HYPERTONIC DISEASE
TUTORIAL

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O‘QUV ADABIYOTINING NASHR RUXSATNOMASI

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TOPIC: Hypertonic disease

Tutorial

In the direction of

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List of abbreviations

AH - arterial hypertension

BP - blood pressure

ADH - antidiuretic hormone

AIR - imidazoline receptor agonists

AK - calcium antagonists

AT - angiotensin

ARBs - angiotensin-II receptor blockers

GB - hypertension

LVH - left ventricular hypertrophy

DBP - diastolic blood pressure

IHD - ischemic heart disease

MI - myocardial infarction

BMI - body mass index

ACE inhibitors - angiotensin-converting enzyme inhibitors

ISAH - isolated systolic arterial hypertension

CT - computed tomography

LV - left ventricle

MI - cerebral stroke

MRI - magnetic resonance imaging

MS - metabolic syndrome

OJ - lifestyle

TPVR - total peripheral vascular resistance

OT - waist circumference

THC - total cholesterol

PA - primary aldosteronism

RAAS - renin-angiotensin-aldosterone system

SBP - systolic blood pressure

SAS - sympathetic-adrenal system

DM - diabetes mellitus

ABPM - ambulatory blood pressure monitoring

HF - heart failure

CVD - cardiovascular disease

CVD - cardiovascular complication

CVR - cardiovascular risk

TG - triglycerides

TIA - transient ischemic attack

Ultrasound - ultrasound examination

RF - risk factor

CRF - chronic renal failure

HDL cholesterol - high-density lipoprotein cholesterol

LDL cholesterol - low density lipoprotein cholesterol

CHF - chronic heart failure

CNS - central nervous system

EG - essential hypertension

ECG - electrocardiography

Echo-KG - echocardiography

YUGA - juxtaglomerular apparatus

α-AB - alpha-blockers

β-AB - beta-blockers

Table of contents

INTRODUCTION

The purpose of the practical lesson is to study clinical, laboratory and instrumental diagnostic criteria, principles of treatment of hypertension in its typical course.This publication is a methodological guide and is intended for students studying faculty therapy, where the most important element of education, however, as in other clinical departments, is the acquisition of various theoretical knowledge and practical skills necessary for future medical practice. The peculiarity of teaching faculty therapy is that, in essence, here is the first acquaintance with many aspects of the work of a doctor of a therapeutic profile. Therefore, the main task of the Department of Faculty Therapy is to form a special type of activity in the student, called clinical thinking, the ultimate goals of which are the diagnosis, the appointment of adequate treatment and the determination of the prognosis. Specific activity (clinical thinking), in turn, consists of a number of practical skills - collecting information about a sick person, information obtained by various laboratory and instrumental research methods (all of the listed skills are verbal, sensory, manual, mental), after which the main process is carried out in diagnostics - comparison of the data obtained about the patient with the "samples" of diseases that the student must know from educational literature. In a medical school, this process is carried out during self-observation (curation) of the patient and subsequent analysis in a practical lesson - the main form of training at the clinical department. Thus, the work of a student in the fourth year is focused on practical activities, regardless of the area in which future doctor will work in clinical medicine. That is why the leading form of education, in addition to listening to a course of lectures and working with textbooks, is the observation by students under the guidance of a teacher of patients with the most important, but by no means all, therapeutic diseases, followed by discussion in practical classes. At the same time, skills are acquired in the preparation of basic medical documentation, namely the medical history of the disease. These features are reflected to a certain extent in the proposed manual. This concerns the most important information about a number of diseases of the internal organs, diagnostic signs, the amount of additional examination

methods required, and the basic principles of treatment. Acquaintance with various aspects of etiology, pathogenesis, clinic and approaches to the treatment of major diseases of internal organs occurs directly in the management of a patient suffering from the corresponding disease. For each disease, the book provides examples of formulating a diagnosis and typical situational tasks. The latter can be used not only to develop still elementary skills in diagnostics and differential diagnostics in fourth-year students, but also as an illustration of a typical clinical picture of a particular disease. The classifications of various therapeutic diseases available to a student starting to study therapy are given. The list of essential drugs is given only in relation to individual diseases, since such information should be operational in nature and it is advisable to update it annually due to the appearance of more and more new drugs on the pharmaceutical market. The same applies to the list of required literature, which should also be constantly updated. The methodological guide was prepared by the staff of the Department of Propieutics of Internal Disease of the Medical Faculty of the Andijan State Medical Institute, who have extensive experience in teaching this discipline.

Relevance

Arterial hypertension (AH) is the most common cardiovascular pathology. The urgency of the problem is determined by the high population frequency of the disease, the impact on the state of health, working capacity and life expectancy of the population. According to G. Mancia, about 40% of the adult population of Europe has a blood pressure (BP) level exceeding 140/90 mm . p t. Art., and in the age groups older than 65 years, AH occurs in 50% of persons and more. In addition, over the past 5 years, there has been a significant increase in the incidence of the disease in this age group.

Despite the efforts of scientists, doctors and health authorities, arterial hypertension (AH) in Uzbekistan remains one of the most significant medical and social problems, which largely determines the level of cardiovascular mortality. This is due both to the wide spread of this pathology (39.5% of the adult population has elevated blood pressure (BP), but only 77.9% of them are aware of their disease), and the fact that hypertension is the most important risk factor for the most important cardiovascular diseases. vascular diseases (CVD) - myocardial infarction (MI) and cerebral stroke (MI), which mainly determine the high mortality in the country.

In addition, the presence of hypertension has a significant impact on the health status, duration and quality of life of patients, because. morbidity and mortality increase in parallel with the increase in diastolic and especially systolic blood pressure. AH is a risk factor for the development of such CVDs as stroke, coronary heart disease (CHD), as well as disability and premature death. Long-term hypertension leads to damage to target organs: heart, brain, kidneys, peripheral vessels. According to the Framingham study, it was found that the higher the level of blood pressure, the higher the risk of developing CVD in both men and women of all age groups. The share of hypertension accounts for up to 90% of all cases of hypertension in the elderly, while in young patients (under 40 years) - 60%. The frequency of complications of hypertension also increases with age. Thus, in patients with mild hypertension at the age of 25-34, the risk of

developing complications within 10 years is less than 1%, while in 65-74 years it is more than 30%.

The complex interweaving of age-related and pathological moments in the development of hypertension in old age creates significant difficulties in diagnosing and solving therapy issues that arise mainly when assessing the nature of hypertension itself - to what extent it is a reflection of age-related involutive processes and phenomena of adaptation of the circulatory system in the body as a whole, and to what extent it depends on the development of systemic or organic pathology.

Modern generally accepted concepts of the pathogenesis of AH disease do not sufficiently take into account the "contribution" of violations of the rheological properties of blood and the functional state of platelets in the formation of the AH syndrome and disorders of central and peripheral hemodynamics. These disorders correlate with the severity of the disease and are considered as additional factors contributing to its progression.

Chapter 1

Anatomist o -physiological features of organs blood circulation

1.1. Heart

1.1.1. The structure of the heart

CARDIOVASCULAR SYSTEM

The heart is located in the chest behind the sternum and in front of the descending aorta and esophagus. It is attached to the central ligament of the diaphragm muscle. On both sides there is one lung. Above are the main blood vessels and the division of the trachea into the two main bronchi.

The main significance of the cardiovascular system is the supply of blood to organs and tissues. Blood is constantly moving through the vessels, which makes it possible for it to perform all vital functions. The circulatory system includes the heart and blood vessels - blood and lymphatics . yo yo

The heart weighs about 300 g and is shaped like a grapefruit (Figure 1); has two atria, two ventricles and four valves; receives blood from two vena cava and four pulmonary veins, and throws it into the aorta and pulmonary trunk. The heart pumps 9 liters of blood a day, making from 60 to 160 beats per minute.

The heart is covered with a dense fibrous membrane - the pericardium, which forms a serous cavity filled with a small amount of fluid, which prevents friction during its contraction. The heart is made up of two pairs of chambers, the atria and ventricles, which act as independent pumps. The right half of the heart "pumps" venous, carbon dioxide-rich blood through the lungs; it is a small circle of blood circulation. The left side ejects oxygenated blood from the lungs into the systemic circulation.

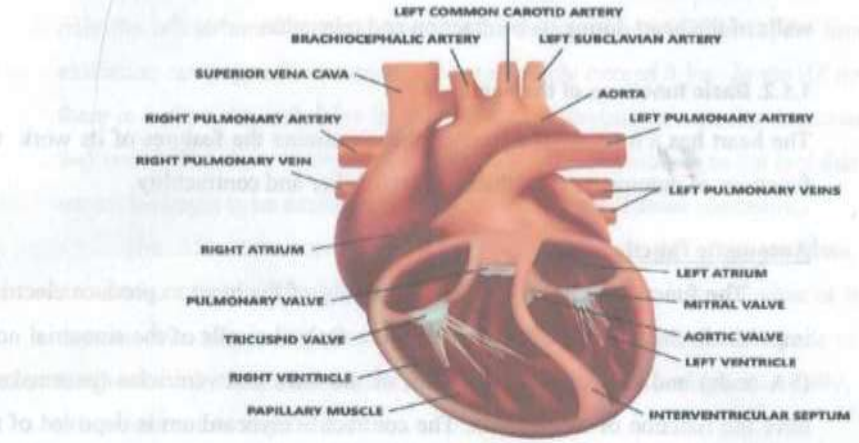


Figure- 1.1.

The wall of the heart consists of three layers: endocardium, myocardium and epicardium. **Endocardium** in the form of a thin (about 0.6 mm) connective tissue membrane, it lines the inside of all the cavities of the heart, valves, chords and papillary muscles (Fig-1.1).

Myocardium consists of individual muscle fibers, each of which includes a large number of muscle cells (cardiomyocytes) connected in series to each other through intercalated disks (nexuses). With the help of nexuses, individual cardiomyocytes are connected into a single muscle network - a functional syncytium, which provides a rhythmic and almost synchronous contraction of all working muscle fibers. The thickness of the atrial myocardium does not normally exceed 2-3 mm, the left ventricle - 7-8 mm, and the right ventricle - 3-4 mm.

epicardium covers the outer surface of the heart, the initial sections of the ascending aorta, the pulmonary trunk and the final sections of the caval and pulmonary veins. The epicardium is composed of connective tissue fused to the muscle layer. At the base of the heart, it passes into the parietal leaf of the pericardium - the pericardial sac that surrounds the heart, the initial sections of the aorta, pulmonary trunk and the mouth of the caval and pulmonary veins and delimits the heart from neighboring organs. Normally, the pericardial cavity

contains about 20-30 ml of a clear serous fluid, which reduces the friction of the walls of the heart during its contraction and relaxation.

1.1.2. Basic functions of the heart

The heart has a number of functions that determine the features of its work: the functions of automatism, conduction, excitability and contractility.

Automatic function

The function of automatism is the ability of the heart to produce electrical impulses in the absence of external stimuli. Only the cells of the sinoatrial node (SA node) and the conduction system of the atria and ventricles (pacemakers) have the function of automatism. The contractile myocardium is deprived of the function of automatism.

There are three centers of automatism (see Fig. 1.2).

1. The center of automatism *of the first order* is the cells of the SA node, which produce electrical impulses with a frequency of about 60–80 per minute.

2. The center of automatism of the *second order* is the cells of the AV junction (zones of transition of the AV node to the bundle of His and the lower sections of the atria), as well as the bundle of His, which produce impulses at a frequency of 40–60 per minute.

3. The center of automatism of the *third order* - the final part, legs and branches of the bundle of His. They have the lowest automatism function, producing about 25-45 pulses per minute.

Normally, the only pacemaker is the SA node, which suppresses the automatic activity of other (ectopic) pacemakers.

Conductivity function

The conduction function is the ability to conduct excitation of the fibers of the conduction system of the heart and contractile myocardium. In the latter case, the speed of the electrical impulse is significant. In the *atria* , excitation spreads from the SA node along three internodal tracts (Bachmann, Wenckebach and Torel) to the AV node and through the interatrial Bachmann bundle to the left

atrium . At the beginning, the right is excited, then the right and left, at the end - only the left atrium. The excitation conduction speed is 30–80 cm/s, the time of excitation coverage of both atria does not normally exceed 0.1 s . In *the AV node* , there is a physiological delay in excitation (the conduction velocity decreases to 2–5 cm/s). The delay in excitation in the AV node contributes to the fact that the ventricles begin to be excited only after the end of a full atrial contraction.

The AV node normally "passes" no more than 180–220 impulses per minute from the atria to the ventricles. With a higher frequency of sinus or atrial rhythm, even in a healthy person, an incomplete atrioventricular blockade of the conduction of impulses from the atria to the ventricles develops. Normally, AV delay does not exceed 0.1 s .

In the ventricles , excitation quickly spreads along the bundle of His, its branches and Purkinje fibers (conduction velocity from 100–150 to 300–400 cm/s). The wave of depolarization spreads from subendocardial to subepicardial areas of the heart muscle . (see Fig . 1.2).

In the first 0.02 s, the left half of the interventricular septum (IVS) is depolarized , as well as most of the right ventricle (RV). After 0.04–0.05 s , a significant part of the left ventricle (LV) is excited . The last ones in the period of 0.06–0.08 s are the basal sections of the LV, RV, and IVS activated. In this case, the front of the excitation wave constantly changes its direction, as can be seen in the figure. The total duration of ventricular depolarization is 0.08–0.09 s .

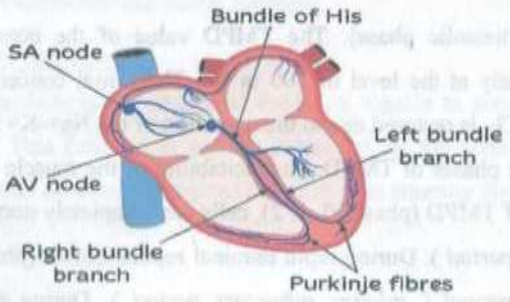


Figure-1.2.

Excitability function

The excitability function is the ability of the cells of the conduction system of the heart and contractile myocardium to be excited under the influence of external electrical impulses.

Excitation of the heart muscle is accompanied by the emergence of a *transmembrane action potential (TMPD*) - a changing potential difference between the outer and inner surfaces of the cell membrane. In the initial state, the outer surface of an unexcited myocardial cell is positively charged, while the inner one is negatively charged (Fig. 1.3).

There are several phases of TMPD of the myocardial cell.

Phase 0 - during which there is a rapid (within 0.01 s) recharge of the cell membrane: its inner surface is positively charged, and the outer one is negatively charged.

Phase 1 - a slight initial decrease in TMPD from +20 mV to 0 or slightly lower (the phase of initial rapid repolarization).

Phase 2 is a relatively long (about 0.2 s) *plateau phase* , during which the TMPD value is maintained at the same level.

Phase 3 (final rapid repolarization), during which the previous polarization of the cell membrane is restored: its outer

the surface is positively charged, while the inner one is negatively charged (–90 m V).

Phase 4 (diastolic phase). The TMPD value of the contractile cell remains approximately at the level of –90 m V . The initial concentration of K+, Na+, Ca2+ and Cl– is restored due to the operation of the Na+-K+ pump.

In different phases of TMPD, the excitability of the muscle fiber is different. At the onset of TMPD (phases 0, 1, 2), cells are completely non-excitable (*absolute refractory period*). During rapid terminal repolarization (phase 3), excitability is partially restored (*relative refractory period*). During diastole (phase 4 of TMPD), there is no refractoriness and the myocardial fiber is fully excitable (Fig. 1.3).

