factor corticotropin (CT). As a result of the activation of the two most important stress-realizing system - sympathetic-adrenal and the hypothalamic-pituitary-adrenal axis (HPA axis).

CT increases the secretion of ACTH by the pituitary gland, and that in turn activates the emission beam in the zone of the adrenal cortex of glucocorticoids (GC). The pulses from the higher activated hypothalamic centers of the sympathetic nervous system through the reticular formation neurons reach the middle horns thoraco-lumbar spinal cord. Further processes of these neurons transmit impulses to the neurons of the sympathetic trunk ganglia that innervate virtually all vessels and internal organs. Adrenal medulla origin is different sympathetic ganglia. His chromaffin cells

have modified postganglionic neurons that have lost their processes and acquired the ability to secrete a neurotransmitter, and in fact - the hormone adrenaline directly into the bloodstream. As a result, activation of CAC selection in adrenaline blood increases.

Under the influence of different stressors in the hypothalamus and pituitary gland and increases production of other hormonal substances; opioid peptides (β-endorphin and metenkefalina

- with pain, severe physical stress, immune response, and others.), antidiuretic hormone (ADH - in blood loss, hypoglycemia "electrical pain stimulation, hypoxia), oxytocin (when immobilized, restriction of movements, swimming) , growth hormone (emotions, pain, a lot of noise), prolactin (emotions, electrical pain stimulation, immobilization, surgery).

The basic mechanisms of activation of stress-realizing system

1. Direct superstrong impact on certain receptive fields (typical for somatic stress):

- Chemoreceptor (hypoxemia, hypercapnia, acidosis and alkalosis decompensated, hypoglycemia, hyperosmolarity and hypoosmolarity);
- Pressosensitive (lowering blood pressure);
- Proprioreceptor (excessive physical activity);
- Painful (superficial and deep nociceptors);
- Termoreseptor (hypothermia and overheating);
- Receptive field analyzers (loud sound and noise, bright, long lasting light, sharp smells and others.)

2. Effect on the hypothalamic neuronal receptors substances produced in tissues, and entering the bloodstream during inflammation (cytokines) 1.

3. Conditional (psychogenic) stimuli.

The first two mechanisms of activation of stress-realizing system lead to the development of physical stress, and a third mechanism - psycho-emotional.

Psycho-emotional stress causes all the things we currently do not expect the time, what we do not want and what are not ready: the deficit and surplus of information; immobilization (immobilization); deprivation of freedom of movement; It is in close proximity to the previously known stress object hazard (predator, fire, etc.); stimulated by the use of the unpleasant taste of food, and others.

Driving the sequence of activation of stress systems in implementing the somatic stress the following:

Somatic stressor → receptors → front tubular region of the hypothalamus → corticotropin → anterior pituitary → ACTH → adrenal → glucocorticoids.

In contrast, somatic, psycho-emotional stress when the signal from the receptor is conventional and requires mandatory processing of sensory information to the cerebral cortex based on previous experience or in the limbic system based on genetically conditioned emotional recognition relevant

factors. Next, from the bark through the limbic system, or directly from the limbic system generates a control signal to the hypothalamus to the central cores stress realizuyushih systems.

Stress criteria. The most important criterion of stress is the degree of activation simpatoadrenalovoj system (estimated, in particular, the level of blood catecholamines, as well as the changes that occur in various organs under the action of neurotransmitters of the sympathetic nervous system, - increase in heart rate, sweating, increased blood pressure, mydriasis, and others.).

The sharp increase in the blood concentration of adrenaline inhibits the activity of neurons in the cerebral cortex and the limbic system, has an inhibiting effect on the hypothalamus. The result is a persistent activation of the hypothalamic structures that produce corticotropin, negative feedback is turned off. This leads to a prolonged hyperactivity of the hypothalamic-pituitary-adrenal system and increase in blood cortisol.

The intensity of the stress may also be evaluated by raising the level of CRF, ACTH or corticosteroids above the basal characteristic of this season, and this time of day. hormone levels proportional to the force acting stressor. However, intensive and long-term (chronic) stress factors increase the allocation of (3-endorphin (stress-limiting effect), which inhibits the release of CRH, ACTH and cortisol. In the future, insufficient glucocorticoid production (stage of exhaustion) can develop with continued exposure to stress factors.

The concept of stress-limiting systems. For these systems apply opioidergic link antinociceptive system and GABAergic neurons in the hypothalamus, which inhibit the secretion of CRH and ACTH opioidergic link antinociceptive system is represented by neurons of the hypothalamus and mid-brain that release opioid peptides (beta-endorphin, metenkefalin et al.) As a neurotransmitter, and adenohypophysis cells that release opioid peptides in the blood. Activation of stress-limiting system occurs under certain stressors (pain, exercise, immobilization and others.) And is capable of reducing the severity of the activation stress implementing systems, thereby limiting the possible negative effect of such activation (in particular, oxygen consumption increase myocardial appearance stressful stomach ulcers, and others.) and preventing the depletion of stress realising systems. Stress at which the activation and isolation of antinociceptive system in blood opioid peptides called opioid. Evolved with such stress opioid peptides act on cells of the immune system and prevent the appearance of adverse immunosuppressive effects of high concentrations of glucocorticoids.

Features of emotional stress

Psycho-emotional stress causes all the things we currently do not expect the time, what we do not want and what are not ready: the deficit and surplus of information; immobilization (immobilization); deprivation of freedom of movement; It is in close proximity to the previously known stress object hazard (predator, fire, etc.); stimulated by the use of the unpleasant taste of food, and others.

Emotional stress, unlike conventional emotion accompanied by a violation of homeostasis. It occurs when an individual is aware of the inability to cope with the demands that are presented to it.

Emotional stress occurs as a result of a special type of stressors - potentially dangerous stimuli, that is, begins to causing real damage to the body, if on the basis of experience, in particular conditioned reflexes, the body assumes the existence of danger.

For example, only one type of leopard enough to have experienced the strongest baboon psycho-emotional stress and screaming drew attention to the danger of the object of the pack.

If emotional stress, as well as in other types of stress, at the initial stage, the pronounced activation sympathetic-adrenal system after it activates the hypothalamic-pituitary-adrenal (ACTH and cortisol content increases in the blood).

Catecholamines cause spasm of the renal vessels. In response, the activation of the renin-angiotensin-aldosterone system. Increasing concentrations of aldosterone in blood plasma leads to delayed excretion of sodium ions and water. As a result of increased CBV and has been an increase in systemic blood pressure.

Development of hypertension is associated with the formation of "vicious circle", which is characterized primarily emotional arousal limbic-reticular structures of the brain, activating the adrenal hormone function (catecholamines), and the second - the reaction of the adrenal hormones on central adrenergic mechanisms of the reticular formation of the midbrain. This marked decrease in sensitivity sinocarotid and aortic baroreceptors to increased blood pressure.

Cardiac activity related to the influence of excessive catecholamines, increase myocardial sensitivity to oxygen. Perhaps the development of point of necrotic changes in the myocardium, cardiac arrhythmias (atrial flutter, atrial fibrillation, and others.), The formation of erosions and ulcers of the gastric mucosa (stress ulcers).

Thus, it is psycho-emotional stress is a major factor leading to stress diseases (hypertension, stress ulcers, atherosclerosis, etc..).

Adverse effects of emotional stress in humans is largely due to the fact that he often can not respond to the stressor reaction to "fight" or "flight", although all the changes taking place in the body it is to this it is prepared. For example, a student before an exam, aware of their lack of preparation, can neither deal with the examiner, no escape from it.

In order to eliminate the adverse effects of emotional stress requires his "acting out" in the form of physical activity (in accordance with certain evolutionary reaction "fight" or "flight", which should provide a stress).

UNDER STRESS

In the development of stress H. Selye identified three steps of voltage, resistance and exhaustion.

Phase voltage (alarm reaction) occurs immediately after the exposure to the stressor, usually takes the least amount of time with respect to the entire duration of the general adaptation syndrome.

Thus, in mice or rats swimming in water at room temperature, this step takes 5-10 minutes for a total duration of swimming (before rats begin to sink) to 1 hour. When stress caused by starvation, the first stage lasts 3-4 days.

At this stage it dominates sympathetic-adrenal system, which occurs almost immediately - immediately after exposure to the stressor. Activation of the HPA axis takes time - usually no earlier than 1 hour from the moment of the impact of acute stressor can not detect an increase in blood cortisol concentrations. At this stage the body is forced to centralize circulation, mobilize and wasteful to spend all the resources to deal with life-threatening or violating homeostasis factor.

Stage of resistance develops in the continuation of the action of the stressor or multiple (for a few days or weeks), its effects (eg, regular physical activity). At this stage the body adapts to the new conditions of existence and begins to economize energy resources. This adaptation is achieved largely due to the adaptive effects of glucocorticoid hormones.

In response to a specific stressor is activated:

- Firstly, the adaptation of the system to this particular factor (system, this specific factor);

- Secondly, stress realising systems (universal, non-specific extreme factors) are activated under the influence of any factor extreme.

Further adaptation of cells in the system, specific to this factor, activated genetic apparatus, the synthesis of nucleic acids and proteins. Formed structural footprint, which increases the functional capacity of the system and creates the possibility of transforming the "urgent", but unreliable adaptation in the "long-term" - stable.

For example, during physical stress adaptation system to the specific factor is the skeletal muscles and the cardiovascular system. When infectious process - lymphocytes, phagocytes and other cells of the immune system, mechanical trauma - cells providing regeneration and repair at the site of injury, etc.

Active systems to adapt to a particular factor is supported by the inclusion of non-specific stress-implement systems that respond to the action of any stressor (sympathoadrenal and the hypothalamic-pituitary-adrenal).

As a result of the activation stress-implement systems it is not just a mobilization of energy and structural resources and their redistribution of systems that do not participate in the adaptation to the specific factor in the system, specifically responsible for this adaptation, in order to maintain their hyperfunction. For example, blood-borne oxygen and glucose it is redistributed from the skin and internal organs to the brain and heart, as well as the muscles in their work; of amino acids enter the muscle through activation of proteolysis in blood and further can be used in place of injury for the synthesis of new proteins, etc.

Formation of the structural footprint, and sustainable adaptation is carried out by potentiating the participation of stress realising system. Repeated stress increases the activity of key enzymes of catecholamine synthesis. Catecholamines increase the functional activity of the cells and their ability to hyperplasia and hypertrophy, which increases system capacity adaptation, specific to a particular

factor. At the stage of resistance also increases the activity of enzymes synthesis of mediators of the stress-limiting systems: gamma-aminobutyric acid, and opioid peptides.

Example 1. Acute swimming stress (strong + exercise room in the unusual environmental conditions). When placing the mouse in a container of water at room temperature, from which they can not escape, the mouse is very active first start swimming, taking a lot of unnecessary movements and wasting large amounts of energy. This goes on for about 4-8 minutes (the alarm reaction - the first stage of stress). Subsequently, mice, firstly, tired, and secondly, resign themselves to the new situation. Their movements are much more economical and effective, sufficient only to maintain the nostrils above the water surface. There comes a stage of resistance that extends {depending on physical fitness swimmers) 40-60 min.