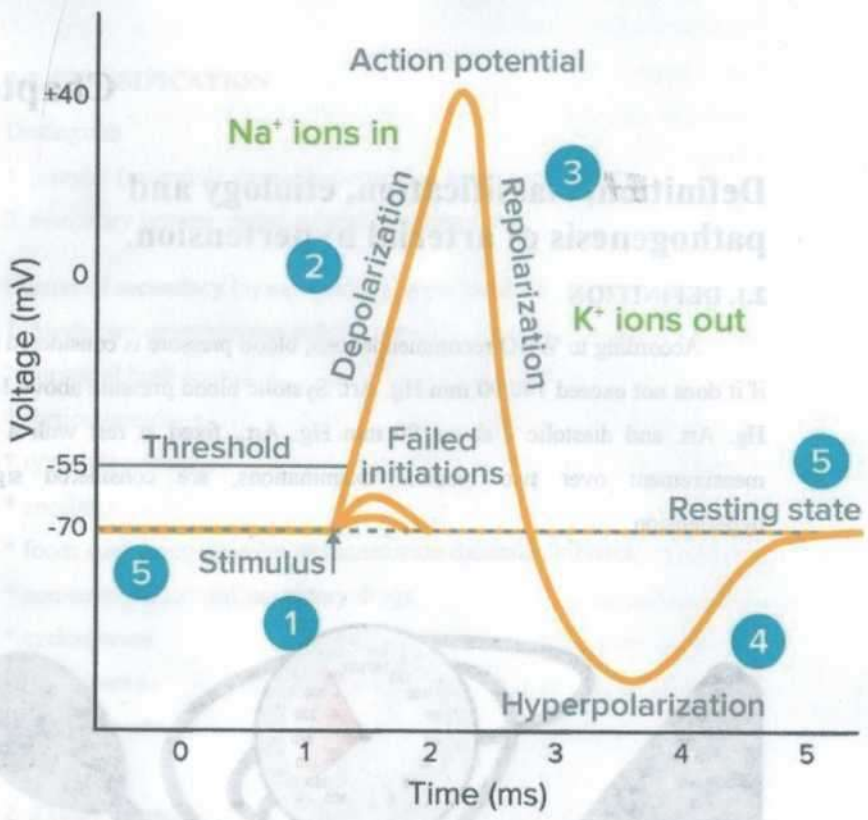


Figure 1.3. transmembrane action potential.

Contractility function

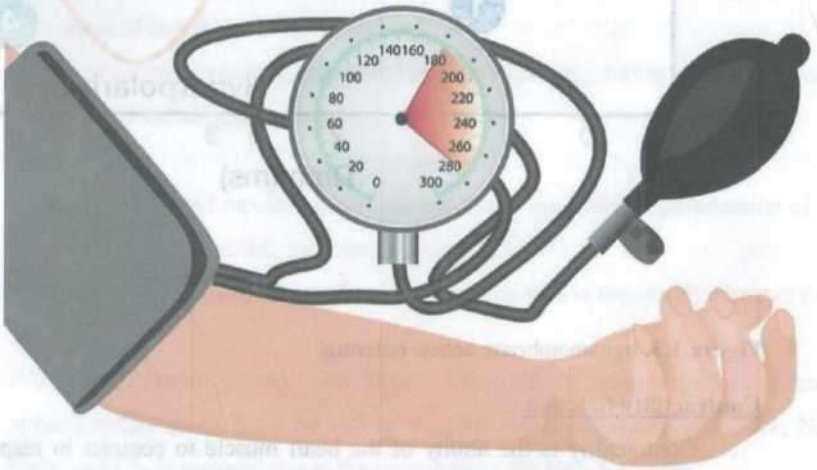
Contractility is the ability of the heart muscle to contract in response to stimulation. This function is mainly possessed by the contractile myocardium. The contraction process is triggered by Ca2+ ions entering the cell during TMPD.

Chapter 2

Definition, classification, etiology and pathogenesis of arterial hypertension.

2.1. DEFINITION

According to WHO recommendations, blood pressure is considered normal if it does not exceed 140/90 mm Hg. Art. Systolic blood pressure above 140 mm Hg. Art. and diastolic - above 90 mm Hg. Art., fixed at rest with a double measurement over two medical examinations, are considered signs of hypertension.



The term "arterial hypertension" means a syndrome of increased blood pressure in "hypertension" and "symptomatic arterial hypertension".

The term "hypertension" (EH), proposed by G.F. Lang in 1948, corresponds to the concept of "essential arterial hypertension" (EH) used in other countries.

2.2. CLASSIFICATION

Distinguish:

1. primary (essential) arterial hypertension (or hypertension)
2. secondary (symptomatic) arterial hypertension.

Causes of secondary (symptomatic) hypertension:

1. *Medicines or exogenous substances –*

* hormonal birth control
* corticosteroids
* sympathomimetics
* cocaine
* foods containing thiamine or monoamine oxidase inhibitors
* non-steroidal anti-inflammatory drugs
* cyclosporine
* amphetamine
* erythropoietin
* alcohol

2. Kidney disease-

* renal parenchymal diseases:
- acute glomerulonephritis
- chronic nephritis
- chronic pyelonephritis
* congenital anomalies of the kidneys:
- polycystic kidney disease
- congenital hypoplasia of the kidneys
- pathologically mobile kidney
* connective tissue diseases
* diabetic nephropathy
* hydronephrosis
* kidney injury

* obstructive nephropathies
* renal amyloidosis
* systemic vasculitis
* kidney infarcts
* kidney tuberculosis
* kidney tumor
* renovascular hypertension (fibromuscular dysplasia, atresia and hypoplasia of the renal arteries, aneurysms of the renal arteries, arteriovenous fistulas, atherosclerosis, calcification, thrombosis of the renal arteries, scarring of the renal arteries, aortoarteritis, stenosis and thrombosis of the renal veins)
* renin-secreting tumors
* renoprival hypertension
* Primary salt retention (Liddle and Gordon syndrome)

3. Hemodynamic -

* heart disease (HCM)
*hyperkinetic state of circulation
* heart defects (aortic valve insufficiency, arteriovenous fistula, open ductus arteriosus)
* violation of conductivity (complete A-B blockade)
* hyperkinetic syndrome
* stiffness of the aorta (atherosclerosis, aortitis)
* hypertension in polycythemia
* circulatory failure
*increased blood volume
* chronic obstructive pulmonary disease

4. Endocrine diseases -

* acromegaly
* hypothyroidism
* primary hyperparathyroidism (hypercalcemia)
* hyperthyroidism
* cancer tumor

A. Damage to the cortical layer:

- Cushing's syndrome

primary aldosteronism

- congenital adrenal hyperplasia

B. Damage to the medulla:

- pheochromocytoma

- a tumor of chromaffin cells located outside the adrenal glands

5. Neurological diseases

* increased intracranial pressure

* brain tumors

* encephalitis

* respiratory acidosis

* sleep apnea

* total paralysis of limbs

*brain injury

* acute porphyria

* lead poisoning

* Guillain-Barre syndrome (Gillian a- Barre)

* poliomyelitis

* chronic stress

6. Complications of pregnancy

7. Surgical complications -

* postoperative hypertension

* post-transplant hypertension

2.3 . _ Etiology and pathogenesis of GB

Essential or primary arterial hypertension develops as an independent chronic disease and accounts for up to 90% of cases of arterial hypertension. Symptomatic or secondary hypertension accounts for 5 to 10% of cases of arterial hypertension and is one of the manifestations of another disease.

Hypertensive disease (essential hypertension) is a multifactorial polyetiological disease .

Risk factors for hypertension (Figure 2.1)

Unchangeable risk factors include:

- Heredity - people who have hypertensive patients among their relatives are most predisposed to developing this pathology in them .
- Age
- Male sex - it was found that the incidence of arterial hypertension in men is significantly higher than the incidence of women. And the fact is that female sex hormones, estrogens, prevent the development of hypertension. But such protection, unfortunately, is short-lived. The climacteric period sets in, the saving effect of estrogen ends , and women equalize in incidence with men and often overtake them.

Modifiable risk factors include :

- Increased body weight - in people who are overweight, the risk of developing arterial hypertension is higher;
- A sedentary lifestyle - otherwise, physical inactivity, a sedentary lifestyle and low physical activity lead to obesity, which in turn contributes to the development of hypertension;

- At alcohol consumption – Excessive alcohol consumption contributes to arterial hypertension.
- Eating a lot of salt in food - a high-salt diet contributes to high blood pressure . This raises the question of how much salt can be consumed per day? The answer is short: 4.5 grams or a teaspoon without a top.
- An unbalanced diet with an excess of atherogenic lipids, excess calories, leading to obesity and contributing to the progression of type II diabetes. Atherogenic, i.e., literally, "creating atherosclerosis" lipids are found in large quantities in all animal fats, meat, especially pork and lamb;
- Smoking is another variable and formidable factor in the development of arterial hypertension and its complications. The fact is that the substances of tobacco, including nicotine, create a constant spasm of the arteries, which, when fixed, leads to stiffness of the arteries, which entails an increase in pressure in the vessels;
- Stress leads to the activation of the sympathetic nervous system, which acts as an instant activator of all body systems, including the cardiovascular system. In addition, pressor hormones, i.e., causing spasm of the arteries, hormones are released into the blood. All this, as with smoking, leads to stiffness of the arteries and arterial hypertension develops;
- Gross sleep disturbances like sleep apnea syndrome , or snoring. Snoring is a real scourge for almost all men and many women. Why is snoring dangerous? The fact is that it causes an increase in pressure in the chest and abdominal cavity. All this is reflected in the vessels, leading to their spasm. Arterial hypertension develops.

Pathogenesis: the main mechanisms for increasing blood pressure

The level of blood pressure, as is known , is determined by three main hemodynamic parameters:

1. The magnitude of cardiac output (MO), which in turn depends on the contractility of the LV myocardium, the magnitude of the preload, and other factors.
2. Veled total peripheral vascular resistance (OPVR), depending on the tone of the vessels of the muscular type (arterioles), the severity of structural

changes in their vascular wall, the stiffness of the elastic type arteries (large and medium arteries, aorta), blood viscosity.

3. Volume of circulating blood (CBV)
4. Changes in the rheological properties of blood, an increase in blood viscosity (when plasma loss , dehydration) leads to an increase in the work of the heart and an increase in blood pressure.

Theoretically, we can assume the following pathogenetic options for the formation of essential hypertension (AH):

1. Hypertension due to a persistent increase in cardiac output, not accompanied by an adequate decrease in peripheral vascular resistance and bcc (for example, due to a decrease in vascular tone and natriuresis).
2. Hypertension caused by a predominant increase in peripheral vascular resistance without a corresponding decrease in MO and BCC.
3. AG, which develops against the background of a simultaneous increase in MO and OPSS without an adequate decrease in BCC.
4. Hypertension due to a predominant increase in BCC, associated with a sharp decrease in natriuresis and diuresis (sodium and water retention in the body).

Mechanisms of development of arterial hypertension

All mechanisms of development of arterial hypertension are divided into 2 groups:

1) vasopressor
2) vasodepressor.

Vasopressor mechanisms:

1. Neurogenic
2. Endocrine
3. Renal

Vasodepressor mechanisms:

1. Centrogenic

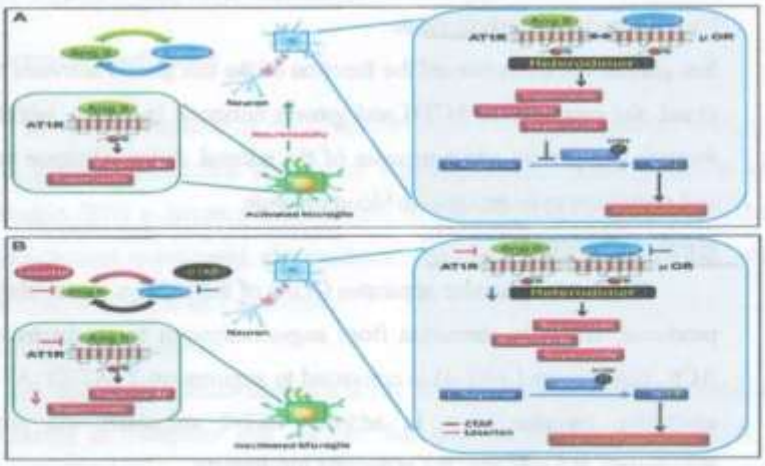
2. Reflexogenic

3. Humoral

VASOPRESSOR MECHANISMS

Neurogenic mechanisms

These mechanisms are leading in the pathogenesis of hypertension. Lang G.F. is the founder of the neurogenic theory of hypertension. Psycho-emotional stress disrupts cortical-subcortical relationships, there is a disorder of neurodynamics, the excitability of the hypothalamus increases. This is also facilitated by cerebral ischemia, hypoxia, traumatic brain injury .. The activity of the hypothalamic structures, the sympathetic nervous system increases, which causes excessive production of catecholamines - adrenaline and norepinephrine. Adrenaline causes excitation $_{of\ 1}$. adrenergic receptors of the myocardium, which leads to its hyperfunction, an increase in cardiac output and an increase in systolic blood pressure. This is a hyperdynamic form of arterial hypertension. With increased secretion of noradrenaline, alpha-adrenergic receptors of the vessels react, diastolic blood pressure increases. This is resistance hypertension. The release of epinephrine and norepinephrine causes an increase in systolic and diastolic blood pressure. This is a mixed form of arterial hypertension.



Endocrine mechanisms

These mechanisms involve the hypothalamus, pituitary gland, adrenal glands, and sex glands. Excessive production of vasopressin in the hypothalamus causes an increase in myogenic tone and an increase in blood pressure. An increase in blood pressure is associated with excitation of the adenohypophysis and hypersecretion of ACTH and growth hormone. These hormones cause an increase in blood pressure indirectly, through vasopressin and hormones of the adrenal cortex. Adrenal glands: Among the hormones of the adrenal cortex, aldosterone plays an important role. Aldosterone retains sodium in the body and promotes its entry into the vascular wall. It swells due to the accumulation of water. The internal diameter of the vessel decreases, which leads to an increase in blood pressure. In addition, sodium increases the sensitivity of the wall to the action of thyroxine and catecholamines, even in their physiological concentration. Against their background, the intake of salt in the body stimulates an increase in blood pressure. An increase in sodium ions in the body leads to water retention in the body, which causes additional stress on the heart and leads to an increase in blood pressure.

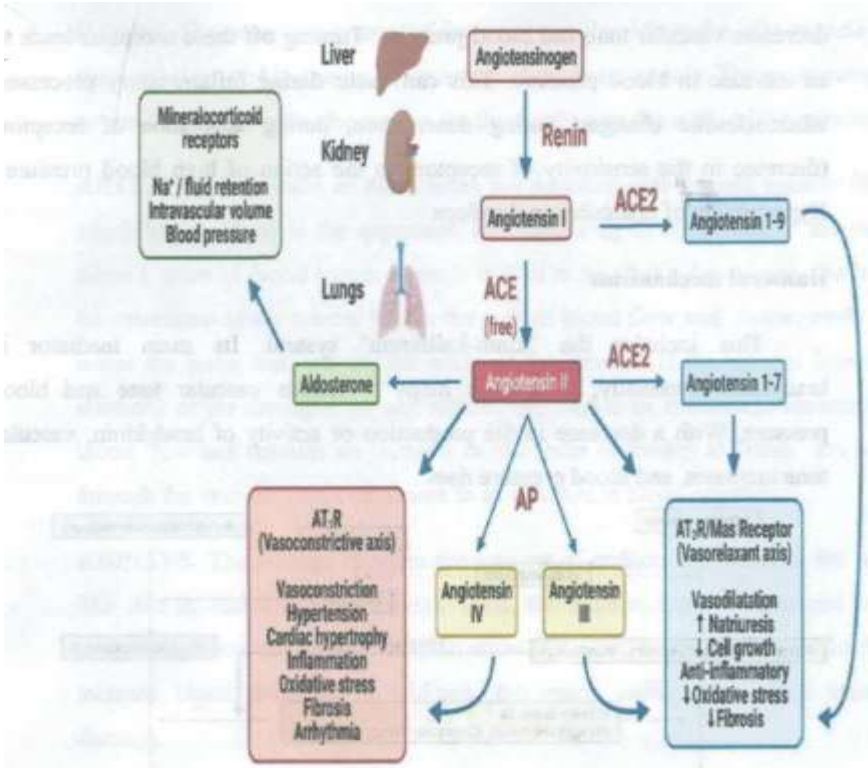
Aldosterone -----Na^+--------- AD

Na^+ Thyroxine, catecholamines

Sex glands: the extinction of the function of the sex glands activates the pituitary gland, the secretion of ACTH and growth hormone increases, which indirectly, through vasopressin and hormones of the adrenal cortex, increase vascular tone and contribute to an increase in blood pressure.

renal mechanism

The juxtaglomerular apparatus (JGA) of the kidneys is stimulated. Renin is produced, which is converted from angiotensinogen to angiotensin-1, through ACE, angiotensin-1 (AT-1) is converted to angiotensin-2 (AT-2). AT-2 increases myogenic vascular tone. In addition, AT-2 stimulates the production of aldosterone and activates the endocrine mechanism.



VASODEPRESSOR MECHANISMS

Centrogenic mechanism

There are structures in the CNS that cause a depressant effect. This is the opiate system. It contains endorphins and enkephalins. This system is anti-adrenergic. With a decrease in the activity of the opioid system, the sympathetic nervous system is activated, the production of catecholamines increases, which leads to an increase in blood pressure.

Reflexogenic mechanisms

In the carotid sinus zone, the aortic arch, depressor zones are localized, represented by receptors that regulate the level of blood pressure. With an increase in blood pressure, excitation of receptors occurs and reflexively

decreases vascular tone and blood pressure. Turning off these receptors leads to an increase in blood pressure. This can occur during inflammatory processes, atherosclerotic changes, during denervation, during adaptation of receptors (decrease in the sensitivity of receptors to the action of high blood pressure). Hypertension of disinhibition develops

Humoral mechanisms

This includes the "kinin-kallikrein" system. Its main mediator is bradykinin. Normally, bradykinin helps to reduce vascular tone and blood pressure. With a decrease in the production or activity of bradykinin, vascular tone increases, and blood pressure rises.

The inclusion of pressor mechanisms and the violation of depressor mechanisms leads to the development of hypertension.

Blood pressure regulation

There are several systems in the body that control blood pressure levels and protect them from excessive drops or increases. These are the heart, arteries, kidneys, a number of hormones and enzymes, as well as the nervous system.

HEART. The necessary amount of force to eject blood from the left ventricle into the aorta is created by the pumping action of the heart muscle. The more pumping power the heart creates, the greater the force acting on the walls of the arteries.

ARTERIES. The walls of the arteries are supplied with smooth muscle fibers, which are involved in the expansion and narrowing of the lumen of the vessel when a wave of blood passes through it. The more elastic the arteries, the lower the resistance of the arterial bed in the path of blood flow and, consequently, the lower the force that acts on the walls of the arteries. If the arteries lose their elasticity or are damaged for any reason, this causes an increase in resistance to blood flow and requires an increase in the force necessary to "push" the blood through the vessels. This contributes to an increase in blood pressure.

KIDNEYS. The kidneys regulate the amount of sodium and water in the body. The rule is: sodium "holds" water. Thus, the more sodium is contained in the body, the greater the volume of fluid circulates with the blood. Excess fluid can increase blood pressure. In addition, too much sodium can cause vascular damage.

OTHER FACTORS. ***The central nervous system, along with hormones, enzymes, and other chemicals,*** can affect blood pressure levels.

Baroreceptors There are tiny nodular structures in the walls of the heart and some blood vessels called baroreceptors. These structures work like a room thermometer in your home. Baroreceptors continuously monitor the level of blood pressure in the arteries and veins. If a pressure change is signaled, the baroreceptors relay it to the brain, where it responds with commands to decrease or increase the heart rate, and to widen or narrow the arteries to maintain a normal blood pressure level.

Adrenaline . The brain responds to impulses from baroreceptors by stimulating the release of hormones and enzymes that affect the functioning of the heart,

blood vessels, and kidneys. One of the main hormones involved in controlling blood pressure is adrenaline, also called epinephrine. Adrenaline is released into the blood under conditions of stress or tension, for example, in case of anxiety and haste when performing a task.

Adrenaline causes the blood vessels to constrict, causing the heart to contract with greater force and speed, resulting in an increase in blood pressure. People often associate the feeling of high blood pressure with the release of adrenaline.

Renin-angiotensin-aldosterone system . There are other hormones in the body that regulate blood pressure levels. Among them is renin, which is formed in the kidneys, it is able to turn into angiotensin I. Once in the bloodstream, angiotensin I turns into angiotensin II. The effect of angiotensin II is to constrict blood vessels and stimulate the release of the hormone aldosterone, which is synthesized in the adrenal glands. As a result of an increase in the concentration of aldosterone, the kidneys begin to retain more water and salts in the body.

According to scientists, some people with high blood pressure have a special version of the gene responsible for the synthesis of angiotensin. As a result, the body produces too much angiotensin.

Endothelium . Arteries are lined with a thin layer of cells called endothelium. The experiment shows that this layer plays a very important role in the regulation of blood pressure - for example, by releasing chemicals that cause blood vessels to contract and relax.

Nitric oxide . A gas called nitric oxide found in the blood can affect blood pressure. This gas helps to relax the wall of the blood vessel and expand its lumen. Nitric oxide levels can be elevated by nitroglycerin, a drug used to treat certain cardiovascular conditions.

Endothelin . The opposite effect of nitric oxide on the vessel wall is exerted by a protein called endothelin . It causes blood vessels to contract. Endothelin-1, a form of this protein, may play a critical role in the development of high blood pressure.

Chapter 3

Diagnosis and clinic of GB

3.1. DIAGNOSTICS GB

The doctor at the reception will first of all find out the complaints that bother the patient and collect an anamnesis (history of diseases and life). Then he will definitely measure the level of blood pressure and conduct a complete examination.

If arterial hypertension is suspected, pressure and pulse should be monitored for at least 1-2 weeks. If blood pressure is above 140/90 mm Hg. more than three times when measured at different times, we can talk about arterial hypertension.

Next, you need to exclude the so-called. symptomatic hypertension, when high blood pressure is a consequence of other diseases and conditions.

At the first appointment in a patient with high blood pressure, it is necessary:

1. Find out the constancy (stability) of the increase in blood pressure (confirm with an entry in the outpatient card - three times during the week / month, elevated blood pressure figures or data from daily monitoring of blood pressure)

2. Exclude the secondary nature of blood pressure

developing cardiovascular complications

modifiable risk factors for cardiovascular disease

5. Assess for the presence of target organ damage, cardiovascular and other comorbidities

6. Determine the clinical variants of hypertension

7. Choose the optimal solution in the selection of antihypertensive therapy

The two main diagnostic methods that allow you to determine the presence of hypertension in a person are:

- blood pressure measurement
- physical examination

3.2 Rules for measuring blood pressure:

The ideal option for measuring blood pressure is considered to be a mechanical sphygmomanometer and a phonendoscope (Figure 3.1). This method is the most accurate. But for self-monitoring at home, you can use an automatic or semi-automatic tonometer (Figure 3.2).

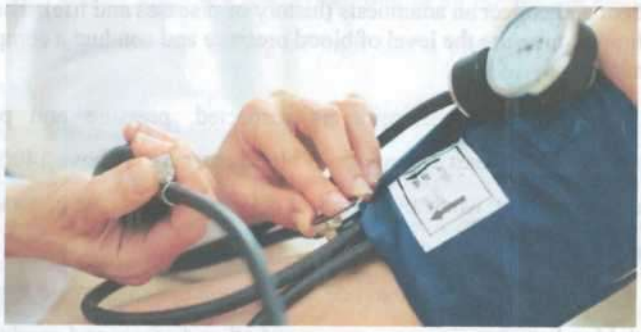


Figure 3.1

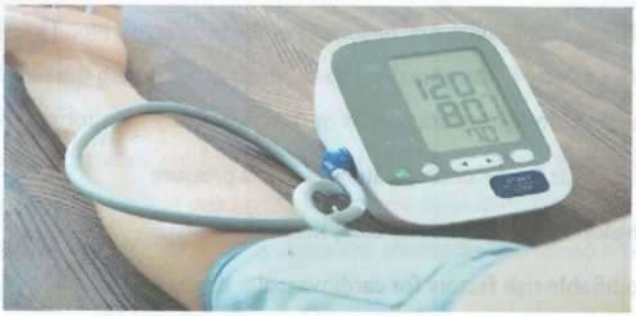


Figure 3.2

- The measurement must be taken after a five-minute rest.
- 30 minutes before this, they do not recommend eating, drinking coffee, alcohol, physical activity, smoking.
- When measuring, the legs should not be crossed, the feet should be on the floor, the back should rest on the back of the chair.
- An emphasis is needed for the hand, the bladder must be emptied before measurement.

Blood pressure is measured after the patient is at rest and in a sitting position for 5 minutes. When measuring blood pressure, it is necessary to take into account the size of the cuff (the rubber part must be at least 2/3 of the length and at least ¾ of the circumference of the arm). The standard cuff should be 10 cm longer than the bladder inside the cuff. The cuff should be placed 2 cm above the antecubital fossa.

Failure to comply with these conditions can lead to an increase in blood pressure. The shoulder should not be squeezed by clothing (measurement through clothing is unacceptable). Blood pressure is measured at least twice on the same arm. If a difference in the level of blood pressure on one arm is 5 or more mm Hg . carry out an additional, third, measurement. Finally, the average value is recorded. During the first measurement, the pressure is measured on both hands, in the subsequent - on the arm where it was higher. The difference in blood pressure on the left and right hand should not exceed 10 mm Hg. Art. Larger differences should be of concern for upper extremity vascular disease.

Previously, it was believed that normally there may be a slight difference in the values of systolic blood pressure in one person when measuring it on different hands. Recent data, however, suggest that a difference of 10-15 mm Hg. Art. may indicate the presence, if not of cerebrovascular diseases, then at least of the pathology of peripheral vessels, contributing to the development of arterial hypertension and other cardiovascular diseases. Moreover, although this feature has a rather low sensitivity (15%), it is distinguished by a very high specificity (96%). Therefore, blood pressure, indeed, as it has always been reflected in the instructions, should be measured on both hands, fix the differences for the appointment of additional examinations, and classify the pressure according to the maximum value from both hands. In order not to be mistaken, it is supposed in each case to measure the pressure on each arm three times at short intervals and consider the lowest pressure indicators to be true (however, it should be borne in mind that there are patients whose pressure values do not decrease with each measurement, but increase).

Factors that distort the true values of blood pressure when measured by an automatic tonometer Table 3.1

FACTOR	SYSTOLIC ("upper") BP	DIASTOLIC ("lower") BP
Lying position	↑ by 3 mm Hg	↓ by 2 - 5 Hg
Deviation of the position of the hand at the level of the heart (for every 10 cm)	Above the level of the heart - ↓ by 8 mm Hg. Below the level of the heart - ↑ by 8 mm Hg.	Above the level of the heart - ↓ by 8 mm Hg. Below the level of the heart - ↑ by 8 mm Hg.
Hand without support	↑ by 2 mm Hg	↑ by 2 mm Hg.s t
Back without support	↑ by 8 mm Hg	↑ by 6 - 10 mm Hg.
Crossed legs	↑	↑
Disproportionately small cuff	↓ by 8 mm Hg	↑ by 8 mm Hg
Rapid air release	↓	↑
Re-inflation of air into the cuff	↑ by 14 - 30 mm Hg.	↑ by 10 -20 mm Hg.
ambient noise	↓	↑
Talk	↑ by 17 mm Hg	↑ by 13 mm Hg
Measurement of blood pressure in a cold room	↑ by 11 mm Hg	↑ by 8 mm Hg
Within and 1 hour after exercise	↓ by 5 - 11 mm Hg.	↓ by 4 - 8 mm Hg.
Full bowel or bladder	↑ by 27 mm Hg	↑ by 22 mm Hg
Intestinal spasms	↑ by 18 mm Hg.	↑ by 14 mm Hg
Within 2 hours after drinking coffee	↑ by 10 mm Hg	↑ by 7 mm Hg
Smoking	↑ by 10 mm Hg	↑ by 8 mm Hg
Decreased hearing in a blood pressure monitor	↓	↑

3.3 Rates of increase in blood pressure

The following blood pressure levels have been adopted by the World Health Organization:

Category	Systolic (mmHg)		Diastolic (mmHg)
Optimal	<120	and	<80
Normal	120–129	and/or	80–84
High normal	130–139	and/or	85–89
Grade 1 hypertension	140–159	and/or	90–99
Grade 2 hypertension	160–179	and/or	100–109
Grade 3 hypertension	≥180	and/or	≥110
Isolated systolic hypertension[b]	≥140	and	<90

BP = blood pressure; SBP = systolic blood pressure.

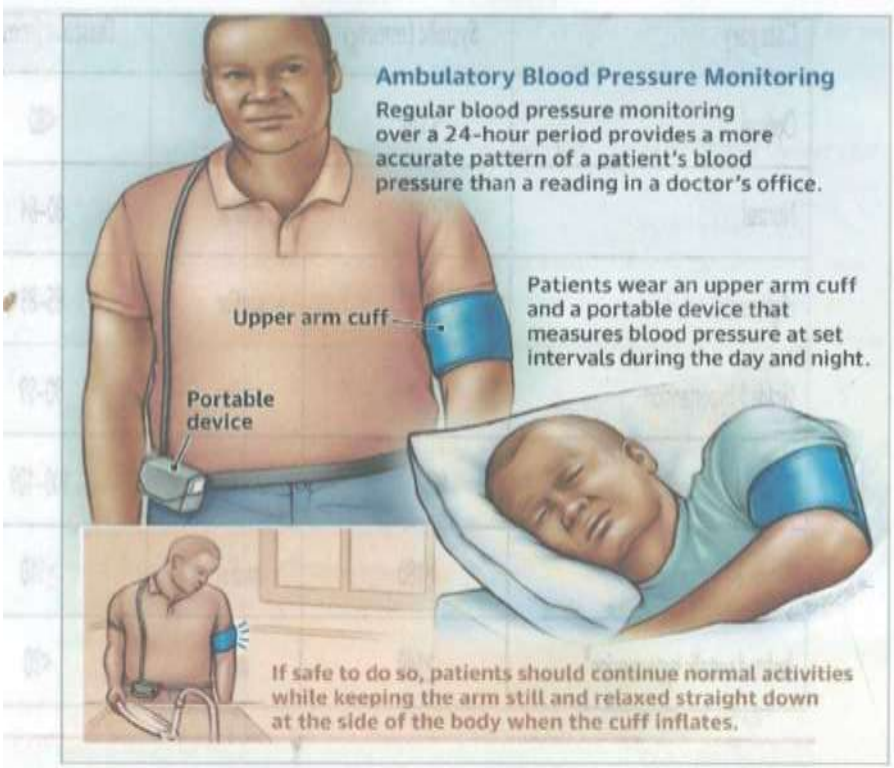
[a]BP category is defined according to seated clinic BP and by the highest level of BP, whether systolic or diastolic.

[b]Isolated systolic hypertension is graded 1, 2, or 3 according to SBP values in the ranges indicated.

The same classification is used for all ages from 16 years.

blood pressure monitoring systems have increasingly entered medical practice . Compact wearable monitors based on the Korotkoff method and / or using the oscillometric method have allowed doctors to monitor not only blood pressure at night

(bedside monitors also provide such an opportunity), but also in the conditions familiar to the patient, with physical and mental stress .



In addition, the accumulated experience made it possible to divide patients ***depending on the nature of daily fluctuations in blood pressure*** into groups in which the risk of developing cardiovascular complications was significantly different:

Dippe s - persons with a normal nocturnal decrease in blood pressure (by 10-22%) - 60-80% of patients with essential hypertension (EAH). This group has the lowest risk of complications.

• **Non-dippe s - individuals with insufficient reduction in blood pressure (less than 10%) - up to 25% of patients with EAH.**

• **Over-dipper, or extreme-dippers - persons with excessive nocturnal drop in blood pressure (more than 22%)** - up to 22% of patients with EAH.

• **Night-peake r s - persons with nocturnal hypertension** , in which nighttime blood pressure exceeds daytime - 3-5% of patients with EAH.