Example 2. Chronic stress caused by the constant action of stress factors (prolonged starvation). When stress caused by prolonged fasting, during the first 3-4 days, the body is extremely wasteful uses its energy resources, down to 1.5% of their body weight daily (alarm reaction - the first stage of stress). When this occurs gradually adjustment and optimization of the metabolism, resulting in the following 2-3 weeks of daily body reduces its mass only 0.4-0.5%, preferably by adipose tissue (stage of resistance).

As soon as a stable adaptation and eliminates the disturbance of homeostasis, stress-realizing system are no longer active. This is possible only with repetitive stress conditions. And this effect is the basis of training for different repeatedly repeated stressors (especially physical stress).

But this is not always the case. With purse acute stress and chronic stress, adaptive mechanisms are unable to achieve a state of sustainable adaptation. Stress goes into its next, final stage - exhaustion.

Stage of exhaustion is characterized by:

- Gradually emerging decrease in the ability of the adrenal cortex secrete glucose and mineralocorticoid (corticosteroid insufficiency);
- Depletion of catecholamines in the synapses of the sympathetic nerve endings and decrease the reserve capacity of the organism.

ntensity of stress and its harmful effects are not always proportional to the intensity of the stressor, and is highly dependent on the genetically determined or acquired stress resistance.

In our examples, the stress in the transition stage of exhaustion observed:

- In the first case - after 40-60 minutes when the mouse after a short burst of activity beginning to sink under the water and drown;
- In the second - after 4-5 weeks of total fasting, when a person is first dipped into a coma - he loses consciousness and response to external stimuli, and then dies of heart failure due to a sharp decrease in mass of the heart and adrenal exhaustion.

CONCEPT OF STRESS DISEASES (ADAPTATION OF DISEASES)

It would be wrong, considering the stress, be limited only to its adaptive role. Any reaction of the body to a damaging factor may not always be appropriate. Therefore there is nothing surprising in the fact that the activation of the stress-implement their systems can be an important pathogenic factor causing disturbances in the body. The last stage of stress - exhaustion - is characterized by a shift in the adaptive response of the pathological.

H. Selye identified a whole group of diseases in development of which an important role is played by the activation of the stress-realizing system, and called them to adapt disease or stress disease (gastric ulcer and duodenal ulcer, acute stress ulcer and duodenal ulcer, hypertension, coronary heart disease heart, atherosclerosis, and others.). In fact, the development of diseases of adaptation occurs in the third stage of stress - the stage of exhaustion.

Thus, the effects of stress reaction to the body can be both positive and negative. In this regard, H. Selye identified the so-called useful stress: eustress (from the Greek eu - good) and harmful - distress (from the Latin dis - poor, broken).

The activation of stress-realizing system, especially in cases when the activation of very intense (severe acute stress), continuing a long time (chronic stress) and does not entail the motor activity (inability to "fight" or "flight" at the psycho-emotional stress) can lead to negative consequences for the organism.

The first of these was noticed even H. Selye - the occurrence of stress ulcer of the stomach and duodenum (one of the signs of the triad Selye). Their development is especially true for severe acute stress (trauma, surgery, extensive burns, etc.) Due to a sharp increase in blood glucocorticoids and acute ischemia of the mucous membranes of the digestive tract. Now it is proved that the severe acute and chronic stress contributes to the aggravation of gastric ulcer and duodenal ulcer had previously.

Prolonged and intensive stress myocardial damage is observed by catecholamines by increasing myocardial oxygen consumption and activation of lipid peroxidation under the influence of catecholamines.

Spasm of vessels in the kidneys under the influence of excess catecholamines activates the renin-angiotensin-aldosterone system. This leads to a delay in excretion of sodium ions and water. The result has been an increase in systemic blood pressure.

Chronic psycho-emotional stress is one of the risk factors of atherosclerosis, since excess glucocorticoids in this case leads to hypercholesterolemia and increase in hepatic synthesis of low density atherogenic lipoproteins.

Severe chronic psycho-emotional stress contributes to the development of secondary immunodeficiency - due to preferential inhibition activity of natural killer cells. This increases the risk of cancer.

Nosological variety of stressful illnesses indicates not so much the many stress factors as a variety of "weak links" in different individuals.

PATHOPHYSIOLOGY OF THE NERVOUS SYSTEM

Etiology and pathogenesis of nervous disorders

The causes and conditions of occurrence of disorders of the nervous system

Pathogenic factors that cause damage to the nervous system, are exogenous or endogenous

nature. Exogenous factors may be pathogenic neurotropic, certain structures affecting the nervous system, ie specific. Non-specific etiological factors damaging not only nervous, but also other tissues. Exogenous factors affecting the nervous system, are biological pathogens: viruses (rabies, polio), microbes (leprosy), plant toxins (strychnine, curare), microbial toxins (botulinum, tetanus), alcohols (ethanol, methanol), pesticides (trichlorfon), chemical agents, etc.. Specific for human pathogenic factor is the word. It can cause disturbances of mental activity, behavior, disorders of various functions on the conditional reflex mechanism.

Endogenous pathogenic factors are divided into primary and secondary. The primary concern hereditary disorders of genetic and chromosomal neurons devices. They are linked hereditary diseases of the nervous system (Down syndrome, endogenous psychosis, etc.), Circulatory disorders in a variety of CNS, ischemia, and others.

The secondary endogenous pathogenic effects include destruction of internal organs and systems, when neural tissue is involved in the pathological process in the course of the underlying disease (hepatic encephalopathy, uremic coma, diabetic neuropathy, and coma, etc.).

Etiologic factors cause changes in the nervous system. The latter play the role of pathogenic factors: changes in neurons, violation of separation and reception of neurotransmitters, acquired alterations in the genome of neurons, changes interneuronal relations nervous trophism, the formation of antibodies to the nerve tissue, disruption of antisystems (analgesic, anticonvulsant, and others.). Typical pathogenic changes may be the formation of aggregates of hyperactive neurons, which are generators of pathologically enhanced excitation (GPEE), the formation of pathological determinants of pathological systems and pathological dominants.

Understanding the pathogenesis and knowledge of the pathological process development mechanisms required for adequate pathogenetic therapy. So, it is useless to treat tetanus toxin induced CNS only tetanus toxoid, tetanus toxin neutralization, as the latter has already contacted the nerve elements and caused corresponding changes in the central nervous system (in particular, damage to the proteins involved in the selection of brake transmitters). Treatment at this stage should be aimed at eliminating the consequences of the action of tetanus toxin (suppression of neuronal hyperactivity, struggle with seizures, etc.). The use of tetanus toxoid in this step is necessary for the neutralization of new portions of tetanus toxin, tetanus produced in the wound rod.

Realization of the pathogenic effects depends on their strength and duration - the stronger and more enduring these effects, the greater its effect. However, even a weak pathogen exposure, if they are long and persistent, can cause deep and lasting changes in the nervous system. For example, if the fractional, repeated administration of neurotropic toxins (tetanus, botulinum, etc.) Of the total dose, causing a pathological effect and the death of the animal, can be less than that which causes a similar

effect with a single administration of the entire dose of the toxin (Bering phenomenon). Daily electrical stimulation of brain structures subthreshold current strength is not accompanied by a visible reaction, it leads to the increase of convulsive readiness of the brain. With the passage of time on the same subliminal exposure to the animal responds already cramps (the phenomenon of "swing" or kindling). In everyday life, there are many long-term stressors, nevrozogennye factors, occupational hazards, etc.

Factors that do not cause disease initially normal nervous system can acquire pathogenic significance for the nervous system, altered previous pathological processes with genetically determined predisposition, hyperexcitability, etc. Limbic structures, particularly the hippocampus, more others are able to develop and maintain a pathological overactivity that It can be caused by even a single pathogenic effects.

An important role in maintaining the pathological effects of playing the plasticity of the nervous system - the ability to consolidate the changes arising. This feature provides the ability of its development, the formation of new relationships, learning, structural rearrangements, etc. However, plasticity - Blind force, it establishes not only a biologically useful, but also pathological changes. Due to the plasticity caused fixed structural and functional abnormalities in the nervous system (e.g., synaptic disturbances generated excitation generators, and other pathological system.). Since plasticity linked in many cases, chronicity of the pathological process and its resistance to therapeutic effects.

Pathogenic changes in the nervous system are the two kinds of phenomena. The first of them - the damage and destruction of the morphological structure, functional relationships and physiological systems. It is indicated by IP Pavlov as "damage" and is the result of the direct action of the pathogenic agent. Another phenomenon is the appearance of new, abnormal integration of modified neural structures.

The very "damage" is not the development of the pathological process. He plays the role of the causes and conditions of this development, which is carried out its own endogenous mechanisms of nervous system damage.

At the level of relations interneuronal such integration is a unit of hyperactive neurons at the level of intercellular relationships - a new organization consisting of altered CNS departments - pathological system. Thus, the actual pathogenesis of neurological disorders characterized not only by the destruction, but also the emergence of pathological formations - the unit and pathological neuronal systems, ie is the destruction of physiological and pathological formation systems.

Receipt of pathogenic agents in the nervous system

There are two basic ways of pathogens entering the CNS - from the blood (through the vascular wall), and the nerve trunks.

In the first case, the pathogenic agent (toxic agent, viruses, and other microbes.) Must overcome the blood-brain barrier (BBB), which is formed of the vascular wall (endothelial cells) and glial

elements (astrocytes). BBB provides active and selective transport from the blood into the brain of nutrients and other biologically active substances required for the activity of the brain. At the same time it protects the brain from the direct action of pathogenic agents found in the blood. In fetuses and newborns go through the BBB more. Some toxic agents (strychnine, alcohols, some pharmacological agents) are relatively well BBB. For biological pathogens (viruses, bacteria) in the normal blood-brain barrier is almost impermeable. However, in pathological conditions by the action of a number of physical and chemical factors enhanced the permeability of the BBB that weigh down the disease process. Thus, a strong prolonged stress contributes to the entry of influenza virus into the brain.

Ways of receipt of a number of pathogenic agents in the central nervous system are nerve trunks. Neural pathway characteristic of tetanus toxin, polio virus, rabies and others. The input gate for the tetanus toxin is mionevralny synapse, where

toxin acts on the motor fibers in the spinal cord and the medulla oblongata. In the CNS, the toxins (tetanus), viruses, antibodies to nerve tissue can spread from neuron to neuron in neural processes (with axo- flow) and interneuronal spaces.

Security mechanisms of the nervous system

By the tissue barrier mechanisms it should be added as a protective function of different brain membranes and nerves. Protection neuron and the surrounding glial processes and provide the Schwann cells, as well as the membrane of a neuron. The nervous system is protected as an immunological barrier.

The protective role played by special regulatory "balancing" (according to Pavlov) mechanisms aimed at prevention and elimination of emerging changes. In pathological conditions this principle is implemented in the activities of antisystems (GN Kryzhanovsky). The anti-activated or formed together to form a pathological system, limiting the development of the latter and inhibiting its activity. For example, if there is excessive pain activated antinociceptive system regulating pain sensitivity. Activation of antinociceptive system suppresses the occurrence of pain.

Antiepileptic system monitors the level of arousal in different parts of the central nervous system. Electrical stimulation of the caudal nucleus of the bridge related to antiepileptic system, suppresses the activity of epileptic foci in the cerebral cortex.

Tonic activity of anti-system is one of maintaining a sustainable health of mechanisms. Insufficient activity antisystems is a condition for the development of the pathological process. For example, the lack of antinociceptive system leads to increased pain sensitivity and the formation of painful syndromes; antiepileptic system failure causes a predisposition to seizures.

The role of the second signal system.

Perception and analysis of signals from the sensory organs receptors and causes a certain reaction of the organism is the common property of all members of the kingdom Animalia. However,

a person in the course of employment and social development appeared to have developed and perfected an additional mechanism of formation of conditioned reflexes associated with verbal signals, united in it. It lies in the perception and analysis of words as conditioned stimuli. Pavlov, studying reflex connections, introduced the concept of "signaling system", dividing them into common to animals and humans first signal system and specific only for a second person.

First alarm system - immediate sensation and perception - is the basis of GNI and is reduced to a set of conditioned and unconditioned reflexes to direct stimuli. In humans, it is more propagation velocity and concentration of nervous processes, its mobility, which ensures fast switching and the formation of conditioned reflexes. It has been found, that the animals better differentiate individual stimuli, while people - their combination.

The second signal system formed in humans on the basis of the first as a system of voice signals (spoken, audible, visible) words. In the words of the first signal contains a synthesis of the signaling system. The process of generalization word is produced during the formation of conditioned reflexes with a group of human activity.

Talking about the features of the higher nervous activity of man, NN Danilova quoted Pavlov: "The specifics of the higher nervous activity of man is the result of a new way of interaction with the outside world, which was made possible with the work of people and that is expressed in speech. It originated as a means of communication between people in the labor process. Its development has led to the emergence of language. "

Thus, considering the evolution of the second signal system, you can build a following logical chain: the objects and the objective world phenomenon - their perception of sensory systems - the corresponding reaction of the body - the desire to transform the surrounding reality to meet the needs - to unite the efforts of several members of the group to obtain a more effective result - the need for Meet for coordinated action - occurrence of words - combining them into a speech - language education system as a generalized reflection of reality, understandable to all members of a given group of people.

The qualitative difference between the second signal system connections from the first is that the word, although it is a real physical stimulus (auditory, visual, kinesthetic), does not reflect the specific and the most important, basic properties and relations of objects and phenomena. That word makes it possible a generalized and abstract reflection of reality, which is formed only in the process of communication, ie, It is defined as biological and social factors.

The first and second signal systems are inseparable. In humans, all perceptions, ideas, and feelings most designated word. It follows that the first excitation signal system caused by specific signals from objects and phenomena of the world, are transmitted to the second signal system. The independent operation of the first signaling system without the participation of the second (with the exception of a pathology) is only possible in a child to master their speech. Any training and any creative activities related to the development and improvement of the second signal system.

During ontogeny identify several phases of development of the joint activity of two signaling systems. Originally (with infants) "... the conditioned reflexes are carried out at the level of the first signal system, ie. E. The direct stimulus comes into direct connection with the autonomic and somatic responses." Conditioned reflexes to verbal stimuli appear only in the second half year of

life, as the maturation of the brain and the formation of new and increasingly complex associative and temporary connections. Word is generally combined with other direct stimuli, and as a result it becomes one of the components of the complex: "... a word Conversion" alarm signal "occurs at the end of the second year of life."

Thus, it can be noted that the second signal system is developed based on a first in humans and is formed only in the process of socialization. With the emergence of human language from a new system of stimuli in the form of words denoting different objects, phenomena of the world and their relationships. The ability to understand and then to pronounce the word develops in humans since childhood in the process of development as a result of the association of certain combinations of sounds (words) with visual, tactile and other impressions of external objects. Joining the direct image of the object or phenomenon, the word identifies its essential features, analyzing and summarizing its quality; thus it carries the meaning of the image in the system of values, clear as to the speaker, and any listener. "In a word a person can gain knowledge about objects and phenomena of the world without any direct contact with them. verbal symbol system extends the capabilities of human adaptation to the environment, the possibility of its orientation in the natural and social world. "

United in particular sign systems - language - words became a powerful stimulus and control human behavior. It is now known more than 2500 live in developing language. Linguistic knowledge, in contrast to the unconditioned reflexes, not inherited. However, a person has the genetic background to language learning and communication through speech. They are incorporated in the features of the central nervous system, speech apparatus, larynx. Mastering the language is a result of learning; so the fact that a person learns the language like a native, depends on the environment in which he lives, and the conditions of his upbringing.

Language is implemented and carried out in the speech - the process of speaking, flowing through time and translate into sound or written form. This speech process has several functions, each of which affects the higher nervous activity of man. When communicative functions (communication between people) is carried out or reference to an object or phenomenon (ie attract attention to his companion), or listener motivation to any action. The regulatory function of speech realizes itself in higher mental functions - conscious forms of mental activity. The programming function is expressed in the construction of meaning schemes of verbal expression, grammatical structure of the sentence, in the transition from concept to an external expanded expression, ie, It produces "internal programming", carried out with the help of inner speech.

Thus, in human speech expressed the common features and the quality of the world, presented in all variety of specific events and feelings, and so the value of the speech for the development of human thought is immense. Generated in the evolution of verbal symbol system expanded possibilities of human adaptation to the environment, the possibility of its orientation in the natural and social world.

Summarizing the above, it should be noted that a person characterized by two types of brain function. The first leads to the transformation of signals in the immediate stimuli of different types of the body's activities pertaining to the system of specific, immediate, sensual images of reality. The second form of the brain responsible for the function of dealing with verbal symbols ("signals of signals") related to the system of generalized reflection of reality in the form of concepts, the content of which is fixed in words, mathematical symbols, images of works of art.

The peculiarity of the integrative activity of the nervous system of the person is carried out not only on the basis of immediate sensations and impressions, but also by manipulating words. This word is not only a means of expression, as well as rebuilds thinking and intellectual functions of man, since the idea is made and formed only by means of words.

Loss of function of the nervous system

Loss of one or another function of the nervous system may be due to either the destruction or inhibition of activity of institutions engaged in this function. An example of a loss function due to damage (destruction) of the structure can be flaccid paralysis of the muscles at the death of its

innervating motor neurons of the spinal cord affected by poliomyelitis virus, either by suspension or degeneration of the motor nerve. If the damage of structures related to the sensory systems, the sensitivity of the corresponding drop types (pain, visual, etc.).

The degree of loss of function is determined not only by the number of affected nerve cells. Around the lesion in the brain tissue occurs reversibly damaged area and inhibited neurons. Inhibition plays the role of protective mechanisms ("protective inhibition" according to Pavlov), protecting neurons reversibly damaged, the functional load, which can contribute to their death. Due to switching off of the function of neurons increases the functional level of the defect; This situation occurs when poliomyelitis, traumas of the central nervous system and others. Recovery in a given volume of function is not associated with the regeneration of neurons in therapeutic effects (neurons do not regenerate), and with the improvement of the condition and the normalization of the damaged neurons and reversibly with the removal of protective inhibition.

Loss of function in the event of structural defects is not immediately. It occurs when the damage has reached such a size that has become insufficient compensation mechanisms and overlapping of impaired function. In other words, at this stage of the disease process has made significant development, and does not begin, as is commonly thought. In such cases, the doctor has to deal with quite a neglected disease. That is why the therapy is not always effective even for this, and such an early stage is important for diagnosis of pathological changes in the preclinical stage of the process.

Loss of function due to the inhibition of activity of the central nervous system structures can also occur when the inhibitory effect of strengthening. So if hyperactivity medulla, which normally have a braking effect on the spinal cord reflexes, the spinal reflexes associated with the function falls. Known reflex sensitivity loss, hysterical paralysis, suggestive (hypnotic) movement disorders and sensitivity, and other phenomena of the inhibitory function of suppression.

Trace reaction in the pathology of the nervous system

After each of the pathological process in the nervous system are structural and functional changes that can be stored in the form of hidden tracks in normal conditions. These changes are functionally manifested not only by weakening them, but also because of the mechanisms of compensation and tonic inhibitory control on the part of various CNS structures, and, in particular, by the antisystems. The action of the new pathogens, activating the hidden changes (eg, inhibited

generators of pathologically enhanced excitation) and breaking the mechanisms of control, these changes may appear functional, which will result in the emergence of certain symptoms. Such reactions are defined as a trace: the pathogenic effects that cause these reactions, A.D.Speransky called "second blow". An example of a trace of reaction, reproducible experiment could be traction bath hind limb of the rat, which was formerly the local tetanus (extensor rigidity) of the limbs. After subcutaneous injection of phenol to the animal on his background in common tremor occurs, said traction bath.

The more significant hidden structural and functional changes and the less effective control mechanisms, the easier it is reproduced trace reaction. Therefore, in the early stages of recovery (the so-called clinical recovery) trace pathological effects may occur under the influence of many pathogenic agents, in the later stages as they played less, only some, more intimate mechanism of action of pathogenic influences. If non-specific secondary pathogenic effects of the disease can not be played, and only a few signs of the former pathological process. Accounting trace reactions is essential for the understanding of this disease process, proper diagnosis and treatment, it emphasizes the importance of history and the need to identify possible hidden abnormalities.

PATHOLOGY NEURON

Violation of excitation

The spread of excitation along the nerve fibers provide a consistent combination of the same process: the depolarization fiber membrane area, the entrance to this site Na +, depolarization of the membrane of the neighboring area, the entrance to this site Na +, etc.

With insufficient Na + entrance disturbed the generation of the action potential, and conducting stops. This effect occurs for Na + channel blockade by local anesthetics (procaine, lidocaine, etc.) And a number of other chemical agents. A specific blocker of Na + -channels is tetrodotoxin - toxin produced by the internal organs of the puffer fish.

Initial concentration difference of Na + and Ca + on both sides of the membrane (Na + 10-15 times more on the outside, K + 50-70 times within increase) required to generate an action potential is restored and maintained by active transport of ions Na + / K + - nacocom. It pumps out Na +, ringing the interior (the cytoplasm) during excitation, in return for the external K +, which came out during arousal. Activities of the pump, which carries out the role of the built-in membrane Na + / K

+ -ATPase, provides the energy liberated in the cleavage of ATP. Energy deficit leads to a malfunction of the pump, resulting in the inability of the membrane to generate an action potential and pursue excitement. This effect causes uncouplers of oxidative phosphorylation (for example, dinitrophenol) and other metabolic poisons, and prolonged ischemia and nerve cooling portion. Inhibit the pump, and as a consequence disturb conductivity cardiac glycosides (e.g. ouabain, strophanthin) in high doses.

Conducting field along the axon is disturbed at various kinds of diseases of the peripheral nerves and nerve fibers in the central nervous system -. In inflammatory processes, scarring of the nerve, and compression of nerve fibers, the fibers demyelination (allergic processes, multiple sclerosis), burns, etc. Carrying out the excitation stops when degeneration axon.