Typical mistakes during daily blood pressure monitoring:

- using an instrument that has not been tested to meet accuracy standards
- incorrect cuff selection, cuff displacement during monitoring
- lack of control measurements of blood pressure before monitoring
- conducting ABPM in patients with severe arrhythmias (permanent form of atrial fibrillation, frequency of extrasystoles more than 10,000 per day)
- incorrectly indicated sleep and wake times during the analysis
- lack of a detailed diary of the patient's well-being and physical activity

Typical errors in the calculation and analysis of the main indicators of ABPM:

- incorrectly set intervals of wakefulness and night sleep
- analysis of variability with a large number of unsuccessful measurements or monitoring intervals of 60 minutes or more
- calculation of variability for mean daily blood pressure
- calculation of variability by average hourly values
- use of the coefficient of variability rather than the standard deviation to describe BP variability
- use as a threshold value of 140/90 mmHg. at night
- analysis of nighttime decrease in blood pressure and its values in severe sleep disorders
- conducting ABPM to control antihypertensive therapy on an outpatient basis, using ABPM data obtained in a hospital as initial data

3.4 Stages of hypertension

Hypertension, depending on the damage to target organs and the development of associated (comorbid) conditions, goes through three stages:

stage I - the absence of objective signs of damage to target organs;

stage II - the presence of at least one of the signs of subclinical damage to target organs: left ventricular hypertrophy (ECG, echocardiography); microalbuminuria or proteinuria (30–300 mg/24 h) and/or creatinine level 1.3–1.5 mg/dl (m), 1.2–

1.4 (w); decrease in creatinine clearance (<60 ml/min); ultrasound signs of atherosclerotic plaque in the carotid artery, thickening of the intima/media >0.9 mm; pulse wave velocity >12 m/ s (carotid - femoral artery); hypertensive angiopathy.

stage III - the presence of clinical manifestations of damage to target organs: the brain (ischemic or hemorrhagic stroke, transient ischemic attack); hearts (myocardial infarction, angina pectoris, chronic heart failure); kidneys (creatinine >2 mg/dl, chronic renal failure); peripheral vessels (stratified aortic aneurysm , to a clinically pronounced lesion of peripheral arteries); retina (hemorrhages or exudates, swelling of the optic nerve papilla).

3.5 Arterial hypertension - 4 risk groups

In order to protect the heart and blood vessels from damage and not to miss the state when it is already too late, you need to know what factors the course of the disease depends on.

4 groups of risk factors:

- low risk;
- moderate;
- high;
- very tall.

To determine your risk group, you need to know the level of blood pressure and the stage of the disease.

3.6 Investigations in hypertension

In all patients with arterial hypertension, the following investigations should be performed:

- general analysis of blood and urine;
- the level of creatinine in the blood (to exclude kidney damage);
- the level of potassium in the blood outside the intake of diuretics (a sharp decrease in the level of potassium is suspicious for the presence of an adrenal tumor or renal artery stenosis);

- electrocardiogram (signs of left ventricular hypertrophy - evidence of a long course of arterial hypertension);
- determination of the level of glucose in the blood (on an empty stomach);
- serum levels of total cholesterol, high and low density lipoprotein cholesterol, triglycerides, uric acid;
- echocardiography (determination of the degree of myocardial hypertrophy of the left ventricle and the state of contractility of the heart)
- fundus examination.

Additional recommended studies:

- chest x-ray;
- Ultrasound of the kidneys and adrenal glands;
- Ultrasound of brachiocephalic and renal arteries;
- C-reactive protein in blood serum;
- analysis of urine for the presence of bacteria (bacteriuria), quantitative assessment of protein in the urine (proteinuria);
- determination of microalbumin in the urine (mandatory in the presence of diabetes mellitus).

In-Depth Research:

- Assessment of the functional state of cerebral blood flow, myocardium, kidneys;
- A study in the blood of the concentration of aldosterone, corticosteroids, renin activity;
- determination of catecholamines and their metabolites in daily urine;
- abdominal aortography;
- computed tomography or magnetic resonance imaging of the adrenal glands and brain.

Blood pressure control

Measurement of blood pressure is carried out using a special apparatus - tonometer , which is a combination of a sphygmomanometer with a

phonendoscope . In addition, at present there are special electronic devices that measure blood pressure, pulse rate, and also allow you to enter blood pressure indicators into the memory of the device.

The normal range of blood pressure in an adult is 120-140/80-90 mm Hg. Art. But some people may have lower blood pressure, at which they feel quite normal, and the seemingly "normal" numbers of 120/80 for them may mean an increase in blood pressure. In most cases, the limits of blood pressure are from 120 to 140 mm Hg. Art. are now considered "prehypertension".

Blood pressure can vary depending on age, heart condition, emotional status, physical activity, and concomitant medications a person is taking. Therefore, if an increase in blood pressure has ever been recorded, this does not mean that the patient has hypertension. It is necessary to measure blood pressure at different times, at least with an interval of 5 minutes.

Medical history

Diagnosis of hypertension also includes a survey of the patient by a doctor. The doctor finds out from the patient what diseases he previously suffered or is currently suffering from. Risk factors are assessed (smoking, high cholesterol, diabetes), plus the so-called. hereditary history, that is , whether the parents, grandparents of the patient and other close relatives suffered from hypertension.

Physical examination

Physical examination of the patient includes, first of all, the study of the heart using a phonendoscope. This method allows you to detect the presence of heart murmurs, changes in characteristic tones (amplification or, conversely, weakening), as well as the appearance of uncharacteristic sounds. These data, first of all, speak of changes occurring in the heart tissue due to increased blood pressure, as well as the presence of defects.

Electrocardiogram (ECG)

An electrocardiogram (ECG) is a method that allows you to register on a special tape the change in the electrical potentials of the heart over time. This is an

indispensable method for diagnosing, first of all, various cardiac arrhythmias. In addition, the ECG allows you to determine the so-called. hypertrophy of the wall of the left ventricle, which is typical for arterial hypertension.

Echocardiography (ECHOCG)

In addition to these diagnostic methods, other methods are used, for example, echocardiography . (ultrasound examination of the heart), which allows you to determine the presence of defects in the structure of the heart, changes in the thickness of its walls and the condition of the valves.

Arteriography

Arteriography, including aortography, is an X-ray method for examining the condition of the walls of the arteries and their lumen. This method allows you to identify the presence of atheromatous plaques in the wall of the coronary arteries (coronary angiography), the presence of coarctation of the aorta (congenital narrowing of the aorta in a certain area), etc.

dopplerography

Dopplerography is an ultrasound method for diagnosing the state of blood flow in vessels, both in arteries and veins. With arterial hypertension, first of all, the doctor checks the condition of the carotid arteries and cerebral arteries. Ultrasound is widely used for this, as it is absolutely safe to use and does not provoke complications.

Blood chemistry

A biochemical blood test is also used in the diagnosis of hypertension. First of all, it turns out the level of cholesterol and high, low and very low density lipoproteins, as they are an indicator of a tendency to atherosclerosis. In addition, the blood sugar level is determined.

In the diagnosis of hypertension, a study of the condition of the kidneys is also used, for which methods such as a general urinalysis, a biochemical blood test (for the level of creatinine and urea), as well as ultrasound of the kidneys and their vessels are used.

Thyroid ultrasound

Ultrasound of the thyroid gland and a blood test for thyroid hormones. These research methods help to identify the role of the thyroid gland in causing high blood pressure.

Additional data revealed during the examination of patients with hypertension: If the ECG revealed the following changes: **Hypokalemia: there** is a downward shift of the ST segment, merging with the negative phase of the T wave , the appearance of a U wave in the chest leads, which often overlaps with the T wave, as if prolonging the electrical systole QRS-T (QU) and sometimes prolongation of the PQ interval. Pronounced signs of hypokalemia in patients with elevated blood pressure (if diuretics have not been taken for a long time) makes one think about the presence of **primary hyperaldosteronism.**

3.7 CLINIC GB

1. **Headache is often the first, and with further progression of the disease, one of the main subjective signs of GB.**

- "typical" headache.
- "liquor" headache.
- ischemic headache.
- "muscular" headache.

"typical" headache

Most patients with GB are characterized by headache, which often occurs at night or early in the morning, after waking up (the patient wakes up with a headache). The pain is usually not very intense and is felt by patients as heaviness or fullness in the back of the head, in the forehead or throughout the head ("dull" headache).

The described nature of the so-called typical headaches is mainly due to a decrease in the tone of the intracranial veins and a violation of the outflow of blood from the cranial cavity. As a result, the veins expand and overflow with blood, and functional venous intracranial hypertension develops. The immediate

cause of pain in these cases is irritation of sensory receptors (nociceptors) of distended intracranial veins.

"liquor" headache

Another type of headache is observed, as a rule, in the later stages of AH, including in persons with a malignant form of AH or during a hypertensive crisis, and is associated with an increase in intracranial pressure. In these cases, patients complain of a diffuse arching headache ("the head seems to be filled with lead"). The slightest tension (straining, coughing, changing the position of the head and body) increases the pain. Sometimes the pain becomes pulsating.

Such a headache usually occurs with a rapid and significant increase in blood pressure, which is accompanied by a deep discirculation of the local (cerebral) circulation. In addition to a decrease in the tone of the intracranial veins, in these cases, as a rule, there is insufficient compensatory spasm of the cerebral arteries. Recall that normally, with transient rises in blood pressure, such a spasm of the cerebral arteries usually protects the cerebral capillary bed from excessive blood overflow (Beilis phenomenon).

In hypertensive patients, during a rapid and significant rise in blood pressure , the described compensatory mechanism does not work completely, and the arteries are in a state of relative hypotension.

As a result, the capillary bed of the cerebral circulation is overfilled with blood, and this overflow is often of a pulsating nature. Since at the same time there is a significant violation of the venous outflow, intracranial pressure rises and irritation of the sensitive endings of the membranes of the brain, vessels and nerves inside the skull occurs, which is the direct cause of throbbing headaches. In severe cases, swelling of the brain is observed.

"ischemic" headache

The third type of headache occurs in some patients with a rapid and sharp increase in blood pressure (for example, in a hypertensive crisis) as a result of an excessively pronounced local spasm of the cerebral arteries that occurs in response to a significant increase in blood pressure. In these cases, headaches are accompanied by general cerebral and focal neurological symptoms caused by a

decrease in intracerebral blood flow and cerebral ischemia. There is a feeling of pressure, bursting or dull headache, accompanied by nausea, non-systemic dizziness, flashing "flies" before the eyes.

"muscle" headache

The possibility of another type of headache in HD patients that is of non-vascular origin should be kept in mind. Muscular headache is caused by tension in the muscles of the soft integuments of the head. Pain occurs, as a rule, against the background of pronounced psycho-emotional or physical stress and subsides after rest and resolution of conflict situations.

Pain of muscular origin is characterized by slow onset and slow regression. Characteristic is the feeling of compression or constriction of the head with a bandage or hoop

2. Shortness of breath a- first during physical exertion, and then at rest, this indicates the development of left ventricular failure.

3. Edema - swelling on the legs up to anasarca.

4. Dizuri - violation of urination up to anuria.

5. Visual impairment

6. Pain in the region of the heart

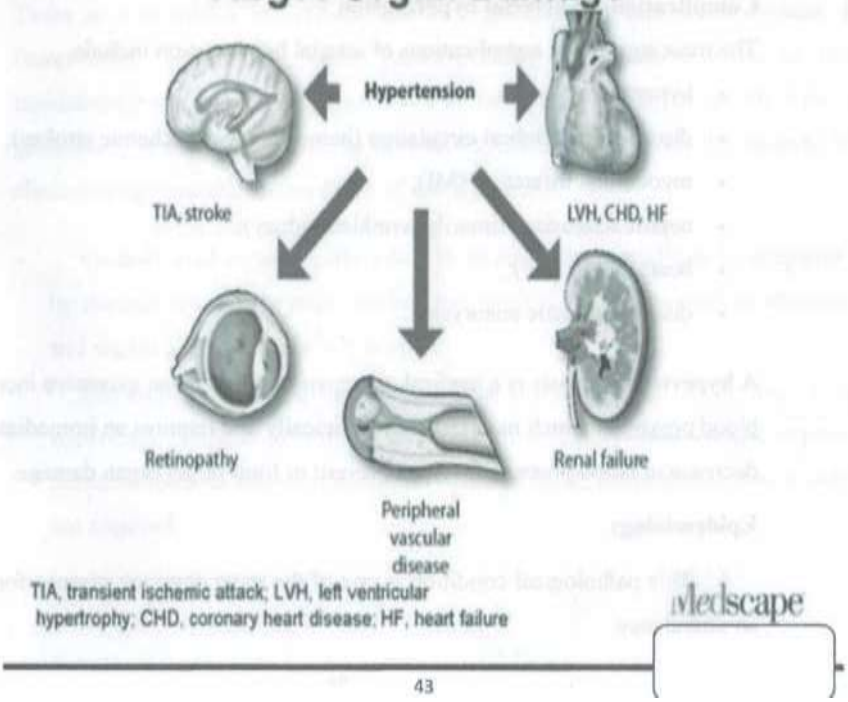
Chapter 4

Complications and differential diagnosis of arterial hypertension

4.1 Complications of arterial hypertension

High blood pressure requires mandatory treatment, because over time, excessive force acting on the arterial walls can lead to serious damage to many vital organs of the body. Arteries, heart, brain, kidneys and eyes are most affected by high blood pressure.

Some of the complications described below may require emergency treatment.



Risk factors for cardiovascular complications in arterial hypertension

Main:

- men over 55;
- women over 65;
- total blood cholesterol > 6.5 mmol/l, elevated low-density lipoprotein cholesterol (> 4.0 mmol/l) and low high-density lipoprotein cholesterol;
- family history of early cardiovascular disease (women < 65 years, men < 55 years) ;
- abdominal obesity (waist ≥102 cm for men or ≥ 88 cm for women);
- level of C - reactive protein in the blood ≥1 mg / dl;
- diabetes mellitus (fasting blood glucose> 7 mmol / l).

Additional:

- impaired glucose tolerance;
- low physical activity;
- an increase in fibrinogen levels.

Complications of arterial hypertension

The most significant complications of arterial hypertension include:

- hypertensive crises;
- disorders of cerebral circulation (hemorrhagic or ischemic strokes);
- myocardial infarction (MI);
- nephrosclerosis (primarily wrinkled kidney);
- heart failure (HF);
- dissecting aortic aneurysm

A hypertensive crisis is a medical emergency caused by an excessive increase in blood pressure , which manifests itself clinically and requires an immediate decrease in blood pressure levels to prevent or limit target organ damage.

Epidemiology

This pathological condition is one of the most common reasons for calling an ambulance.

In Western European countries, there is a decrease in the incidence of hypertensive crises in patients with arterial hypertension - from 7% to 1% (as of 2004). This is due to improved treatment of arterial hypertension [1] and an increase in the frequency of timely diagnosis of the disease.

In Russia, the situation remained at an unsatisfactory level: according to data for 2000, only 58% of sick women and 37.1% of men knew about the presence of the disease, despite the fact that the prevalence of the disease among the population was 39.2% in men, 41 in women, one%. Only 45.7% of women and 21.6% of men received medical treatment [1].

Thus, only about 20% of patients with arterial hypertension received medical treatment of varying degrees of adequacy. In this regard, the absolute number of hypertensive crises naturally increases.

In the CIS countries, there is currently no single generally accepted classification of hypertensive crises.

In the USA, Canada, the concept of "hypertensive crisis" does not exist. There is a definition of "critical arterial hypertension", that is, in essence, a complicated hypertensive crisis (uncomplicated hypertensive crisis is not considered there, since it is characterized by low mortality). In the world, in most guidelines, preference is given to clinical classification based on the severity of clinical symptoms and the presence of complications.

- **Complicated hypertensive crisis** is an emergency condition accompanied by damage to target organs; can be fatal, require immediate medical attention and urgent hospitalization in a hospital.
- **Uncomplicated hypertensive crisis** is a condition in which there is a significant increase in blood pressure with relatively intact target organs. Requires medical attention within 24 hours of onset; hospitalization is usually not required.