Violation of axonal transport and dendrites

Axonal transport from the cell body to the nerve endings and nerve endings of the neuron in the body is carried out with the participation of neurofilaments, microtubules and actin contractile proteins and miosinosimilar, reduction depends on the content of Ca2 + in the environment and energy from ATP cleavage. The substances, which destroy microtubules and neurofilaments (colchicine, vinblastine, etc.), Lack of ATP, metabolic poisons, creating an energy deficit (dinitrophenol, cyanide), violate axo- flow. Axonal transport suffers from axon degeneration, caused by lack of vitamin B6 and vitamin B (beri-beri), industrial poisons (acrylamide hexachlorophorum), salts of heavy metals (lead), pharmacological drugs (disulfiram), alcohol, diabetes, nerve compression and dystrophic neuronal damage. When a break occurs Wallerian axon degeneration (decay) of its peripheral parts and retrograde degeneration of the central part. These processes involve a violation trophism in both parts of the axon.

Disorders of axonal transport trophogenic and substances necessary for the formation and release of mediators of nerve endings that cause the development of degenerative changes of neurons and innervated tissues and disruption of synaptic processes. Distribution pathotrophogenic with axonal transport, antibodies to neural tissue and neurotransmitters leads to the involvement of a pathological process in other neurons depatment CNS.

Dendrites and spines are the most vulnerable structures of the neuron. With aging spines and dendritic branches are reduced, in some degenerative diseases of the brain and atrophic (senile dementia, Alzheimer's disease), they disappear. Dendrospinule apparatus suffers from hypoxia, ischemia, concussion of the brain, stress and neurotic effects.

Pathology of the structural elements of the neuronal

A significant role in the pathology of a neuron playing a violation of intracellular structural homeostasis. The normal process of wear and decay of intracellular structures and neuronal membranes balanced process of renewal and regeneration. The combination of these processes is the dynamic structural homeostasis.

Damage as a cell (cytoplasmic) and intracellular membranes arise in various pathogenic effects and are themselves a cause of further pathology neuron.

Increased lipid peroxidation (LPO) neuronal membranes affects not only the membrane but also to other intracellular processes.

There is little of the pathological process in the nervous system, in which there would be no enhanced lipid peroxidation. It occurs in epilepsy, endogenous psychoses (eg, schizophrenia, manic-depressive syndrome), with nervousness, stress and injury, ischemia, chronic hypoxia, functional neurons overload and so on. It involves further hyperactivation of neurons.

Due to the increase in membrane permeability is exited neuron various substances including antigens, which cause the formation of antibodies antineuronal that leads to the development of the autoimmune process. Violation of the barrier properties of the membrane causes an increase in current of Ca2 + ions and Na + into the neuron and K + - of the neuron; these processes in combination with the lack of energy-dependent Na + -, K + - and Ca2 + pump (their activity also varies under the

influence of intensive POL) lead to partial depolarization of the membrane. The increased Ca2 + entry not only causes hyperactivation neuron, but the excessive content of it in the cell leads to pathological changes of intracellular metabolism and damage.

Normalization of lipids and stabilizing neuronal membranes peroxidation should be part of the complex pathogenetic treatment of various pathologies of the nervous system.

For the life of the neuron, which is a highly differentiated cell is not able to divide mitotically, intracellular regeneration is the only way the structural renovation of neurons and maintain their integrity. It includes protein synthesis, formation of intracellular organelles, mitochondria, membrane structures, receptors, nerve growth processes (axons, dendrites, dendritic spines), and others.

Intracellular regeneration processes require high energy and trophic provision and proper cell metabolism. In damaged neurons, occurrence of energy and trophic deficiency disorders genome activity suffers intracellular regeneration falls plastic potential of the cell, the disintegration of intracellular structures is not counterbalanced by them.

The energy deficit

Need neurons in the energy supply - the highest of all body cells, and disruption of energy supply is one of the common causes of neuron pathology. Energy deficiency can be primary - under the influence of metabolic poisons (such as dinitrophenol, cyanide), or secondary -. Under various injuries, circulatory disorders, shock, edema, general convulsions, enhanced functional load and other energy deficiency refers to the category of typical intracellular pathological processes.

The main conditions of energy deficit is the lack of oxygen and the significant damage to the mitochondria, which is synthesized by the main carrier of energy - ATP. The reason for the energy deficit may also be lack of oxidation of the substrate, in particular glucose which is a substrate for oxidation of primary brain. The neurons of the cortex do not have reserves of glucose and consume it directly from the blood (glucose passes freely BBB), so they are particularly sensitive to hypoglycemia. Brain consumes 20% of the glucose being in the blood. Insulin shocks, used to treat some psychoses associated with profound hypoglycemia and proceed with loss of consciousness and sometimes with convulsions. In a number of pathological conditions (traumatic shock, hemorrhage) brain can longer be provided with oxygen and glucose due to redistribution of the blood and reduce their consumption of other tissues. For the speedy recovery of brain activity after total seizures requires a fairly high level of glucose in the blood. Energy shortage is aggravated breach of the Krebs cycle.

With deep violation of oxidative phosphorylation and synthesis macroergs energy source becomes anaerobic glycolysis. He has the character of a compensatory mechanism, but its effect can not make up for the energy deficit, and the growing increase of lactic acid in the brain has a negative effect on the activity of neurons and aggravate cerebral edema.

The effects of ischemia and hypoxia

Due to the high energy demand of CNS neurons oxygen it needs significant maintenance. Neuron cortex consumes 250-450 l O2 / min (for comparison - gliacyte hepatocyte and consume up to 60 l O2). Reduction of brain oxygen consumption is only 20% may cause loss of consciousness in humans. The disappearance of the impulse activity of neurons occurs in the first ten seconds of

cerebral ischemia. After 5-6 minutes after the start of asphyxiation comes profound and often irreversible damage of brain activity. Neuronal loss in ischemia is the result of complex interconnected intracellular processes.

When cerebral anoxia primarily affected cortex. The death of the whole brain is "brain death", which appears in the complete disappearance of the bioelectric activity. Phylogenetically older structures of the central nervous system (spinal cord, brain stem) are less sensitive to asphyxia than younger (subcortex and especially the bark). Therefore decortication may occur if belated revival of the organism.

It is very sensitive to anoxia brakes. One consequence of this is a disinhibition of CNS structures intact. In the early stages of ischemic brain neurons when still capable of giving a reaction, they can hyperactivity. In the later stages of ischemia hyperactivation of neuronal changes to their inactivation.

With the arrival of Na + into the neuron is connected first, acute phase of injury neuron. The increase in Na + concentration in the cytosol of the neuron leads to increased osmolarity, which causes the water input into the neuron and its swelling. Further increasing the osmolarity of the neuron it is also associated with the accumulation of Ca2 + in it, lactic acid, inorganic phosphorus. Since Ca2 + entry in the second phase is associated neuron neuron damage. Increasing the amount of Ca2 + entering the neuron is determined by the activation of glutamate receptors due to enhanced release of glutamate in nerve endings during ischemia. Antagonists of glutamate receptors and Ca2

+ antagonists (blockers of Ca2 + channels) capable of preventing ischemic neuronal degeneration and to provide a therapeutic effect.

Neuron damage occurs not only during ischemia, but also in connection with renewal of cerebral reperfusion and the blood circulation. They may be the main danger. A major role in the post-ischemic reperfusion injury play: a new wave revenues Ca2 + into the neuron, POL (lipid peroxidation), and the processes of free radical oxidation, enhanced due to the influence of the incoming oxygen. Increased content of lactic acid due to receipt of glucose in violation of the conditions of oxidative phosphorylation, and increased anaerobic glycolysis. There is a swelling of the brain due to water inflow from the blood circulation at the resumption.

The complex set of intracellular Ca2 + - inducible damage include: alteration of intracellular proteins, increased phospholipase hydrolysis and proteolysis, the destruction of intracellular structures, damage to the cytoplasmic and intracellular membranes, swelling of neurons, violation of genome activity. On a critical increase in the intensity of these processes irreversible damage and death of a neuron, a so-called calcium death.

In the later stages of the pathological process caused by cerebral ischemia, as well as chronic process, a new set of secondary changes -. Degenerative-dystrophic processes, violation of enzyme and metabolic systems, vascular changes, the formation of antibodies to brain tissue, autoimmune aggression, etc. They constitute the pathogenetic structure post-ischemic encephalopathy, which can continue to develop (a progressive development). These processes, as well as changes in other systems and organs with their consequences occur after the resuscitation of the body, especially if it

has been a long and late. Taken together, they constitute a pathogenetic structure postresuscitative disease (VA Negovsky).

Hypoxia varying degrees accompanied by many (if not all) forms of brain pathology. As a standard and non-specific process, it may, however, make a significant contribution to its development. However, moderate hypoxia can stimulate the metabolic and plastic processes in the neuron, to promote the adaptation and increase resistance, increase the trophic and plastic potential of the neuron, to enhance the adaptive capacity of the brain.

Synaptic stimulation and neuronal damage

Excitatory synaptic stimulation can play an important role in the development of neuron pathology. Strong and long-term synaptic stimulation itself causes functional overstrain of the neuron, which can be completed by degeneration of intracellular structures. These lesions are amplified in violation of microcirculation and cerebral circulation, the action of toxic factors.

Of paramount importance is the synaptic stimulation of the development of anoxic (ischemic) injury. Culture neuronal tissue becomes sensitive to anoxia only after the establishment of synaptic contacts between neurons. Synaptic stimulation is realized through the action of excitatory amino acids (glutamate, aspartate, L-homocystein), these lesions are similar to those that occur during ischemia and are associated with increased intracellular Ca2 + content. This effect is known as a neurotoxic (or cytotoxic) action of excitatory amino acids. With synaptic hyperactivation, the action of excitatory amino acids and hypoxia-associated damage and neuronal death during status epilepticus in the postischemic period. In doing so, the pathogenic action of these factors joined energy deficit.

In connection with the become clear beneficial effects (ie, the weakening of the synaptic effects) reduce a functional load, to prevent additional irritation, "protective" for IP Pavlov, inhibition of reversibly damaged neurons.

Violation of neuron activity when changing the processes of intracellular signaling After perceptual signal receptor (neurotransmitter receptor binding, hormone, etc.) Occurs in

the neuron chain cascade of metabolic processes that provide the necessary activity of the neuron. The important role played in these processes, so-called reinforcing or launchers, and enzymes produced under their influence intermediary substance second messengers.

The set of cascaded membrane processes and intracellular amplification of the endogenous neuron system that can provide multiple input gain and an increase in its effect on the output of the neuron. Thus, a cascade of metabolic processes adenylate cyclase pathway can enhance the effect of the stimulus 107-108 times. This enables the identification and implementation of a weak signal, which is of particular importance in the context of pathology, in violation of synaptic.