PATHOGENESIS

In the development of a hypertensive crisis, an important role is played by the ratio of the total peripheral vascular resistance to the value of cardiac output. As a result of violations of vascular regulation, spasm of arterioles occurs, resulting in an increase in heart rate, a vicious circle develops and a sharp rise in blood pressure occurs, and due to spasm, many organs are in a state of hypoxia, which can lead to the development of ischemic complications.

It has been proven that during a hypertensive crisis, hyperactivity of the renin-angiotensin system is observed, which leads to a vicious circle that includes vascular damage, an increase in ischemia and, as a result, an increase in renin production. It was found that a decrease in the content of vasodilators in the blood leads to an increase in the total peripheral vascular resistance. As a result, fibrinoid necrosis of arterioles develops and vascular permeability increases. The presence and severity of the pathology of the blood coagulation system is extremely important in determining the prognosis and associated complications.

CLINIC

Hypertensive crisis is the result of a sharp violation of the mechanisms of regulation of blood pressure, which, in turn, leads to a strong increase in blood pressure and a disorder of blood circulation in the internal organs. During a hypertensive crisis, symptoms of impaired blood supply to the brain and heart are observed. Patients have the following complaints and symptoms:

- A sharp and often unusually significant increase in blood pressure (in usually normotensive and hypotensive patients with a hypertensive crisis, the pressure may not reach significant values)
- Loss of performance, fatigue
- Redness of the face, chest
- "Mushki", flickering before the eyes

- Insomnia, anxiety, fear
- Headaches, especially in the back of the head
- Noise, ringing, tinnitus, deafness
- Dyspnea
- Chest pain
- Neurological disorders, dizziness, confusion

A hypertensive crisis can be complicated (life-threatening), when in order to save life, medical care must be sought to be provided within an hour, uncomplicated (up to 24 hours). With malignant hypertension, a patient's life can be saved even with a longer delay. But it is better to start treatment as soon as possible in all cases, since target organ damage depends on the time before the start of treatment and occurs in all crises and in malignant hypertension.

A hypertensive crisis is always considered complicated in the following cases:

- hypertensive encephalopathy ;
- acute violation of cerebral circulation ;
- acute coronary syndrome ;
- acute left ventricular failure;
- dissecting aortic aneurysm ;
- pheochromocytoma ;
- GC against the background of taking amphetamines , cocaine , etc.
- preeclampsia and eclampsia ;
- severe hypertension associated with subarachnoid hemorrhage or brain injury;
- AH in postoperative patients and with the threat of bleeding.

A hypertensive crisis is dangerous for patients both without and with pre-existing diseases of the heart and brain. Hypertensive crises occur in patients with pheochromocytoma (including against the background of hypotension) and often in patients with essential hypertension (hypertension) periodically. Adrenergic (catecholamine) crises similar to pheochromocytoma crises are observed with the

use of cocaine, amphetamines, an overdose of ephedrine and norepinephrine , with the abolition of clonidine or methyldopa, often after severe burns, such autonomic crises occur with somatoform autonomic dysfunction of the heart and cardiovascular system. Those who have undergone a hypertensive crisis have a tendency to relapse. Hypertension and pheochromocytoma can also be combined with other arterial hypertension. Malignant hypertension can be a complication of any arterial hypertension. In case of complicated hypertensive crises (*hypertensive emergency*), medical care must be provided within several tens of minutes (in extreme cases, up to an hour), with exfoliating aortic aneurysm - a few minutes. It is necessary to differentiate hypertensive crises with other similar conditions accompanied by an increase in blood pressure - preeclampsia (occurs only in pregnant women), eclampsia (a complication of preeclampsia, including undiagnosed, can also be during and after childbirth), autonomic crisis with somatoform heart dysfunction and cardiovascular system, panic attack in panic disorder , generalized anxiety disorder, obsessive compulsive disorder, phobias, post-traumatic stress syndrome, headaches (especially hypertension headaches and migraines), angina attacks, renal colic, nephroptosis (may be due to enteroptosis) , thyrotoxic crises, erythremic crises, the onset of malignant arterial hypertension, exacerbation of chronic kidney disease, etc. These conditions can also be combined with a hypertensive crisis. A hypertensive crisis may be the first manifestation of previously undiagnosed arterial hypertension.

Treatment of a hypertensive crisis begins with an installation for the patient to rest and an accurate measurement of pressure. When providing first aid (not conventional first aid) and in a medical facility, according to indications (taking into account the absolute and relative contraindications of each drug), enalaprilat is administered parenterally (especially indicated for left ventricular failure of the myocardium, with malignant hypertension without renal artery stenosis, with crises with high plasma renin activity, but contraindicated for emergency care for myocardial infarction, since ACE inhibitors cannot be administered intravenously on the first day after a heart attack), nitroglycerin (with acute coronary syndrome and acute left ventricular failure); sodium nitroprusside (is the drug of choice for

hypertensive encephalopathy, but it should be borne in mind that it can increase intracranial pressure and cause azotemia), beta-blockers

(metoprolol , esmolol Esmolol) are preferred for dissecting aortic aneurysm and acute coronary syndrome, as well as for high plasma renin activity and contraindications for enalaprilat); antiadrenergics (phentolamine for suspected pheochromocytoma); diuretics (furosemide for acute left ventricular failure); antipsychotics (droperidol); hydralazine, labetalol for pre-eclampsia and eclampsia, magnesium sulfate (slowly with a live fetus and stopped at least two hours before delivery of a live baby) for eclampsia; ganglion blockers pentamine , for example, in particular, if beta-blockers are usually prescribed for such a crisis, and this patient has chronic obstructive pulmonary disease. For the treatment of hypertensive crisis with pheochromocytoma, alpha-blockers are used (phentolamine , 5-10 mg intravenously or intramuscularly, followed by an infusion of 2-3.5 mcg / kg / min). After the elimination of hypertension in the presence of severe tachycardia and (or) cardiac arrhythmias, beta-blockers are prescribed . As prescribed by the doctor, for the relief of repeated and subsequent uncomplicated hypertensive crises, the patient uses captopril , less often labetalol , prazosin , with systolic blood pressure of more than 200 mm Hg. Art. - clonidine sublingually or orally. The sublingual agents prescribed by the doctor should be carried by the patient prone to crises. With the availability of medical care in a hospital, intravenous administration of enalaprilat , labetalol , prazosin , nifedipine is possible .

Complications of a hypertensive crisis: retinopathy , edema of the optic nerve papilla, visual impairment and loss, arrhythmic heart disease, heart failure , myocardial infarction , disseminated intravascular coagulation syndrome (DIC), hemolytic anemia, acute cerebrovascular accident , pulmonary edema , cerebral edema , kidney failure , lethal outcome .

During a hypertensive crisis, symptoms of impaired blood supply to organs and systems, most often the brain and heart, are observed:

- Of systolic blood pressure above 200 mmHg]

- Headache.
- Dyspnea.
- Pain in the chest.
- Neurological disorders: vomiting, convulsions, impaired consciousness, in some cases clouding of consciousness, strokes and paralysis.

A hypertensive crisis can be fatal.

A hypertensive crisis can be especially dangerous for patients with pre-existing diseases of the heart and brain.

The prognosis in the case of a complicated crisis is unfavorable. 1% of patients suffering from chronic arterial hypertension suffer from hypertensive crises. Once developed, a crisis tends to relapse.

Mortality within 90 days after discharge from the hospital among patients with hypertensive crisis is 8%. 40% of patients within 90 days after discharge from the hospital due to a hypertensive crisis are again admitted to the intensive care unit. If uncontrolled arterial hypertension is accompanied by 2% mortality in 4 years, then in patients against the background of uncontrolled arterial hypertension with crises, 17% mortality is accompanied by 4 years.

ARTERIOSCLEROSIS . Healthy arteries, like healthy muscles, must be flexible, strong and elastic. Their walls are smooth from the inside, not creating obstacles to blood flow. However, over the years, under the influence of high blood pressure, they can become thicker and more rigid . Under the influence of high blood pressure, the deposition of cholesterol within the arterial wall and between its layers can be accelerated. If the wall of an artery is damaged from the inside, blood cells called platelets settle in this place. Cholesterol also tends to be deposited in a certain area of the wall. Initially, the deposition of cholesterol is only a layer of fat-containing cells. As cholesterol accumulates, the process spreads to the deep layers of the arterial wall, causing damage to it. Large deposits of cholesterol are called plaque. Over time, the plaque becomes harder. The greatest danger of cholesterol plaques is damage to the vascular wall. The

organs and tissues supplied by such altered arteries do not receive enough oxygen and nutrients brought in by the blood. To ensure adequate blood flow, the body responds by increasing blood pressure. In turn, this leads to further damage to the vessels . And arteriosclerosis and atherosclerosis can develop in any arteries of the body. However, the arteries of the heart, brain, kidneys, abdominal aorta, and legs are most commonly affected.

ISCHEMIC HEART DISEASE . One of the main causes of death in patients with untreated arterial hypertension is coronary heart disease.

This disease affects the arteries that feed the heart muscle (coronary arteries). In patients with high blood pressure, the formation of cholesterol plaques in the coronary arteries is a common phenomenon.

Plaques reduce blood flow to the heart muscle, which can lead to a myocardial infarction if the volume of inflowing blood drops to a critical level. This condition requires immediate hospitalization for medical treatment or transluminal balloon angioplasty, a surgical procedure to relieve narrowing of the coronary arteries. Normalization of blood pressure leads to a decrease in the number of myocardial infarctions by about 25 percent.

ANEURYSM . When blood vessels lose their elasticity, their walls can stretch and thin. Such a place in an artery is called an aneurysm. Aneurysms most often form in the arteries of the brain and in the lower part of the aorta, at the level of the abdomen. The biggest danger of any aneurysm is that it ruptures, resulting in life-threatening bleeding.

In the early stages of aneurysm formation, as a rule, they do not affect well-being. As the aneurysm grows, being in the artery of the brain, it can cause very severe headaches that do not go away. A large abdominal aortic aneurysm can cause persistent pain in the abdomen or lower back. Rarely, an abdominal aortic aneurysm is discovered on physical examination, when gentle pressure on the abdomen reveals a pulsatile vessel. Sometimes a thrombus lining the cavity of the aneurysm can come off and block the branches extending from the aorta.

HEART FAILURE . In this condition, the heart is not able to pass the blood flowing to it quickly enough. As a result, blood stasis occurs, which causes fluid to accumulate in the lungs, lower extremities, and other tissues. This condition is called edema. Stagnation of blood in the lungs leads to shortness of breath. The accumulation of fluid in the lower extremities leads to swelling of the feet and ankles. With effective treatment of hypertension, the risk of developing heart failure is reduced by about 50 percent.

BRAIN.

Arterial hypertension significantly increases the risk of STROKE.

Strokes most often occur against the background of high blood pressure. However, people who have received medical treatment for high blood pressure have a reduced risk of stroke.

A stroke, or acute cerebrovascular accident, is damage to brain tissue that occurs either due to occlusion of the lumen or due to rupture of an artery supplying the brain. According to these reasons, there are two main types of strokes: *ischemic* and *hemorrhagic* .

Ischemic stroke . Ischemic strokes account for 70-80 percent of all strokes. Ischemic stroke usually affects the parts of the brain that control movement, speech, and the senses.

A stroke develops as a result of thrombosis of an artery supplying the brain. The likelihood of thrombus formation increases in the presence of a cholesterol plaque, since the surface of the plaque facing the lumen of the vessel is uneven, and the blood flow in this place is disturbed. More than half of ischemic strokes are due to the formation of a blood clot in one of the arteries extending from the aorta and supplying the brain.

A less common cause of ischemic strokes is the detachment of a piece of blood clot formed in an artery and the movement of this piece (embolus) through larger arteries into smaller arteries in the brain. The source of emboli can also be a thrombus located in the chambers of the heart. If a moving clot stops in a small-

diameter artery and completely blocks blood flow, then a stroke develops in the corresponding part of the brain.

Sometimes cerebral blood flow is disturbed for a short time - less than 24 hours. This condition is called a **transient ischemic attack (TIA)** or minor stroke. A transient ischemic attack is a warning sign that a stroke may develop.

Hemorrhagic stroke . Hemorrhagic stroke develops as a result of a rupture of the wall of a cerebral artery. In this case, the blood impregnates the surrounding brain tissue, which causes damage to them. Brain cells located at a distance from the source of bleeding are also damaged, as they are deprived of the influx of fresh arterial blood. One of the causes of hemorrhagic stroke is arterial aneurysm. Small tears in the arterial wall can also lead to leakage of blood into the surrounding tissues.

Normalization of blood pressure figures due to effective treatment is accompanied by a significant reduction in risk. Even if you've already had a stroke or a transient ischemic attack, lowering your high blood pressure will help prevent it from happening again.

DEMENTIA .

Dementia is acquired dementia. Scientific studies show that high blood pressure can lead to memory impairment and other mental impairments over time. The risk of dementia increases significantly at age 70 and older. From the moment of diagnosis of arterial hypertension to the appearance of signs of dementia, it can take from several decades to several years.

It has now been proven that medical control of high blood pressure can reduce the risk of dementia.

KIDNEYS

About one fifth of the volume of blood pumped out by the heart passes through the kidneys. The tiny structures of the kidneys that act as filters are called nephrons. With their help, the blood is cleansed of the metabolic products of our body, which are then excreted in the urine. The function of the kidneys is to control the balance of salts, acids and water in the body. Except

To this end, substances are synthesized in the kidneys that regulate the diameter of blood vessels and their function. High blood pressure can interfere with this complex process.

If atherosclerosis develops due to arterial hypertension in the arteries supplying the kidneys (renal arteries), blood flow to the nephrons decreases, the efficiency of removing waste products from the blood decreases. Over time, the concentration of these products in the blood increases, the kidneys begin to "shrink" and lose their functions.

High blood pressure and diabetes are the most common causes of kidney failure.

If the kidneys are ineffective, hemodialysis or even a kidney transplant may be required. Hemodialysis is the process of removing metabolic products from the blood using special equipment.

Damage to the kidneys can cause or worsen hypertension because the kidneys are involved in controlling blood pressure by regulating the amount of sodium and water in the blood. This situation is a vicious "vicious" circle, which ultimately leads to an increase in blood pressure and a gradual decrease in the ability of the kidneys to remove metabolic products from the body.

Normalizing high blood pressure can slow the progression of kidney disease and reduce the need for hemodialysis and kidney transplantation.

EYES.

High blood pressure leads to accelerated aging of the tiny blood vessels in the eye. In severe cases, it can even lead to loss of vision.

Sometimes the presence of arterial hypertension is detected by a simple examination of the fundus. Directed into the eye, light makes visible the thin arteries located on the inner surface of the eye (the retina). Already in the early stages of arterial hypertension, the walls of these arteries begin to thicken and

their lumen narrows. The arteries of the eye can compress nearby veins and interfere with venous outflow. It is believed that the state of the arteries of the fundus reflects the state of the vessels of the brain.

High blood pressure can also rupture the walls of the arteries and bleed into the underlying tissues of the eye. In severe cases, swelling of the optic nerve, which transmits visual signals from the retina to the brain, may develop. This can cause vision loss. Retinal damage can in most cases be prevented by controlling blood pressure levels.

4.2 DIFFERENTIAL DIAGNOSIS OF GB:

The diagnosis of hypertension should only be made by ruling out secondary symptomatic hypertension. But this is often a very difficult task. Persons with secondary hypertension account for about 10%, and in the age group under 35 years - 25%.

Diagnosis of true hypertension is carried out by excluding secondary arterial hypertension. High blood pressure syndrome is represented by several groups of diseases.

Renal hypertension - anomalies in the structure of the kidneys and their vessels. Chronic diffuse glomerulonephritis, atherosclerosis, thrombosis, renal artery embolism.

a) In chronic diffuse glomerulonephritis; in the anamnesis, there is often an indication of renal pathology, from the very beginning there are at least minimal changes in the urine - slight hemauria, proteinuria, cylindruria. With GB, such changes occur only in advanced stages. BP is stable , may not be particularly high, crises are rare. A kidney biopsy helps.

b) In chronic pyelonephritis: a disease of a bacterial nature, there are signs of infection. Dysuric disorders. In history - an indication of acute inflammation with chills, fever, back pain, sometimes renal colic. With pyelonephritis, the concentration function of the kidneys suffers (but only with 2-sided damage), early thirst and polyuria occur. Often positive s-m tapping on the lower back. In

the analysis of urine leukocyturia, slight or moderate proteinuria. Nechiporenko test - the number of leukocytes in 1 ml of urine; normal - up to 4000. Urine culture is of some importance - a large number of colonies are detected. There may be bacteriuria. Urine must be sown repeatedly, because. outside of an exacerbation, the number of colonies may be small, but they are constant (a sign of the permanence of colonies). When setting up the Zimnitsky test: hypo and isosthenuria. Sometimes, when bacteriuria is detected, provocative tests are resorted to: pyrogenacle or a test with IV prednisolone , then a Nechiporenko test is performed. With pyelonephritis there is a latent leukocyturia. Pyelonephritis, even 2- sided , is always asymmetrical, which is detected by radioisotope renography (separate kidney function is determined). The main diagnostic method is excretory urography, which determines the deformation of the pelvicalyceal apparatus, and not just dysfunction.

c) Polycystic kidney can also cause an increase in blood pressure. This is a congenital disease, so often an indication of the family nature of the pathology. Polycystic often occurs with an increase in the size of the kidneys, which are clearly palpable, the concentration function of the kidneys is disturbed early, early thirst and polyuria. The method of excretory urography helps.

Vasorenal hypertension. Associated with damage to the renal arteries, narrowing of their lumen. Causes: in men, often as an age-related atherosclerotic process, in women more often as fibromuscular dysplasia - a kind of isolated lesion of the renal arteries of unclear etiology. Often occurs in young women after pregnancy. Sometimes the cause is thrombosis or thromboembolism of the renal arteries (after surgery, with atherosclerosis).

Pathogenesis: As a result of the narrowing of the vascular process, changes in the kidneys occur, microcirculation decreases, the renin-angiotensin system is activated, and the aldosterone mechanism is activated for the second time.

Signs: rapidly progressive high stable hypertension, often with a malignant course (high renin activity). vascular murmur over the projection of the renal artery: on the anterior abdominal wall just above the navel, in the lumbar region. Noise is heard better on an empty stomach.

Additional research methods:

The function of the ischemic kidney suffers, the other kidney compensatory increases in size. Therefore, an informative method for a separate study of the kidneys is radioisotope renography, in which the vascular part of the segment is reduced, the curve is stretched + asymmetry.

Excretory urography - the contrast agent enters the ischemic kidney more slowly (slowdown in the first minutes of the study) and is more slowly excreted (in the last minutes of the delay of the contrast agent). Described as late arrival and late hyperconcentration - that is, contrasting asynchronism takes place - a sign of asymmetry.

When scanning, the diseased kidney is reduced in size due to wrinkling and is poorly defined, the healthy kidney is compensatory enlarged.

Aortography is the most informative method, but, unfortunately, unsafe, therefore it is used last

Vessel plasty leads to a complete cure. But early surgery is important, before irreversible changes in the kidney occur. It must also be remembered that there is a functional stenosis.

Nephroptosis occurs due to pathological mobility of the kidney.

The pathogenesis of hypertension consists of 3 moments: tension and narrowing of the renal artery ---> kidney ischemia ---> vasospasm ---> hypertension; violation of the outflow of urine through a stiffened, sometimes twisted, with bends ureter, the attachment of an infection ---> pyelonephritis, irritation of the sympathetic nerve in the vascular pedicle ---> spasm.

Signs: more often at a young age, hypertension with crises, severe headaches, severe autonomic disorders, but in general, hypertension is labile; in the supine position, blood pressure decreases. For diagnosis, aortography and excretory urography are mainly used. Surgical treatment: fixation of the kidney. From other hypertension of renal origin: with amyloidosis, hypernephron, diabetic glomerulosclerosis. Hypertension due to damage to the heart and large blood

vessels. Hemodynamic arterial hypertension is associated with a primary lesion of large main vessels.

a) Coarctation of the aorta is a congenital disease associated with a thickening of the muscular layer in the region of the isthmus of the aorta. There is a redistribution of blood - the vessels are sharply overflowing with blood up to or above the constriction, i.e. vessels of the upper half of the body; the vessels of the lower extremities, on the contrary, receive little and slowly blood. The main symptoms of the disease appear by puberty, usually by the age of 18. Headaches, a feeling of heat or a flush to the head, nosebleeds are subjectively noted.

Obectivno:

Disproportion; powerful upper half of the body and poorly developed lower; hyperemic face; the pulse on the radial artery is full, tense; cold feet, weakened pulse in the legs; to the left of the sternum, a rough systolic murmur; the apical impulse is sharply increased; BP on the brachial artery is high, on the legs - low; patterns of ribs on the radiograph; the main diagnostic method is aortography.

With timely diagnosis, treatment leads to a complete recovery. If left untreated, nephrosclerosis appears after about 30 years.

b) Pulseless disease, or Takayashi's syndrome. Synonyms: panaortitis, panarteritis of the aorta and its branches, disease of the aortic arch. A disease of an infectious-allergic nature, most often found in young women. There is a proliferative inflammation of the walls of the aorta, mostly intima, as a result of necrosis, plaques are formed, and fibrinoid swelling occurs. She has a history of prolonged subfibrillation, resembling a feverish state, and allergic reactions.

Ischemic syndrome appears in the vessels of the extremities and the brain, which is manifested by fainting, dizziness, loss of vision, short-term loss of consciousness, weakness in the hands. Arterial hypertension is detected as a result of redistribution of blood. This disease is also called reverse coarctation. On the hands, the pressure is lowered, and asymmetrically, and on the legs, the pressure

is greater. Further, vasorenal or ischemic hypertension, which is malignant, joins. A renal shunt appears.

Diagnosis: the use of the aortography method is mandatory, the ESR is often increased, the content of gamma globulin is high , a test with aortic antigen (UANE) is proposed.

Endocrine hypertension:

a) Itsenko-Cushing's syndrome is associated with damage to the cortical layer of the adrenal glands, the production of glucocorticoids sharply increases. A typical appearance of patients is characteristic: a moon-shaped face, redistribution of fatty tissue.

b) Pheochromocytoma: this is a tumor of mature cells of the chromophinous tissue of the medulla, less often a tumor of the paraganglia of the aorta, sympathetic ganglions and plexuses. Chromophine tissue produces epinephrine and norepinephrine. Usually, with pheochromocytoma, catecholamines are released into the bloodstream periodically, which is the reason for the occurrence of catecholamine crises. Clinically, pheochromocytoma can occur in two ways:

1. Crisis arterial hypertension.

2. Permanent arterial hypertension. Blood pressure rises suddenly, within a few minutes over 300 mm Hg. Accompanied by pronounced vegetative manifestations of the "storm": palpitations, trembling, sweating, fear, anxiety, skin manifestations. Catecholamines actively interfere with carbohydrate metabolism - the blood sugar level rises, so thirst is observed during a crisis, and after polyuria. There is also a tendency to an orthostatic drop in blood pressure, which is manifested by loss of consciousness when trying to change the horizontal position to a vertical one (hypotension in orthostasis). With pheochromocytoma, a decrease in body weight is also observed, which is associated with an increase in basal metabolism.

Diagnostics:

Hyperglycemia and leukocytosis during a crisis; hypertrophy and dilatation of the left ventricle develop early; there may be tachycardia, changes in the fundus; the main diagnostic method: determination of catecholamines and their metabolic

products; vanilmandelic acid, with pheochromocytoma its content exceeds 3.5 mg / day, the content of adrenaline and norepinephrine exceeds 100 mg / day in the urine;

- test with alpha-blockers: phentolamine (Regitin) 0.5% - 1 ml IV or IM or tropafen 1% - 1 ml IV or IM. These drugs have an antiadrenergic effect, block the transmission of adrenergic vasoconstrictor impulses. The decrease in systolic pressure is more than 80 mm Hg, and diastolic pressure by 60 mm Hg. 1-1.5 minutes after the administration of the drug indicates the sympathetic-adrenal nature of hypertension, and the test for pheochromocytoma is considered positive. The same drugs (phentolamine and tropafen) are used to relieve catecholamine crises.

- provocative test: histamine dihydrochloride 0.1%, 25-0.5 ml is injected intravenously (histamine is produced in 0.1% - 1 ml). Pheochromocytoma is characterized by an increase in blood pressure by 4O/25 mm Hg. and more 1-5 minutes after the injection. The test is indicated only if the blood pressure without seizures does not exceed 170 / 110 mm Hg. At a higher pressure, a test is carried out only with phentolamine or tropafen. In about 10% of cases, a histamine test may be positive even in the absence of pheochromocytoma. The mechanism of action of histamine is based on reflex excitation of the adrenal medulla.

- resacral oxysuprarenography (oxygen is injected into the perirenal space and a series of tomograms is made).

- pressure during palpation in the kidney area can lead to the release of catecholamines from the tumor into the blood and be accompanied by an increase in blood pressure.

- also helps to study the vessels of the fundus and ECG.

c) Kohn's syndrome or primary hyperaldosteronism. This disease is associated with the presence of an adenoma or a benign tumor, rarely carcinoma, as well as with 2-sided hyperplasia of the glomerular zone of the adrenal cortex, where aldosterone is produced. The disease is associated with an increased intake of aldosterone into the body, which enhances tubular reabsorption of sodium, resulting in the replacement of intracellular potassium with sodium, with the

distribution of potassium and sodium leads to the accumulation of sodium, followed by water intracellularly, including in the vascular wall, which narrows the lumen of blood vessels and leads to an increase in blood pressure. An increase in the content of sodium and water in the wall of blood vessels leads to an increase in sensitivity to humoral pressor substances, resulting in arterial hypertension of the diastolic type. A feature of hypertension is stability and a steady increase, stability, lack of response to conventional antihypertensive drugs (except for veroshpiron, an aldosterone antagonist).

The second group of symptoms is associated with excessive excretion of potassium from the body, therefore, in the clinical picture there will be signs of severe hypokalemia, manifested primarily by muscle disorders: muscle weakness, adynamia, parasthesia, there may be paresis and even functional muscle paralysis, as well as changes in the cardiovascular vascular system: tachycardia, extrasystole and other rhythm disturbances. On the ECG, the lengthening of the electrical systole, an increase in the ST interval, sometimes a pathological U wave appears. Cohn's syndrome is also called "dry hyperaldosteronism", because. with it there are no visible edema.

Diagnostics:

- a blood test for potassium and sodium: the potassium concentration falls below 3.5 mmol / l, the sodium concentration increases above 130 mmol / l, the potassium content in the urine is increased, and the sodium content is reduced; - Urine catecholamines are increased (see above); urine reaction is usually neutral or alkaline; a test with hypothiazide is of some importance: first, the content of potassium in the blood serum is determined, then the patient receives hypothiazide at 100 mg / day for 3-5 days. Further, blood potassium is examined again - in patients with Kohn's syndrome, there is a sharp drop in the concentration of potassium, in contrast to healthy ones;

- test with veroshpiron - an aldosterone antagonist, which is prescribed at 400 mg / day. This leads to a decrease in blood pressure after a week, and potassium in the blood rises;

- determination of aldosterone in the urine (the method is not clearly established);

- determination of renin, with primary hyperaldosteronism, the activity of the juxtaglomerular apparatus of the kidneys is sharply inhibited, little renin is produced;

- X-ray: tomography of the adrenal glands, but only a tumor weighing more than 2 g is detected;

if the tumor is small: exploratory laparotomy with revision of the adrenal glands.

If the disease is not diagnosed in time, kidney disease joins - nephrosclerosis, pyelonephritis. There is thirst and polyuria.

d) Acromegaly. Blood pressure rises due to the activation of the function of the adrenal cortex.

e) Kimmelstiel-Wilson syndrome: diabetic glomerulosclerosis in diabetes mellitus.

f) Thyrotoxicosis: there is an increased excretion of calcium through the kidneys, which contributes to the formation of stones and ultimately leads to an increase in blood pressure.

g) Hyperreninoma - a tumor of the juxtaglomerular apparatus - but this is more of a casuistry.

h) Contraceptive arterial hypertension, when using hormonal contraceptive drugs.

Pulmonogenic hypertension

Medicinal arterial hypertension:

a) When using adrenergic drugs: ephedrine, adrenaline.

b) With long-term treatment with hormonal agents (glucocorticoids).

c) When using drugs that have a damaging effect on the kidneys (phenacetin).

d) From taking hormonal contraceptives.

Chapter 5

Treatment and prevention of hypertension

5.1. How to control blood pressure .

On the way to the normalization of blood pressure, changing habits and lifestyle is of no small importance. Simple rules for a healthy diet, regular physical activity, and smoking cessation can significantly lower blood pressure levels. Sometimes, in the initial stages of the disease, these conditions are enough to maintain blood pressure within normal limits.

Unfortunately, drug therapy is often required in addition to the general rules. Therapy for arterial hypertension is selected individually and serves to prevent rises in blood pressure. Drugs should be taken daily (usually 1-2 times a day). Rarely, one drug is effective - more often, a combination of two, and sometimes three types of drugs is required. Such combinations (which are often included in one tablet) allow you to achieve the desired effect with the minimum dosage of each of the components.

If blood pressure still rises above normal values, there are drugs for quick help - they help to quickly and effectively reduce blood pressure "here and now". Such emergency receptions in hypertensive patients should be as small as possible - daily planned antihypertensive therapy should be selected as efficiently as possible .

It should be remembered that arterial hypertension is a chronic disease from which it is impossible to cure forever, therefore, normal blood pressure figures require PERMANENT medication

5.2. Treatment of arterial hypertension

The main goal of treating patients with arterial hypertension is to minimize the risk of developing cardiovascular complications and death from them. This is achieved through long-term, lifelong therapy aimed at :

- lowering blood pressure to normal levels (below 140/90 mm Hg). When arterial hypertension is combined with diabetes mellitus or kidney damage, a decrease in blood pressure < 130/80 mm Hg is recommended. (but not lower than 110/70 mm Hg);
- "protection" of target organs (brain, heart, kidneys), preventing their further damage;
- active influence on adverse risk factors (obesity, hyperlipidemia, carbohydrate metabolism disorders, excessive salt intake, physical inactivity) that contribute to the progression of arterial hypertension and the development of its complications.

Indications for hospitalization of patients with arterial hypertension are:

- Uncertainty of the diagnosis and the need for special, often invasive, research methods to clarify the form of arterial hypertension;
- Difficulties in the selection of drug therapy - frequent hypertensive crises, refractory arterial hypertension.

Indications for emergency hospitalization:

- Hypertensive crisis that does not stop at the prehospital stage;
- Hypertensive crisis with severe manifestations of hypertensive encephalopathy (nausea, vomiting, confusion);
- Complications of hypertension requiring intensive care and constant medical supervision: cerebral stroke, subarachnoid hemorrhage, acute visual impairment, pulmonary edema, etc.

Non-drug treatment of arterial hypertension

- to give up smoking;
- normalization of body weight a (body mass index < 25 kg/m2);
- reduced consumption of alcoholic beverages < 30 g of alcohol per day in men and 20 g per day in women;
- increase in physical activity - regular physical activity for 30-40 minutes. at least 4 times a week;
- reduction in salt intake to 5 g / day;
- a change in diet with an increase in the consumption of plant foods, a decrease in the consumption of vegetable fats, an increase in the diet of potassium, calcium contained in vegetables, fruits, grains, and magnesium contained in dairy products.

The basic principles of drug therapy for arterial hypertension: Drug treatment should begin with minimal doses of any class of antihypertensive drugs (taking into account the relevant contraindications), gradually increasing the dose until a good therapeutic effect. The choice of the drug should be justified, the antihypertensive drug should provide a stable effect during the day and be well tolerated by patients.
It is most advisable to use long-acting drugs to achieve a 24-hour effect with a single dose.

The use of such drugs provides a milder hypotensive effect with more intense protection of target organs.
With a low efficiency of monotherapy (therapy with a single drug), it is advisable to use optimal combinations of drugs to achieve the maximum hypotensive effect and minimal side effects.
Long-term (almost lifelong) medication should be taken to maintain an optimal level of blood pressure and prevent complications of arterial hypertension.