Many changes in the functions of a neuron associated with the action of pathogenic agents on specific units of intracellular signaling systems. Pharmacological correction of neuron activity and the effects of therapeutic agents also are implemented through appropriate changes in these systems. For example, cholera and pertussis toxins act on the processes associated with the activity of membrane G-protein adenylate cyclase activating or depressing. Xanthines (theophylline, caffeine) are responsible for the accumulation of cAMP, which leads to increased activity of the neuron. Under the action of a number of anticonvulsants (eg diphenylhydantoin, carbamazepine, benzodiazepines)

and psychotropic drugs (eg, triftazine) inhibited phosphorylation of proteins different ways, which reduces neuronal activity. Lithium ions are used in the treatment of certain endogenous psychoses, impaired system operation phosphoinositol. With enhanced Ca2 + entry associated epileptization neurons, blockade of Ca2 + entry antagonists suppress seizure activity.

Hyperactivity neuron

Hyperactivity neuron caused significant emerging out of control imbalance between excitation and inhibition in favor of the neuron excitation. Functionally, it is the production of neuron amplified pulse stream, which can have a different character: the high-frequency action potentials; individual level; digits, grouped in packs, and so on. A special kind of hyperactivity is a paroxysmal depolarization shift (PDS) in the membrane, which occurs at the height of the high-frequency discharge. This type of hyperactivity is seen as a manifestation of epileptization neuron.

This shift in the balance between excitation and inhibition may be due to a primary enhanced neuronal excitation, overcoming the braking control, or primary failure of the brake control. The first mechanism is a significant membrane depolarization and increased input of Na + and Ca2 + into the neuron, the second - a disorder mechanisms for hyperpolarization of the membrane: breach of release of K + of the neuron and the neuron input C1.

An important endogenous regulator of the neuron activity is γ-aminobutyric acid (GABA). It causes inhibition of the neuron upon binding to its receptor. As a result in enhanced neuron C1 delivery.

When a neuron disinhibition due to the weakening of inhibition and membrane depolarization occurs gain admission Ca2 + into the neuron. Furthermore, Ca2 +, while in the cytosol delivery SH

gives a neuron, thereby weakening, inside GABAergic inhibition. A related epileptization neuron that occurs under the influence of a convulsant that violate GABAergic inhibition. Many convulsant (eg, penicillin, korazol et al.) Have a complex effect on the neuron, stimulating at the same time activating and inactivating the brakes.

Chronic stimulation of the neuron (e.g., by direct electrical stimulation, synaptic effects influenced by excitatory amino acids, etc.), Even low intensity over time can lead to hyperactivation neuron.

TIPICAL PATHOLOGICAL PROCESS NERVOUS SYSTEM

Inhibition deficit. Disinhibition.

At rest and activity of neurons able to experience persistent inhibitory influences. Upon excitation of neurons occurs weakening of inhibitory processes. This disinhibition is metered, it is monitored and the required level of neuron activity, so it is a physiological nature.

If disinhibition having pathological neuron becomes hyperactive and out of control. Pathological disinhibition occurs when a significant deficiency and uncontrolled braking. This condition occurs in direct damage to the brake mechanisms with selective action on them some toxins (e.g., tetanus toxin strychnine).

Deficiency of braking and brake release are found in almost all forms of pathology of the nervous system, so they are typical pathological processes of the nervous system. inhibition deficit plays a significant role in the formation and activities of GPEE.

A typical experimental release syndrome is decerebrate rigidity. She called on Sherrington, transection of the brainstem between the front and rear quadrigemina. In these circumstances, there is loss of inhibitory influences from supraspinal structures and especially the red nuclei, and manifested tonic excitatory influence of the vestibular nuclei of Deiters on spinal cord motoneurons, especially γ-motor neurons that are normally under inhibitory control of the red nuclei. Break (for example, by sectioning the dorsal root) disinhibited, pathologically enhanced in-loop at the level of the spinal cord leads to the disappearance of the rigidity of the respective muscles. Therefore, this type of decerebrate rigidity is also called γ-rigidity (R. Granit).

At loss of inhibitory influences disinhibited hyperactivity and especially those neurons which normally are in a state of excitation of the tonic. In humans and many animals such neurons are neurons of the muscles that perform the function of anti-gravity. As a consequence, decerebrate cat throws up his head, front and hind legs are extended, the tail is raised, etc. In humans, a roll of motor cortical influences (eg after hemorrhagic stroke) occurs spastic flexor setting the upper and lower limb extensor installation (Wernicke-Mann pose).

A number of pathological reflexes occurs in a loss of influences from the cortex and subcortical structures; These reflexes are the result of release centers or spinal medulla. They are exaggerated uncontrolled reactions that are normal in the early postnatal period and then were suppressed during the development of regulatory influences from the higher parts of the CNS. These include the Babinski reflex (rastopyrivanie toes instead of bending at the foot of irritation), grasping, sucking, and other reflexes.

A full break of the spinal cord may occur and incorporated genetically suppressed with age spinal automatism in a relatively coordinated flexor-extensor movements. If giperaktiviruyutsya disinhibited and inhibitory neurons, there is a pathologically enhanced braking effect which can be manifested in the form of oppression and loss of function.

Denervation syndrome

Denervation syndrome is a set of changes that occur in the postsynaptic neurons, organs and tissues after loss of neural influences on these structures. Denervated structure (muscle, neuron) becomes sensitive to a physiologically active substance (Cannon-law Rosenbluth). The main manifestation of the syndrome in the muscle denervation is the disappearance of endplate - muscle fiber area where concentrated all his cholinergic apparatus. Instead, new acetyl choline receptors

throughout the muscle fibers, and therefore is an increase in overall sensitivity to acetylcholine total fiber (AG Ginetsinskii NM Ashmarina). This effect is mainly due to loss of nerve trophic effects. Another characteristic feature - fibrillar twitching denervated muscles. This effect reflects the response of denervated muscle fibers coming to them from various third-party sources of acetylcholine.

With denervation in muscle and other tissues appears inherent properties early in particular stages of embryonic development. This phenomenon occurs as a result of pathological release suppress normal genes.

Deafferentation

Impulses coming into the neuron, from whatever source it may come, is to afferent neuron. Disabling this afferent neuron is a deafferentation. The latter may be due to either loss of incoming impulses (with a break in the nerve pathways, neurotransmitter release violation presynaptic terminal), or blockage sensing receptors on the postsynaptic neuron (the action of toxins, pharmacological agents, and others.).

Many phenomena in deafferentation neuron denervation are an expression of the syndrome. Full deafferentation neuron does not occur, as the central nervous system neurons have a large number of afferent inputs. Nevertheless, with the partial deafferentation occurs increase in the excitability of the neuron or its individual sections and a violation of the brakes. Because of this, when a group of neurons deafferentation can acquire properties GPEE.

In the clinic at a phenomenon mean deafferentation syndromes resulting from the loss of afferent stimulation from the periphery. These syndromes can be reproduced in the experiment by the respective sectioning dorsal root of the spinal cord. Movement limbs innervated deafferentized thus the spinal cord segments are sweeping, poorly co-ordinated. Moreover, such a limb is capable of spontaneous motion in time with the breathing (Orbeli phenomenon-Kunstman) due to disinhibition and increased excitability of spinal cord neurons deafferentized.

Spinal shock

Spinal shock occurs after spinal cord break and represents a profound but reversible inhibition of motor and autonomic reflexes that take place below the break. Inhibition of reflexes associated with loss of activation by stimulation of the brain. Frogs, whose dependence on the spinal cord head is considerably less than in higher animals, spinal shock lasts a few minutes, apes and humans - some months.

A person complete areflexia after spinal cord break is the initial stage of complete paraplegia. In the future, there is a gradual recovery of motor and autonomic reflexes. Initially appear flexor reflexes fingers having the character of pathological reflexes (Babinski et al.), Then made more significant and then generalized spinal reflexes and movements such as spinal automatism.

Violation of the nervous trophism. neurodystrophic process

Trophico cells and dystrophic process. Trophico cells - a complex process, ensuring its ability to live and maintain a genetically inherent properties. The disorder is trophicity dystrophy, dystrophic changes constitute a dystrophic process.

Neurodystrophic process. It is developing a violation trophism, which is due to loss or change of neural influences. It can occur in both the peripheral tissues and in the nervous system itself. Loss of nerve influences is: 1) termination of stimulation innervated structures in connection with the violation of the neurotransmitter release or action; 2) in violation of secretion or action komediatorov - substances that are released along with neurotransmitters and neuromodulators play a role to ensure the regulation of the receptor, membrane and metabolic processes; 3) in violation of separation and action trophogenic. Trofogeny (trofiny) - various substances, mainly protein nature, carrying out proper maintenance of the trophic effects of life and genetically inherent properties of the cells. Trophogenic source are: 1) the neurons of which come from the anterograde trofogeny (orthograde) axoplasmatic current in recipient cells (neurons or other peripheral tissues innervated);

peripheral tissue cells that act on nerves trofogeny with retrograde axoplasmatic current in neurons; 3) Schwann cells and glial that communicate with the neurons and their processes trophic substances. Substances that act as trophogenic, also formed of serum and immune proteins. Trophic effects can have some hormones. The regulation of trophic processes participate peptides, gangliosides, some neurotransmitters.

By normothrophogenic include various kinds of proteins that promote growth, differentiation and survival of neurons and somatic cells to preserve their structural homeostasis (e.g., nerve growth factor).

In the context of the pathology of the nervous system produced trophic substances that cause persistent pathological changes of the recipient cells (pathothrophogen by GN Krizhanovsky). Such materials are synthesized, eg in the epileptic neurons - axoplasmatic acting with current in other neurons, they can induce these neurons recipient epileptic properties. Pathothrophogen can spread through the nervous system, both in the food web, which is one of the mechanisms for the spread of the pathological process. Pathothrophogen formed in other tissues.

Degenerative processes in the denervated muscle. Synthesized in the body of the neuron and transported to the terminal with the current axoplasmatic substances secreted nerve endings and muscle fibers come in, performing the function trophogenic. neurothrophogenic effects seen from experiments with cutting motor nerve: the higher the transection is made, ie, The more trophogenic preserved in the peripheral nerve segment, the later comes denervation syndrome. Neuron with them innervated structure (eg, muscle fiber) forms regional trophic circuit, or a regional trophic system. If you implement a cross-reinnervation of muscles with different initial structural and functional characteristics (reinnervation "slow" muscle fibers of neurons innervate "fast" muscles, and vice versa), reinnervirovannaya muscle gains largely new dynamic characteristics "slow" becomes "fast" , "fast" - " slow".

In denervated muscle fiber there are new trofogeny that activate the proliferation of nerve fibers (sprouting). These effects disappear after reinnervation.

Neurodystrophic process in other tissues. Mutual trophic influence exist between each cloth and its nervous apparatus. When transection of afferent nerves arise degenerative skin changes. Sciatic nerve, which is a mixed (sensory and motor), causes the formation of dystrophic ulcers in hock. Over time, the ulcer may increase in size and cover the entire foot.

Classic experience F. Magendie (1824), which served as the beginning of the development of the whole problem of the nervous trophism, is transection of the rabbit of the first branch of the trigeminal nerve. As a result of this operation is developing ulcerative keratitis, an inflammation around the ulcers, and in the limb with side vessels grow into the cornea, which it normally absent. vascular ingrowth is an expression of abnormal release of vascular cells - degenerative changes in the cornea disappears factor that inhibits the normal growth of blood vessels in it, and there is a factor that activates the growth.