When choosing antihypertensive therapy, it is necessary to consider:

1. Gender
2. Age
3. Nationality
4. Profession
5. Blood pressure level
6. Variability of blood pressure during the day
7. Risk factors
8. Presence of comorbidities
9. Target organ damage
10. Type of hemodynamics
11. Renin level
12. Pharmacodynamic effects of antihypertensive drugs
13. Side effects of antihypertensive drugs
14. Additivity of action of antihypertensive drugs in their combination
15. Action on various pressor mechanisms
16. Taking other drugs for comorbidities
17. Patient tolerance to antihypertensive drugs
18. Convenient dosage and frequency of administration
19. Ability to reduce the risk of cardiovascular events and mortality while maintaining quality of life
20. Cost of the drug

Choice of appropriate drugs:

Currently, seven classes of drugs are recommended for the treatment of arterial hypertension:

- diuretics;
- b-blockers;
- calcium antagonists;
- angiotensin-converting enzyme inhibitors;
- angiotensin receptor blockers;

- imidazoline receptor agonists
- a-blockers.

1. Beta-blockers - are a group of pharmacological drugs, the introduction of which into the human body occurs blocking beta - adrenergic receptors . They are conditionally divided into two groups, the first includes β_1 -adrenergic receptor blockers (selective, or selective), the second - β_1 -adrenergic receptor blockers and β_2 -adrenergic receptor blockers

Mechanism of action and main pharmacodynamic effects
Cardiac pharmacodynamic effects of b-adrenergic blockers are associated with the blockade of predominantly b1-adrenergic receptors of the heart. b-blockers, binding to b1-adrenergic receptors, prevent the interaction with them of endogenous catecholamines (norepinephrine, adrenaline), which leads to a decrease in the stimulating effect of Gs-protein associated with b1-adrenergic receptors on adenylate cyclase. Its activity drops sharply, which manifests itself in slowing down the synthesis of cAMP. A decrease in the content of intracellular cAMP leads to the fact that cAMP-dependent protein kinases remain inactive, cannot phosphorylate membrane calcium channels, which remain closed and, thus, the current of calcium ions from the extracellular space decreases, which could play the role of a "calcium spark" necessary for the massive release of calcium ions from the depot (sarcoplasmic reticulum). In the "working" cardiomyocytes, the absence of calcium ions leads to the fact that the calcium-troponin C complex cannot be formed , which can "free" the binding sites of the contractile proteins of actin and myosin, the consequence of this is the impossibility of the formation of the actin-myosin complex and a decrease in the strength of heart contractions (negative inotropic effect).

A decrease in the concentration of ionized calcium in the cells of the conduction system of the heart (sinoatrial node - SA node) leads to a decrease in heart rate (negative chronotropic effect) and inhibition of conduction (negative dromotropic effect), to a greater extent in the antegrade direction through the AV node and Kent's bundle, as well as a decrease in automatism (negative

bathmotropic effect), especially in the cells of the SA-node, AV-node, atria, and to a lesser extent - the ventricles. Reducing the strength of heart contractions and heart rate contribute to a decrease in myocardial oxygen demand, which justifies the possibility of using b-blockers as antianginal drugs in patients with coronary artery disease. The presence in this group of drugs the ability to inhibit conduction and automatism determines the antiarrhythmic effect of b-adrenergic blockers. A decrease in the content of intracellular calcium due to blockade of b1-adrenergic receptors in the cells of the juxtaglomerular apparatus (JGA) of the kidneys is accompanied by inhibition of the release of renin into the blood, a decrease in the formation of angiotensin II, which, along with a decrease in cardiac output (due to a decrease in the strength of heart contractions and heart rate) leads to a decrease in blood pressure and determines the effectiveness of b-blockers as antihypertensive drugs.

Pharmacokinetics

Features of the pharmacokinetics of various b-blockers are largely determined by the degree of their solubility in lipids and water. On this basis, 3 groups of b-blockers are distinguished: lipophilic, hydrophilic, lipo- and hydrophilic.

• Lipophilic b-blockers (betaxolol, carvedilol, metoprolol, oxprenolol, propranolol, timolol, etc.) are quickly and completely (about 90%) absorbed from the gastrointestinal tract, easily penetrate the blood-brain barrier (accompanied by an increase in the frequency of side effects from the central nervous system - insomnia, general weakness, drowsiness, depression, nightmares, hallucinations, etc.). Some lipophilic b-blockers (carvedilol, talinolol) are substrates for glycoprotein-P1. All lipophilic b-blockers undergo biotransformation by oxidation with the participation of cytochrome P450 2D6 isoenzyme (CYP2D6), and the first pass metabolism of b-blockers during the first passage through the liver is up to 80%. It should be noted that the biotransformation of lipophilic b-blockers under the influence of CYP2D6 is stereoselective: CYP2D6 metabolizes R-enantiomers of b-blockers to a greater extent than S-enantiomers. It should be borne in mind that the metabolism of b-blockers with the effect of "first pass" through the liver can change even with normal functional activity.

hepatocytes: lipophilic b-blockers, reducing hepatic blood flow (propranolol, for example, by 30%), can slow down their own metabolism in the liver and thus lengthen the half-life (T 1 / 2) with prolonged use. So, with long-term administration of T 1 / 2 propranolol can increase by 2-3 times compared with a single dose. Propranolol, like other lipophilic b-blockers, can slow down the excretion of other drugs from the blood that are metabolized in the liver (eg, lidocaine, hydralazine, theophylline). Decreased biotransformation of b-blockers with a pronounced first pass metabolism is especially pronounced in patients with cirrhosis of the liver, congestive circulatory failure and in old age (in these groups of patients, the dose of b-blockers should be reduced). Lipophilic b-blockers are intensively associated with plasma proteins (propranolol - 80-93%). Lipophilic b-blockers have a large volume of distribution.

• Hydrophilic b-blockers (atenolol, nadolol, sotalol, etc.) are not completely (30-70%) and unevenly absorbed in the gastrointestinal tract and are usually metabolized to a small extent (0-20%) in the liver. They are excreted by the kidneys in unchanged form (40-70%), or as metabolites. Hydrophilic b-adrenergic blockers have a longer T 1 /2 (from 6 to 24 hours) than lipophilic ones. T 1 /2 hydrophilic b-blockers increases in patients with reduced glomerular filtration rate (GFR), ie. with renal failure, as well as in the elderly; in such cases, the daily dose of drugs should be reduced due to the frequency of administration. With severe renal failure, it is safer to prescribe not hydrophilic , but lipophilic b-blockers (bisoprolol, etc.), which are metabolized in the liver. Since the excretion of hydrophilic b-blockers is little dependent on liver function, they do not interact with drugs that are metabolized in the liver and are more preferable in patients with severe liver disease.

• The third group includes b-blockers, soluble both in fats and in water (acebutolol, bisoprolol, pindolol, celiprolol, etc.), they are partially biotransformed in the liver (40-60%) under the influence of CYP2D6, the rest excreted by the kidneys unchanged. b-adrenergic blockers with balanced clearance usually have a small T 1 / 2 (from 3 to 12 hours). Thus, the balanced clearance of bisoprolol explains the low probability of interaction of this drug

with other drugs and the greater safety of their use in patients with moderate hepatic or renal insufficiency.

Contraindications **Absolute contraindications** to the use of b-blockers include severe bradycardia at rest (less than 50), sick sinus syndrome, AV block II and III degree (except for patients with an artificial pacemaker), cardiogenic shock, pulmonary edema, bronchial asthma and chronic obstructive bronchitis (for non-selective b-blockers), arterial hypotension (systolic blood pressure below 100 mm Hg).

Relative contraindications to the use of b-blockers include: peripheral circulatory disorders ("intermittent" claudication, Raynaud's syndrome), depression, pheochromocytoma.

Mention should be made of the potential for withdrawal syndrome with abrupt discontinuation of b-blockers. Abrupt discontinuation of b-adrenergic blockers is dangerous, first of all, for patients with coronary artery disease, so they should be canceled gradually. When using drugs with BCMA, the risk of exacerbation of the disease is less. The body responds to any intervention in the adaptive mechanisms, therefore, with blockade of b-adrenergic receptors, sensitivity may increase compensatory or the number of b-adrenergic receptors may increase. Other likely causes of "withdrawal" syndrome may be an increase in platelet aggregation and thyroid hormone activity. Sudden discontinuation of the use of b-blockers can be manifested by a symptom complex (tachycardia, increased blood pressure, worsening of angina pectoris, sometimes the development of acute myocardial infarction up to death), due to increased activity of the sympathetic nervous system. The latter adversely affects the course of diseases of the cardiovascular system. In addition, the protective effect of b-adrenergic blockers allows patients with coronary artery disease to endure higher workloads associated with their work. With a sharp discontinuation of the drug, patients do not have time to "rebuild" (they do not adequately limit physical activity), and therefore their condition may deteriorate significantly.

Indications for use

The main indications for the use of b-blockers include:

- angina with episodes of myocardial ischemia, accompanied or not accompanied by pain;
– arterial hypertension (AH);
- prevention of the development of ventricular and atrial arrhythmias;
– primary prevention of stroke and coronary artery disease in patients with hypertension;
- secondary prevention of myocardial infarction (MI) after myocardial infarction;
- prevention of sudden death in patients with congenital long QT interval syndrome;
- improvement of the "pumping" function of the heart in chronic heart failure (CHF) - carvedilol, metoprolol and bisoprolol;
- systemic diseases with impaired adrenergic activity (thyrotoxicosis, Marfan syndrome, essential tremor, alcohol withdrawal).

b-blockers are also used for the following indications: dissecting aortic aneurysm, hypertrophic obstructive cardiomyopathy, digitalis intoxication; mitral valve prolapse, tetralogy of Fallot, mitral stenosis (tachysystolic form), autonomic dystonia syndrome.

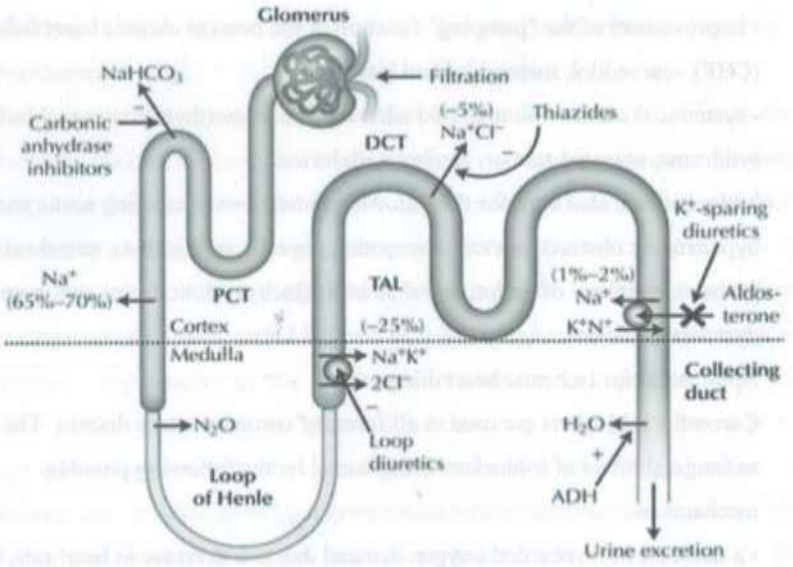
Application for Ischemic heart disease

Currently, b-blockers are used in all forms of coronary artery disease. The antianginal effect of b-blockers is explained by the following possible mechanisms:

- a decrease in myocardial oxygen demand due to a decrease in heart rate, blood pressure and myocardial contractility;
– an increase in coronary blood flow due to an increase in the time of diastolic perfusion in conditions of a decrease in heart rate;
– improvement of collateral blood flow, redistribution of blood flow to the zones of myocardial ischemia;
- reduction of microvascular damage to the myocardium;
– stabilization of cell and lysosomal membranes;
- improved release of oxygen from oxyhemoglobin;
- inhibition of platelet aggregation.

2. Diuretics

Diuretics (from the Greek . διούρησις - urination ; diuretics) - agents of various chemical structures that inhibit the reabsorption of water and salts in the tubules of the kidneys and increase their excretion in the urine; increasing the rate of urine formation and thus reducing the fluid content in the tissues and serous cavities. Diuretics that decrease sodium reabsorption and increase natriuresis are called *saluretics* .



I. _ Potent, or potent ("loop") diuretics

Torasemid - Torasemidum (solution 5 mg / ml in amp . 4 ml in tab. 5-10 mg :)) - loop diuretic. The maximum effect during the first two hours, the effect lasts up to 18 hours. Normalizes electrolyte imbalance. Torasemide has a long half-life, reduces the synthesis of thromboxane, thereby ensuring the prevention of vasospasm; does not affect the excretion of K, Mg, C a . At a dose of 2.5 mg-5 mg, it is used as an antihypertensive drug .

II. Medium strength diuretics (thiazide diuretics)

benzothiazine derivatives (thiazide diuretics) — dichlothiazide, polythiazide;

III. Potassium-sparing diuretics

Aldosterone antagonists

Spironolactone (veroshpiron; Spironolactonum, Verospironum, Gedeon Richter, Hungary; tab. 0.025 each) is a weak potassium-sparing diuretic.

IV. Carbonic anhydrase inhibitors

Diacarb as a diuretic also belongs to weak diuretics.

Diacarbum (Diacarbum; phonurite, diamox; in powders and tablets of 0.25 or in ampoules of 125; 250; 500 mg). The drug is a diuretic of medium speed and duration of action (the effect occurs after 1-3 hours and lasts about 10 hours, with intravenous administration - after 30-60 minutes, for 3-4 hours).

V Osmotic diuretics

Mannitol, urea, concentrated glucose solutions, glycerin - osmotic diuretics

Mannitol (Mannitol; Mannitolum) is a six-hydric alcohol, which is the most powerful of the existing osmotic diuretics. It is able to increase diuresis by 20% of the total sodium filtered in the glomeruli.

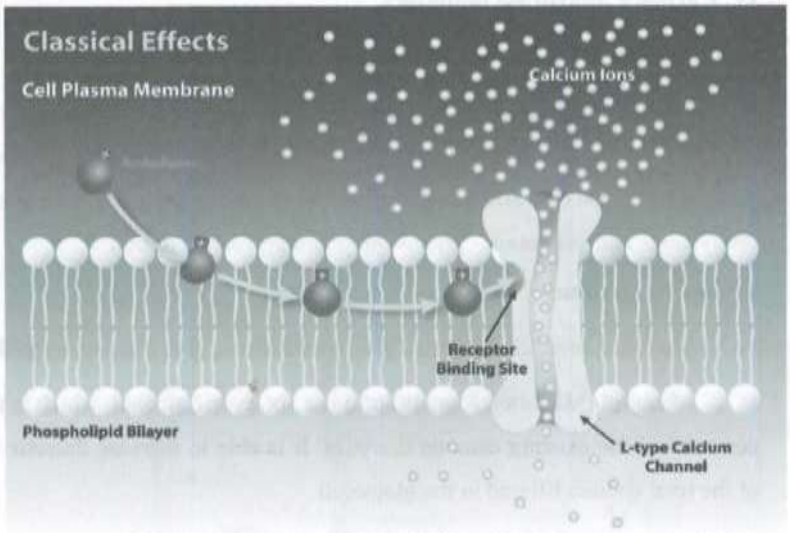
3. Calcium channel blockers (Calcium antagonists , ACC)

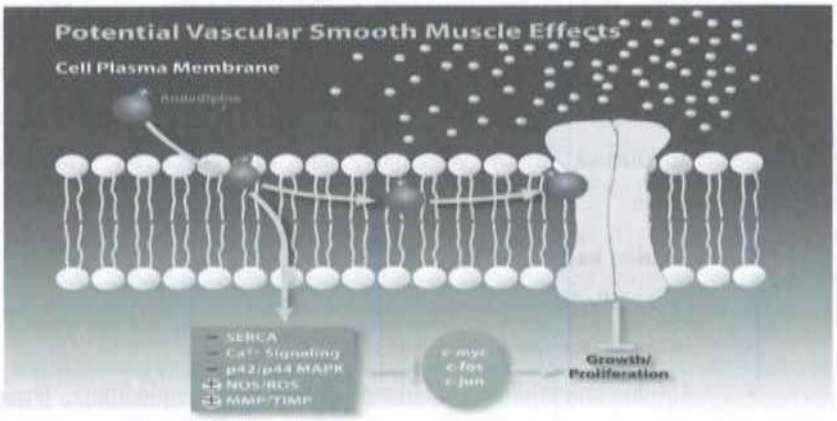
Calcium antagonists (drugs that block L-type calcium channels ; slow calcium channel blockers (SCC)) are a heterogeneous group of drugs that have the same mechanism of action, but differ in a number of properties, including pharmacokinetics, tissue selectivity, and the effect on frequency heart contractions.