Additional factors neurodystrophic process. The factors involved in the development process neurodystrophic include: vascular changes in the tissues, violations hemo- and lymphomicrocirculation, abnormal vascular permeability, violation of transport into the cell nutrient and plastic substances. An important pathogenetic link is the appearance of dystrophic tissue antigens as a result of the new changes in the genetic apparatus and protein synthesis, produced antibodies against tissue antigens, there are autoimmune and inflammatory processes. In pathological processes said complex also includes secondary infections of ulcer and development of infectious and inflammatory lesions. Overall neurodystrophic tissue damage are complex multifactorial pathogenesis (NN Zayko).

Generalized neurodystrophic process. If nervous system damage can occur generalized forms neurodystrophic process. One of them is shown in the form of gum lesions (ulcers, aphthous stomatitis), tooth loss, hemorrhages in lung, mucous erosion and hemorrhage in the stomach (pylorus frequently in) in the intestine, especially in buagynievoy flap in the rectum. As these changes occur relatively regularly and can take place at different chronic nerve damage, they are called the standard form of the nervous dystrophy (AD Speransky). Often these changes occur in

case of damage of higher vegetative centers, particularly the hypothalamus (in trauma, tumors), in the experiment with the application of a glass ball on the Turkish saddle.

All the nerves (motor, sensory, autonomic), whatever function they are performed, are both trophic (AD Speransky). Disorders of the nervous trophism constitute important pathogenetic link diseases of the nervous system and the somatic nervous regulation bodies, so correction trophic changes is a necessary part of the complex pathogenetic therapy.

GENERATORS pathologically enhanced excitation

Concept and general characteristics

Disorders of the central nervous system occurs when the impact of a powerful stream of pulses that can overcome the mechanisms of regulation and control of other brake parts of the central nervous system and cause a pathological activity. Such a powerful stream of pulses produced by a group of hyperactive neurons, forming a generator of pathologically enhanced excitation (GN Kryzhanovsky).

GPEE - a unit of interacting neurons hyperactive, producing an uncontrolled stream of pulses. The intensity and nature of the flow does not match the incoming signal and is only determined by the peculiarities of structural and functional organization of the generator. Because the generator is activated neurons to each other, the generator is capable of self-sustaining its activity, without the need for constant further stimulation from the outside.

Appearing with nervous system damage, the generator becomes pathogenic factor in the development process. His education has the character of a universal mechanism and is a typical pathological process is carried out at the level of interneuronal relations. Electrophysiologic generator expression activity are total potentials of its constituent neurons. As such potentials example, electrical activity, to be registered in the generator giant cell nucleus of the medulla oblongata and in epileptic foci in the cerebral cortex, which is one of the generator types.

Pathogenetic value GPEE. Main pathogenetic significance of the generator is that it giperaktiviruet the CNS department in which it arose or to which it is directly connected, so that this department becomes important determinants of pathological forming pathological system. Since the pathological system lie in the basis of the relevant nerve disorders (neuropathological syndromes), the formation of the generator is the initial link these disorders.

The formation and operation of generators of pathologically enhanced excitation

The generator can be formed under the influence of various substances of endogenous or exogenous nature that cause any violation braking controls (which entails disinhibition and hyperactivation neurons) or direct neuronal hyperactivation. In the latter case, the brakes are saved, but they are functionally inefficient and not able to normalize the activity of neurons. In all cases, the prerequisite education and generator business is lack of inhibition of its constituent neurons.

An example of the formation of the generator at a primary violation of braking can be generators, arising under the action of tetanus toxin, strychnine, penicillin and other convulsant. An example for primary formation generator neurons may be hyperactive generators arising from prolonged and enhanced synaptic stimulation, effects of excitatory amino acids (such as glutamate), shallow and postischemic reperfusion ischemic CNS. The generator can also occur when neurons deafferentation after transection of the spinal cord and nerves, with associated deafferentatsionnye pain syndromes.

In the early stages of the generator when the brakes are still preserved, and neuronal excitability is low, the generator is activated sufficiently strong stimuli coming through a specific component of the entrance to his group of neurons. In the later stages, when there is a profound failure of brake mechanisms and significantly increased neuronal excitability, the generator can be activated by various stimuli from different sources, as well as spontaneous.

PATHOLOGICAL DETERMINANTS

Concept and general characteristics

Education generator does not always have the effect of occurrence of pathological reactions. When the siege spread generated by the excitation of the brake control mechanisms generator is functionally isolated and does not cause systemic pathological effects. The pathology occurs when giperaktiviruemy influenced generator CNS department actively affect other CNS education, involves them in a pathological reaction and combines them into a new organization - a pathological system (GN Kryzhanovsky). In many cases, particularly in the early stages of the system and formation of pathological acute cases such hyperactive CNS Department defines pathological nature of the system, it becomes important pathological determinant. The role of the pathological determinants can play any formation of the central nervous system (the department, the core nerve center and so on.).

Pathogenetic determinants of pathological significance. Pathological determinant is forming a key link in managing and pathological systems. The emergence of the determinants belongs to the category of typical pathological processes that are realized at the system level.

An example of a pathological determinants in the cerebral cortex is a powerful epileptic focus, which is formed under the influence of a set of disparate, weaker foci of epileptic activity. This generates an epileptic focus center, which is a pathological (epileptic) system. If suppress pharmacologically or surgically remove a determinate center, the complex decomposes and instead re-emerge some epileptic foci.

The emergence and activity of pathological determinants

Determinant may combine CNS pathological structures in the system and determine the nature of the activity of these structures. If the regulation is weakened structures that perceive impulses from the neuron determinants, the determinant of subjects them to its effects.

In the early stages of development of nervous disorders pathological determinant activated by specific stimuli, ie, irritations, which are adequate for the formation of the central nervous system, which became the determinant (eg, light stimuli, if the determinant is education in the visual analyzer system, pain - if there was a determinant in the system sensitivity to pain and so on.). This rule also applies to disorders of higher nervous activity, neurotic reactions: their determinant relief activated by the action of the stimuli that led to its formation (for example, the same conflict neurotic situation and so on.). These features determine the specificity of provoking actions that cause bouts of nervous disorders.

In the later stages of the determinant can be activated by stimuli of different nature, in connection with which attacks can be triggered by different influences. Furthermore, pathological determinant may be activated accidentally due to spontaneous activation of the generator.

CNS experiencing long-term effects of pathological determinants over time may themselves become determinants. First, such a secondary determinant is dependent on the primary: it disappears when liquidated the primary determinant. In the future, the secondary determinant may acquire an independent pathogenetic significance. Sometimes secondary determinant is stronger than the original, and becomes the leader. The establishment of primary and secondary determinants is essential for the understanding of the pathogenic features of nervous disorders and their proper diagnosis and pathogenetic therapy.

Pathological determinant is the most resistant part of the pathological system. During the suppression of the pathological system or its natural elimination determinant structure is retained even when other education system has returned to normal and went out of its composition ("determinant of the last to die"). When you restore a pathological system under the influence of new actions before the other activated determinant structure ("determinant resurrected first").

PATHOLOGICAL SYSTEM

Concept and general characteristics

Pathological system - a new organization pathodynamic arising in the central nervous system in terms of damage, the activity of which is biologically negative (GN Kryzhanovsky). The main feature of the system is its pathological or maladaptive direct pathogenic significance for the

organism. This feature distinguishes pathological from the physiological system, whose activity has an adaptive value and is aimed at achieving the desired result for the body.

In some cases, the pathologic system is the result of hyperactivity and out of control of the physiological system, in others - through the involvement of the central nervous system intact and damaged structures in a new, not pre-existing structural and functional organization.

The emergence of a pathological system represents the next stage of development of the pathological process. Formation and activity of pathological systems belong to the category of typical pathological processes realized in the system of relations level.

A good example of the pathological activity of the system is abnormal carding reflex. It occurs when you create a generator brachial department spinal apparatus carding reflex. Apparatus carding reflex becomes pathological determinant that turns carding physiological reflex in the pathological. The animal begins to comb the back paw reflex zone projection. These combing arise spontaneously. Over time, as the development of pathological system, they are becoming more frequent, persistent, and fierce, and may be terminated by lacerations of tissues. The animal is not able to stop the combing, despite their uselessness and harming effect. Such unrestrained violent behavior occurs in many forms of diseases of the nervous system in humans.

Structural and functional organization and activity of pathological features of the system

The key control element is a determinant of its pathological hyperactivation mechanism in the

form of a generator. Intermediate and central efferent links develop an activity that corresponds to the peculiarities of the activity of pathological determinants. If abnormal system has access to the periphery, in its structure includes a peripheral body, which becomes the target organ. In this case, the pathological activity of the system is manifested in the form of altered organ function - pathological effect. If the final link in the system is abnormal brain structure, then its effect is in violation of the relevant functions of the brain.

From all parts of the system are abnormal negative feedback to the same links and determinant. However, in contrast to the physiological system, where such ties to regulate the activities of the system, in a pathological system functionally they are ineffective because they do not correcting (or correcting bad) pathological determinant that is due to insufficient brake out of control. Brakes relatively scarce in other parts of the pathological system. Therefore, the system as a whole is almost getting out of the total CNS integrative control. At the same time, thanks to the constant activity of the positive connection between the parts of system consolidates pathological, conduction of excitation in these relations easier. As a result, over time, abnormal system is becoming more resistant to regulatory influences on the part of anti-system and the brain, and in general to the treatment modality.

In the early stages of the pathological system after pathological determinant activated by specific stimuli for her, in the later stages, it can be activated by different, including random stimuli, and spontaneously. Therefore, in the later stages of the attacks that are typical of the activity of this pathological system (eg, seizures, emotional affects, twinges, etc.), Can be triggered by different stimuli occur spontaneously, becoming more frequent, persistent and intense.

In the initial stage of a pathological system dependent on the pathological determinants, it is activated when excited determinants and disappears when its liquidation. In the later stages due to the consolidation of the pathological structure of the system is less dependent on the last determinants and can continue to operate and after its removal.

Pathogenetic significance of pathological system

Pathological system underlie a variety of neurological disorders related to various fields of activity of the nervous system, so their education is virtually universal value of pathogenetic factors.

Activities pathological system is clinically expressed as a neuropathological syndrome or symptoms. Each has its syndrome pathological system. Simple, linear pathological system are manifested as symptoms or syndromes monomorphic. An example of a relatively simple system is abnormal pathological system carding pathological reflex described above. Multi-unit, branched

pathological systems are pathogenetic basis of complex polymorphic syndromes. As an example of such pathological systems can cause parkinsonism, emotional and behavioral disorders, and others.

Consistently implemented pathogenic triad "generator - pathological determinant - pathological system" is a mechanism of occurrence of various nervous disorders.

This position is the basis of the playback experimental models of various neuropathological syndromes: central pain of spinal origin (generator in the dorsal horns of the spinal cord); trigeminal neuralgia (generator in the caudal nucleus of the trigeminal nerve); thalamic pain syndrome (generator intralaminar thalamic nucleus); vestibulopathy - rat revolves around the longitudinal axis of the body (the generator in the vestibular nucleus of Deiters); photogenic epilepsy (generator in the visual analyzer system - in the lateral geniculate body); pathologically elongated sleep (generator somnogennoy system); psychoaffective complex pathological condition (emotiogenic generator system); abnormal food-getting behavior such as violent behavior (generator in the lateral hypothalamus); parkinsonian syndrome (generator in the caudate nuclei).

One important pathological mechanisms functioning in the system is that it inhibits the physiological systems including antisystems and compensatory processes. This mechanism contributes to the development of the pathological process, especially with the continued action of the etiological factor.

Liquidation and restoration of pathological system

In contrast to the physiological system, which after reaching the programmed biologically useful (adaptive), the result is eliminated, abnormal system can operate indefinitely. This is due to the persistence of pathological determinants and fixing the positive relations between the parts of the pathological system. The elimination of the system due to the weakening of pathological effects of pathological determinants and activation antisystems. It can occur naturally in mobilizing sanogenetic mechanisms and the action of therapeutic agents.

The elimination of the pathological system is carried out by a single pattern - there is a consistent normalization of those parts of the system, who experience the least impact from the pathological determinants. Therefore, reduction of pathological system at the expense of an exit from it less dependent on the determinants of pathological parts of the system. Longer other saved pathological determinant. When her disappearance may remain local, attenuated generator that does not cause significant pathological effects. Then disappears and the generator. When you activate traces of the former system of pathological latter can recover. Since relapse occurs nerve disorders which are based on pathological system.

Removal pathological system through efferent central portions at respective therapeutic effects leads to the disappearance of clinical symptoms or syndromes, as in these circumstances it may not be manifested as impaired function of the target organ. However, there are other parts of the pathological system and the threat of its recovery. Treatment aimed at normalizing the only efferent links and target organ pathologic system is not pathogenic and symptomatic.

However, this reduction of pathological system may be clinically effective. Removal of pathological system leads to a reduction in the remaining part of the resistance due to the decrease in the number of positive relationships that strengthen the system. Reducing the number of parts of the system contribute to its destabilization and elimination. It is important that decreases disruptive effect on the system other pathological CNS system.

In the early stages of the elimination of pathological determinants leads to the elimination of a pathological system. In the later stages due to the formation of secondary determinants of pathological

system can either recover or continue to exist even after the elimination of the primary determinants of pathological. Securing the pathological system leads to a chronic disease process and related nervous disorders.

Fighting pathological systems, especially with complex and age-old forms, is very difficult and is not always effective. It requires complex pathogenetic therapy aimed at eliminating pathological determinants and normalization of other parts of the pathological system activation antisystems, strengthening overall control and other sanogenetic mechanisms, and should be

combined with etiologic therapy to prevent action of pathogenic factors supporting pathological system.

BREACH OF DOMINANT RELATIONSHIP

Concept and general characteristics of the dominant

The dominant feature is, by definition, AA Ukhtomskogo is prevailing at the moment the functional structure of the central nervous system - the center, the physiological system. The dominance of this structure over the other is done by the dual inhibition of these structures. Dominant attitudes are essential for the activity of the nervous system: thanks to the inhibition of other operating systems currently physiological system is not experiencing interference. This achieves the result programmed to the extent necessary, without distortion. Violations of dominant relationships can occur in various forms of pathology of the nervous system, they are a typical pathological process is carried out on the system-level relations.

Types of violations of the dominant relations and their pathogenetic significance

Violation dominant relationship expressed either in the form of failure, either in the form of

excessive amplification. And in fact, in both cases there is a pathology.

In case of insufficiency of the dominant relations activities currently active system is disturbed due to the influence on it of other systems. Under these conditions, the system did not result corresponds to the operations that should be achieved. With deep abuse of dominant relations that result in general can not be achieved.

When excessive strengthening relationship dominant pathology is that physiological system and other CNS structures suffer strong inhibition activity due to the dominant system. Hyperactive pathological value system acquires pathological dominant - it causes inhibition of physiological systems.

Under normal physiological dominant and determinant are the working principles of the nervous system. The dominant through inhibition of other systems enables normal activities currently active system, the determinant determines the characteristics of the activity of this system. Dominant is the mechanism of intersystem relations, the determinant - the mechanism of intersystem relations.

DISEASES OF THE NERVOUS REGULATION

Concept and general characteristics

Function disorders occur due to damage to not only the molecular and cellular processes, but also result in dysregulation of these processes. If dysregulation plays a major pathogenic role occurring disorders have disregulatory character pathology or disease regulation. When suffering from nervous regulation, there are diseases of the nervous regulation (GN Kryzhanovsky).

In diseases of the nervous regulation of the initial part of the pathological process are the changes in the regulation of the unit or the primary target organ damage. Pathological changes of regulation of this body is the factor that determines the development of secondary or further changes in the target organ.

Disorders of the nervous regulation may be due to changes in both the central and peripheral links of the regulation unit. The clinical expression of the activity of these systems are appropriate pathological syndromes. In that case the target organs are organs occurs neurovistceral pathology. If pathological determinant autonomic centers are emerging syndromes are vegetative pathology.

Examples of diseases of the nervous regulation. Diseases of the nervous regulation constitute a broad class of various disorders. These include the neurogenic form of cardiac arrhythmias and hypertension, autonomic diencephalic paroxysms, neurogenic dyskinesia internal abdominal organs (stomach, intestine, gall bladder, fallopian tubes, uterus, and so forth.), Some forms of gastric and duodenal ulcers, bronchial asthma, diabetes, glaucoma , various vegetative crises, known as paroxysmal condition and so on.

Those forms of pathology, which in common parlance is often referred to as "neurosis of the internal organs" (such as "cardiac neurosis", "gastric neurosis" and so forth.), Is a disease of the nervous regulation. They are neurotic disorders with specific pathological systems, target organs which are relevant visceral organs. Involvement of a pathological structure formation in the system depends on whether overcome this formation mechanisms regulating influences determinants. Also important are the own mechanisms of regulation of the target organ. So, under normal conditions in experimental cardiac arrhythmia caused by the creation of a generator in the central nervous system, heart rhythm disturbances begin to appear only after prolonged operation of the generator. If the pre-cardiac cause changes in reactivity or minor damage, which in itself does not appear, under these conditions the formation generator arrhythmias occur quickly.

Diseases of the regulation, including the regulation of nervous illness, the doctor usually refers to the so-called functional patolo¬gii, saying that there is no organic change. The target organ pronounced structural changes may occur in the later stages of the process.

Principles of treatment of diseases of the nervous regulation

Treatment aimed only at normalizing the changed internal organ function, is not pathogenic and symptomatic. Its result is usually of short duration, and the abolition of maintenance therapy may be a relapse. Pathogenetic treatment should be to eliminate pathological system, normalization of the

nervous regulation of the device. It is important to use complex pathogenetic therapy in the form of a combined effect on the regulation of the unit, other parts of the pathological system and target organ. The etiological therapy should be to eliminate the factors that cause and support the nervous regulation disorders.

PATHOPHYSIOLOGY OF PAIN

Concept and general characteristics

Pain is a complex psycho-emotional unpleasant sensation, is realized with a special system of pain sensitivity and the higher parts of the brain. It indicates actions that cause tissue damage, or of existing injuries. The system of perception and transmission of the pain signal is also called nociceptive system.

There are physiological and pathological pain. Physiological pain is important adaptive defense mechanism. It indicates the action of damaging agents, on the already incurred damage and the development of pathological processes in tissues. Physiological pain activates protective processes and behavioral responses to address the action of pain (algogenic) factors and the consequences of this action.

People with congenital or acquired (for example, trauma, infectious lesions) pathology of the nociceptive system, devoid of pain sensitivity, do not notice the damage that can lead to serious consequences.

Pathological pain is maladaptive and pathogenic significance. Various types of pathological pain occur as characteristic for it syndromes and symptoms which are absent at physiological pain. These include causalgia, hyperpathia, primary and secondary hyperalgesia, expansion and new algogenic receptive areas, persistent pain, spontaneous episodes of pain, preservation of pain after the termination of the provoking stimulus and other phenomena. Pathological pain is nociceptive done the same system, but the changes in the conditions of disease.

Pathological pain causes the development of structural and functional changes and damage to internal organs, particularly in the cardiovascular system, degeneration of tissues, violation of autonomic reactions, changes in neural activity, endocrine and immune systems, psycho-emotional sphere and behavior. Extreme pain can cause severe shock, uncontrollable chronic pain can be the cause of disability. Pathological pain becomes pathogenic factor in the development of new pathological processes and acquires the value of self-neuropathological syndrome or disease. Pathological pain is poorly corrected and with it the struggle difficult. If abnormal pain occurs a second time (with severe somatic diseases, malignancies, etc.), Then often it becomes the main target of treatment interventions that aim to reduce patient suffering.

Pathological pain of peripheral origin

This form of pathological pain occurs in chronic stimulation of pain receptors (nociceptors), damaged nociceptive fibers, spinal ganglia and dorsal root. These structures are often a source of intense and constant nociceptive stimulation. Nociceptors are activated in chronic inflammation (such as arthritis), the action of the decay products of tissues (eg, in tumors), and others. Chronically damageable (for example, when squeezed scars, overgrown bone and so forth.) And regenerating the sensory nerves, degenerative changed (under the action of various hazards, endocrinopathy) and demyelinated fibers are very sensitive to various humoral effects, even those for which they do not react under normal conditions (for example, to the action of epinephrine, K +, etc.). Sites such fibers are ectopic source of constant and significant nociceptive stimulation.

A special role is played by such a source neuroma - the formation of randomly overgrown nerve fibers, which occurs when they are disordered and difficulty increase. These endings are sensitive to a variety of mechanical, thermal, chemical and endogenous factors (eg, catecholamines). Therefore, the pain attacks with neuroma, as well as nerve damage can be triggered by different factors (for example, emotional stress, adrenaline action).

Nociceptive stimulation from the periphery of attack may cause pain if she overcomes the so-called "gating control" in the rear horns (Melzak, wall) consisting of a brake unit substantia gelatinosa neurons. These neurons control the flow entering the posterior horns and the ascending nociceptive stimulation. This effect can occur when intense afferent stimulation or by brake failure "gate-control."

Pathological pain of central origin

This form of pathological pain associated with hyperactivation of nociceptive neurons in the spinal and supraspinal levels. Such neurons form aggregates which are pathologically enhanced excitation generators. In the formation of the generator in the posterior horns of the spinal cord there is a center of origin of spinal pain syndrome in education in the nuclei of the trigeminal nerve - trigeminal neuralgia, in the nuclei of the thalamus - thalamic pain syndrome.

In the early stages of the disease process twinge due to the activation of the generator is triggered by nociceptive stimuli with certain directly related to the receptive field generator; the late stages of an attack provoked by stimuli of various intensities from different fields of the receptor, and can also occur spontaneously. Feature bout of pain (paroxysmal, continuous, short, long, and so forth.) Depends on the characteristics of the generator function and pathological systems. Character same pain (dull, sharp, localized, diffuse, and others.) Is determined by what education systems have become parts of nociceptive pathological algic system.

The generator in the central office can occur nociceptive system, such as in dorsal horns after prolonged nociceptive stimuli from the periphery. In these circumstances, the pain of peripheral origin initially becomes the central component and becomes pain of spinal origin. This situation occurs when causalgia, neuromas and damages afferent nerves, neuralgia, etc.

The generator in the central nociceptive apparatus may also occur when deafferentation, due to increased sensitivity deafferentized nociceptive neurons and the violation of the brake control. Deafferentatsionnye pain syndromes can occur after limb amputation, nerve transection and posterior roots, after a break or transection of the spinal cord. Thus the patient may feel pain sensitivity or lacking in nonexistent body (e.g., non-existent in the limbs of the body parts following transection of

the spinal cord). This type of pathological pain is called phantom (from the word «fantom» - a ghost). It is due to the central generator activity, the activity of which is not dependent on nociceptive stimulation from the periphery.

The generator in the central parts of the nociceptive system may occur in infectious lesions of these departments (herpetic and syphilitic lesions), trauma, toxic effects. In the experiment, these generators and associated pain syndromes are reproduced by introducing appropriate department system nociceptive substances causing violation brake (tetanus toxin, penicillin) or activate nociceptive neurons (potassium ions and so forth.).

The central office of the nociceptive system may form secondary generators. Thus, after the generator rear horns of the spinal cord after a certain time in the thalamus secondary generator may occur. Often, the localization of the primary generator in the spinal cord in order to prevent the receipt of his impulses in the brain, producing a partial (break of the ascending tracts), and in severe cases even a complete transection of the spinal cord of conductive paths.

Pathological algic system

Emerged in the afferent input (dorsal horns of the spinal cord or caudal trigeminal nucleus) generator itself is not able to cause pathological pain. Local generator regional changes may lead to spinal cord: a relief flexor reflex, changes in motor neuron activity, and others.

Pathological pain as suffering and as a syndrome occurs when the process involved and other departments of pain sensitivity system, in particular brain structures responsible for manifestation of the feelings of pain and its emotional coloring.

Participation in these structures forming pathological pain is not just in their responses to nociceptive signals received, both in physiological pain. Department of pain sensitivity system, in which there was a generator, becomes hyperactive and acquires the ability to change the functional state of the neurons of other levels. From primary and secondary educational change processes plastic is formed and fixed pain sensitivity system integration of new pathologic - abnormal algic system (PAS). That pain sensitivity system department, which is formed under the influence pathologic algic system plays the role of determinants of PAS.

If abnormal algic system is unformed, if it does not include the higher parts of the pain sensitivity of the system - the thalamus and the cerebral cortex - pain does not appear behaviorally. This situation can occur if the nociceptive neurons in the dorsal horn and are not active enough or do not form a generator if the higher parts of pain sensitivity have an effective braking system control. In both cases, the role of the supervisory mechanism that prevents the formation and activity of pathological algic system plays antinociceptive system.

The following table shows the levels of education and pain sensitivity of the system, included in the pathological algic system, which is due to the enhanced nociceptive stimulation from the periphery. These structures constitute the main trunk of PAS, on them are due to the different departments of the central nervous system, involvement in the pathological process which causes

additional syndromes. The latter include autonomic disturbances, changes in the cardiovascular system and microcirculation, disregulation functions of internal organs, endocrine and immune systems, psycho-emotional disorders, and others.

Current pain and nature of attacks of pain depends on the characteristics of activation and activity of PAS. An important role in this process is played particularly activation of the generator, which is connected with the activity of PAS. With a significant violation of the brake and increased excitability of neurons is their gipersinhronizatsiya and discharge pulse generator bystronarastajushchih flow. If this flow is as fast and enhanced activation algic pathological system, it has a twinge of paroxysmal character. If the generator develops its activity slowly and slowly activated PAS, the intensity of pain during an attack is slowly growing; when the tonic activity of the generator and PAS constant pain.

Table. Levels of education and altered pain sensitivity system constituting the main trunk system pathological algic

Peripheral units	Sensitize nociceptors, ectopic excitation foci (and regenerating damaged nerves, demyelinated areas nerve neuroma); giperaktivirovannyh group of neurons of the spinal ganglia
spinal level	Units of hyperactive neurons (generators) in afferent nociceptive relay - in the dorsal horns of the spinal cord and in the nucleus of the spinal tract of the trigeminal nerve (caudal nucleus)

supraspinal level	The nuclei of the reticular formation of the barrel, nucleus of the thalamus, and the sensorimotor orbitofrontal cortex, emotiogenic structure

Antinociceptive system

Nociceptive system has a functional antipode - antinociceptive system, which controls the activity of the nociceptive system structures.

Antinociceptive system consists of a variety of nerve structures belonging to different departments and organizations CNS levels ranging from afferent inputs in the spinal cord and cerebral cortex ending. Each relay switch in the nociceptive system has its own control unit for the active constituent of nociceptive neurons. Nociceptive and antinociceptive systems form a common system of pain sensitivity, which determines the nature of nociceptive signaling, measure its perception and the reaction to it.

Antinociceptive system plays an essential role in the mechanisms of prevention and elimination of pathological pain. Joining the reaction at nociceptive stimuli, it weakens the upward flow of nociceptive stimulation and the intensity of pain, so pain is under control and does not acquire pathological character. If any of the activities antinociceptive system nociceptive stimuli of small intensity even cause excessive pain. This effect takes place, for example, congenital or acquired deficiency antinociceptive mechanisms of the spinal cord, in particular when failure "gating control", in violation of the excitation by the thick fibers, activating this control, with injuries, infectious lesions of the central nervous system and so on.

In cases of failure antinociceptive system, it must be additional and special activation. The latter is carried out in various ways. Effective anti-nociceptive direct electrical stimulation of the brain structures that can cause suppression of even severe pathological pain. Many analgesics, including opioids exert their effect not only by a direct downward pressure on nociceptive neurons and blockade of excitatory synaptic transmission, but also via activation of antinociceptive system structures. Through activation of antinociceptive system function and non-pharmacological means of suppression of pain (eg, acupuncture). Electrical stimulation of thick fibers, activating "gating control" and other mechanisms of antinociceptive system, used clinically to suppress many kinds of pain, in particular peripheral origin.

However hyperactivation antinociceptive system may lead to inadequate hypoalgesia and even profound suppression of pain sensitivity. These effects occur in the formation of structures in antinociceptive generator system. Hysterical loss of pain sensitivity, analgesia occurs in severe stress and some psychoses, it is also associated with increased activity of antinociceptive system.

The neurochemical mechanisms of pain

The functional activity of the neurophysiological mechanisms of pain sensitivity system implemented neurochemical processes at various levels of nociceptive and antinociceptive systems.

Peripheral nociceptors are activated under the influence of many of the endogenous biologically active substances -. Histamine, substance P, kinins, prostaglandins, etc. An important role in the field in primary nociceptive neurons plays substance P. It is considered as a mediator of pain. Capsaicin (a substance found in red pepper) is a violation of substance P synthesis; intrathecal administration of capsaicin in the region of the spinal cord is a long analgesia; with the effect of capsaicin could be linked to the analgesic effect of pepper patch. At the higher levels of the nociceptive system also has a substance P, but holding them in excitation is carried out mainly by the neurotransmitters, which are inherent in the neurons of these levels. In the processes of excitation in different parts of the nociceptive system involving various neuropeptides, which, as in other parts of the central nervous system, act as neuromodulators.

The neurochemical mechanisms of activity of endogenous antinociceptive system implemented neuropeptides and neurotransmitters classic. Analgesia is caused, as a rule, the combined or sequential action of several transmitters.

Effective endogenous opioid analgesics are neuropeptides (the enkephalins, endorphins). They depressing effect on transmission neurons and activating it - on neurons antinociceptive system,

stimulate the system of diffuse nociceptive inhibitory control (DNIC), change the activity of neurons in the higher parts of the brain that perceive nociceptive stimulation and involved in the formation of painful sensations. Their effects are also realized through the action of serotonin, norepinephrine, and other neurotransmitters. Also induce analgesia and other neuropeptides (neurotensin, cholecystokinin, bombesin, angiotensin, vasopressin and others.). Substance P may also cause analgesia and inhibition of pathological pain, even when it is in the antinociceptive action of the structure, such as the dorsal nucleus of the seam.

From classical neurotransmitters important role in the analgesic effects play serotonin, norepinephrine, dopamine, GABA. Serotonin is a neurotransmitter antinociceptive systems at the spinal level. However, one of the parts of the serotoninergic system activity participates in nociceptive system, it enhances the sensitivity of nociceptive field.

Norepinephrine is also the mediator of the descending antinociceptive system, it inhibits the activity of nociceptive neurons in the posterior horns of the spinal cord and the nuclei of the trigeminal nerve. Furthermore, norepinephrine suppresses pain mechanisms and at the supraspinal level. Its analgesic effect is associated with the activation of α-adrenergic receptors, as well as

involving the serotoninergic system. Therefore, an activator of the central α-adrenergic clonidine causes a pronounced analgesic effect.

GABA is involved in the suppression of activity of nociceptive neurons and pain at the spinal level. Violation of GABAergic inhibitory processes (for example, by exposing the posterior horns of tetanus toxin, penicillin, and others.) Causes the formation therein generator and heavy pain of spinal origin. In the middle and medulla can inhibit GABA neurons antinociceptive structures and weaken the mechanisms of pain relief at this level.

Principles of treatment of pathological pain

The basic principle of treatment of pathological pain is nociceptive neurons suppressing hyperactivity and formed by them and generators to eliminate pathological algic system underlying the pain.

This object is achieved by a combination of two effects: 1) the impact on the non-specific standard basic processes hyperactivation of neurons, formation and activity of the generator, which is fundamentally the same in different parts of the central nervous system; 2) the impact on specific neurochemical processes which are associated with the activity of nociceptive neurons, generators and various pathological nociceptive system (pathological algic system).

Correction of the basic processes of hyperactivity of neurons and the formation of the generator may be effected by anticonvulsants (antiepileptics). Thus, a high therapeutic effect is the use of the antiepileptic drug carbamazepine (Tegretol, finlepsin) for the treatment of trigeminal neuralgia and other pain syndromes, especially acute paroxysmal character. Suppress some pain syndromes and other anticonvulsants.

Of paramount importance for the suppression of hyperactivity nociceptive neurons has blockade of admission to their Ca2 +, which is carried out by means of Ca2 + antagonists.

Since nociceptive and antinociceptive effects are realized at different levels, and that not one, but several mediators, it is advisable to use complex pathogenetic therapy in the form of a combined impact on the different links of the pathological algic system with the aim of suppression and antinociceptive system in order to activate it. Furthermore, it is also important influence on the psycho-emotional, vascular and other vegetative tissue components and pathological pain. It is necessary to eliminate the effect of the etiological factor that supports the pathological changes in the nociceptive system.