Classification based on chemical structure:

- phenylalkylamines (verapamil , gallopamil)
- benzothiazepines (diltiazem , clentiazem)
- 1,4-dihydropyridines (nifedipine , nimodipine , amlodipine , lercanidipine)

The main mechanism of action of calcium antagonists is that they inhibit the penetration of calcium ions from the intercellular space into the muscle cells of the heart and blood vessels through slow L-type calcium channels. By reducing the concentration of Ca^{2+} ions in cardiomyocytes and vascular smooth muscle cells, they dilate the coronary arteries and peripheral arteries and arterioles, and have a pronounced vasodilating effect.





CCBs are prescribed:

- in monotherapy or combination therapy of arterial hypertension; - isolated systolic hypertension in the elderly; - hypertension and the presence of concomitant conditions (diabetes mellitus, bronchial asthma, kidney disease, gout, dyslipoproteinemia); - IHD: stable exertional angina, vasospastic angina pectoris; - IHD with supraventricular arrhythmias; - MI without Q wave (diltiazem); - IHD in the presence of concomitant conditions (diabetes mellitus, bronchial asthma, gout, gastric ulcer, dyslipoproteinemia);
- IHD in combination with arterial hypertension; - relief of paroxysms of supraventricular tachycardias (tachycardia with a narrow QRS complex < 0.12 s); - verapamil, diltiazem; - decrease in heart rate with paroxysms of atrial fibrillation and flutter (verapamil, diltiazem); - presence contraindications or poor tolerability of β -blockers - CCB as an alternative therapy.

Contraindications for CCB

Absolute: pregnancy (first trimester) and breastfeeding, arterial hypotension (SBP below 90 mm Hg), acute myocardial infarction (first 1–2 weeks), left ventricular systolic dysfunction (clinical and radiographic signs of pulmonary congestion, ejection fraction less than 35-40% of the left ventricle), severe aortic stenosis, sick sinus syndrome, II-III stage AV block, atrial fibrillation in WPW syndrome with anterograde conduction through accessory pathways, hemorrhagic stroke in patients with suspected hemostasis disorder.

Relative: 1) for the verapamil and diltiazem groups - pregnancy (late terms), cirrhosis of the liver, sinus bradycardia (less than 50 beats / min), combination with β - blockers (especially when administered intravenously), amiodarone, quinidine, disopyramide, ethacizine , propafenone, prazosin, magnesium sulfate, etc.;

2) dihydropyridine - pregnancy (late terms), cirrhosis of the liver, unstable angina pectoris, hypertrophic cardiomyopathy with severe obstruction, combination with prazosin, nitrates, magnesium sulfate, etc.

4. ACE inhibitors (ACE inhibitors)

(ACE - Angiotensin converting enzyme)

mechanism of action

The main clinical and pharmacological effects of ACE inhibitors are based on their ability to suppress the activity of the enzyme that converts angiotensin I to angiotensin II (kininase II, or ACE), and thus affect the functioning of the renin-angiotensin-aldosterone system (RAAS).

Only 10-15% of angiotensin II in the body is formed due to the participation of ACE, there is an alternative way of its biosynthesis with the participation of the chymase enzyme and the chymase-like enzyme CAGE. In addition, the transformation of angiotensin I into angiotensin II is possible with the participation of tissue plasminogen activator, cathepsin G, tonin and other biologically active substances. At the same time, in some organs and tissues, the classical pathway for the formation of angiotensin II (the right parts of the heart) prevails, in others, the alternative (left parts of the heart, the outer shell of the blood vessels). In some tissues (vascular endothelium), the formation of angiotensin II is carried out in a balanced way in different ways.

Pharmacodynamic effects of ACE inhibitors are associated with blocking ACE and reducing the formation of AT II in the blood and tissues, eliminating its pressor and other neurohumoral effects. At the same time, according to the feedback mechanism, the level of plasma renin and A TI can increase, as well as a transient decrease in the level of aldosterone.

ACE inhibitors can inhibit the secretion of aldosterone and vasopressin, reduce the synthesis of other vasoconstrictor and antinatriuretic substances (norepinephrine, arginine-vasopressin, endothelin-1) involved in the pathogenesis of cardiac dysfunction and arterial hypertension. In addition, ACE is identical to the kininase II enzyme involved in the degradation of bradykinin. Bradykinin is a powerful vasodilator that regulates microcirculation and ion transport. Bradykinin has a short lifespan and is present in the bloodstream (tissues) in low concentrations, and therefore exhibits its effects as a local hormone (paracrine). Bradykinin promotes an increase in intracellular Ca 2 +, which is a cofactor for NO synthetase involved in the formation of endothelial relaxing factor (nitric oxide or NO). The endothelium-relaxing factor, which blocks vascular muscle

contraction and platelet aggregation, is also an inhibitor of mitosis and proliferation of vascular smooth muscle, which provides an anti-atherogenic effect. Bradykinin also stimulates the synthesis in the vascular endothelium of PGE 2 and PGI2 (prostacyclin) - powerful vasodilators and platelet antiplatelet agents. Thus, bradykinin and the kinin system are counteracting for the renin-angiotensin-aldosterone system . Blocking ACE potentially increases the level of kinins in the tissues of the heart and vascular wall, which provides antiproliferative, antiischemic, antiatherogenic and antiplatelet effects. Kinins contribute to an increase in blood flow, diuresis and natriuresis without a significant change in the glomerular filtration rate. PG E2 and PGI2 also have diuretic and natriuretic effects and increase renal blood flow.

Thus, the following main pharmacological effects are distinguished ACE inhibitors:

Neurohumoral

Hemodynamic

Cardiac

Vascular

Renal

metabolic

Pharmacokinetics

According to pharmacokinetics, ACE inhibitors are divided into two main groups - active drugs forms (captopril and lisinopril) and prodrugs (inactive substances that form an active diacid metabolite after transformation in the liver and / or in the gastrointestinal mucosa. For example, enalapril is converted to enalaprilat, fosinopril is converted to fosinoprilat).

Renal excretion is the main route of elimination of all known active ACE inhibitors and active diacid metabolites of most initially inactive drugs. In this regard, in patients with renal insufficiency, it is usually recommended to start therapy with the appointment of lower doses of inhibitors than in patients with normal renal function. Among ACE inhibitors, there are several drugs whose active diacid metabolites are excreted not only through the kidneys (lipophilic),

but also with bile and feces (hydrophilic). ACE inhibitors with two main routes of elimination or with predominantly hepatic elimination include ramipril, moexipril, trandolapril and fosinopril. These ACE inhibitors are safer in long-term use than drugs with predominantly renal elimination.

The pharmacokinetics of various ACE inhibitors - active dosage forms and prodrugs is characterized by some differences.

Differences in individual representatives of the ACE inhibitors group in terms of bioavailability do not have significant clinical significance. The degree of lipophilicity plays a much larger role. Hydrophilic ACE inhibitors, such as lisinopril, ceronapril, are not metabolized in the body and are excreted unchanged by the kidneys. Lipophilic drugs are partially metabolized in the liver, as well as in the gastrointestinal mucosa and extravascular tissues with the formation of active metabolites, some of which have biological activity:

According to the duration of action, ACE inhibitors are usually classified into :

- short-acting drugs that need to be taken 2-3 r / day (for example, captopril);
- long-acting drugs that provide daily control of blood pressure levels when taken 1-2 r / day

Place in therapy

In cardiology

In view of the positive clinical and prognostic value of the action of ACE inhibitors, these drugs are widely used in **cardiology** . The use of ACE inhibitors in cardiac practice is justified in the following cases:

- In the treatment of systolic dysfunction of the left ventricle, regardless of the presence or absence of signs of CHF.
- Left ventricular hypertrophy
- In the treatment of arterial hypertension and most forms of symptomatic hypertension.
- As an independent element of the treatment of various types of nephropathy, including diabetic .

- In the system of measures of secondary prevention in patients after myocardial infarction.
- Increased activity of the renin-angiotensin system (including unilateral renal artery stenosis)
- Non-diabetic nephropathy
- Atherosclerosis of the carotid arteries
- Proteinuria/microalbuminuria
- Atrial fibrillation
- metabolic syndrome

They are shown to all patients with **CHF** and **asymptomatic cardiac dysfunction** , regardless of etiology, stage of the process and myocardial contractility. Treatment with ACE inhibitors begins with minimal doses, gradually increasing them to effective (target) ones, which provide the most complete blockade of the RAAS. The predominant role of ACE inhibitors in reducing left ventricular hypertrophy over other classes of antihypertensive drugs has been proven, and there is no relationship between the severity of the hypotensive effect and regression of left ventricular hypertrophy (they can prevent the development of left ventricular hypertrophy and myocardial fibrosis even in the absence of a decrease in blood pressure). ACE inhibitors exhibit **a vasoprotective** effect, reducing the effect of AT II on the AT1 receptors of blood vessels, on the one hand, and on the other hand, activating the bradykinin system, improving endothelial function and exerting an antiproliferative effect on vascular smooth muscle.

In **arterial hypertension** , ACE inhibitors can be used both as monotherapy and in combination with other antihypertensive drugs. The hypotensive effect is due not only to a decrease in the formation of ATP, but also to the prevention of the degradation of bradykinin, which potentiates endothelium-dependent relaxation of vascular smooth muscles, through the formation of vasodilating prostaglandins and endothelial relaxing factor (NO). Diabetes mellitus develops during treatment with ACE inhibitors statistically

significantly less frequently than during treatment with a diuretic and / or β - blocker (on average by 21%), and in hypertensive patients with type 2 diabetes, captopril therapy is accompanied by a more pronounced decrease in the frequency of cardiovascular events. complications (average 41%) compared with diuretics and / or β-blockers. The combination of ACE inhibitors with dihydropyridine calcium antagonists is effective in the treatment of isolated systolic hypertension.

Due to the protective effect on the processes of remodeling heart and **blood vessels,** increase in coronary reserve due to improved endothelial function, reduced myocardial oxygen demand by reducing pre- and afterload, improving diastolic function of the heart muscle, ACE inhibitors are considered as a means of treating patients ischemic heart disease .

These drugs are used both in the treatment of MI and for long-term therapy in the postinfarction period. ACE inhibitors are the means of choice in the treatment of hypertension or cardiac dysfunction in patients **with** obliterating atherosclerosis of the arteries of the lower extremities (due to the frequent combination of atherosclerotic lesions of the peripheral and renal arteries), widespread atherosclerosis with lesions of the coronary and carotid arteries, moderate hyperkalemia (from 5 to 5, 5 mEq / l), as well as **in** women of childbearing age who do not receive effective contraception (given the possible adverse effects of drugs on intrauterine development of the fetus).

atherogenic effect of ACE inhibitors consists in anti-proliferative and anti-migration effects on vascular smooth muscle cells and monocytes, a decrease in the formation of a collagen matrix, antioxidant and anti-inflammatory effects, as well as potentiation of endogenous fibrinolysis and antiplatelet effects (inhibition of platelet aggregation). As a result, there is a decrease in plasma atherogenicity (decrease in LDL and triglycerides and an increase in HDL) and prevention of atherosclerotic plaque rupture and atherothrombosis.

In neurology

Secondary and primary prevention of stroke , stroke or transient ischemic attack, regardless of baseline blood pressure, the use of other drugs, including antihypertensives, by sex, age and race, is also an indication for the appointment of ACE inhibitors. During treatment, there is a significant reduction in the risk of recurrent stroke - by an average of 28%, the frequency of fatal/disabling (by 38%) and hemorrhagic (by 50%) stroke decreases, the overall risk of cardiovascular complications, especially non-fatal myocardial infarction (by 38 %) decreases. %).

In Nephrology

In nephrology, the preferred use of ACE inhibitors is justified in the treatment of nephropathy due to their ability to reduce the level of proteinuria and microalbuminuria, as well as the risk of microvascular complications. ACE inhibitors prevent the progression of kidney failure. The nephroprotective effect is specific and characteristic of all drugs. Dilatation of predominantly efferent arterioles of the renal glomerulus is accompanied by a decrease in intraglomerular filtration pressure, filtration fraction and hyperfiltration, resulting in a decrease in proteinuria (mainly low molecular weight proteins) in patients with diabetic and hypertensive nephropathy. Renal effects, due to the high sensitivity of the renal vessels to the vasodilatory effect of ACE inhibitors, appear earlier than the decrease in total peripheral resistance and are only partially mediated by the hypotensive effect. The mechanism of the antiproteinuric effect of ACE inhibitors is an anti-inflammatory effect on the glomerular basement membrane and an antiproliferative effect on the mesangial cells of the glomerulus, which reduces its permeability to medium and high molecular weight proteins. In addition, ACE inhibitors eliminate the trophic effects of AT II, which, by stimulating the growth of mesangial cells, their production of collagen and epidermal growth factor of the renal tubules, accelerates the development of nephrosclerosis.

In endocrinology

In endocrinology, the use of ACE inhibitors is justified in the patient has diabetes mellitus **and** diabetic nephropathy . With obesity and insulin resistance , ACE inhibitors increase tissue sensitivity to insulin, which is accompanied by a decrease in new cases of diabetes mellitus during treatment. In addition, all ACE inhibitors slow down the progression of kidney damage in type I and type II diabetes mellitus, regardless of the level of blood pressure. ACE inhibitors slow down the progression of chronic renal failure in other nephropathies. Long-term use of ACE inhibitors is accompanied by a decrease in the incidence of complications of diabetes mellitus and cardiovascular complications.

5. Angiotensin II receptor antagonists (ARA, ARB, Sartans)

Angiotensin (AT) II receptor blockers (sartans) are a class of antihypertensive drugs that act on the renin-angiotensin-aldosterone system (RAAS) . They selectively block AT II receptors, eliminating the adverse biological effects of ATP (vasoconstriction, aldosterone secretion, SAS activation, proliferation of vascular and myocardial smooth muscle).

Mechanism of action

Unlike ACE inhibitors, sartans block the formation of AT II without affecting the entire chain of transformation of AT I into AT II, including enzymes - angiotensin-converting enzyme, chymases, endothelial and renal peptidases, tissue plasminogen activator - tPA, etc.

At present, two types of AT II receptors that perform different functions are best studied: AT_1 and AT_2:

AT_1

- Vasoconstriction.
- Stimulation of the synthesis and secretion of aldosterone.
- Tubular reabsorption of Na^+.
- Decreased renal blood flow.
- Proliferation of smooth muscle cells.

- Hypertrophy of the heart muscle.
- Increased release of norepinephrine.
- Stimulation of vasopressin release.
- Inhibition of renin formation.
- Thirst stimulation.

AT_2

- Vasodilation.
- Natriuretic action.
- Release of NO and prostacyclin.
- antiproliferative action.
- Stimulation of apoptosis.
- Differentiation and development of embryonic tissues.

$AT_{1\ receptors}$ are localized in the vascular wall, adrenal glands, and liver. Through $AT_{1\ receptors}$, undesirable effects of AT II are realized: vasoconstriction, secretion of aldosterone, vasopressin, norepinephrine, fluid retention, proliferation of smooth muscle cells and hyperplasia of cardiomyocytes, activation of the sympathetic-adrenal system (SAS), as well as the negative feedback mechanism of RAAS - the formation of renin. $AT_{2\ receptors}$ are also widely represented in the body: CNS, vascular endothelium, adrenal glands, reproductive organs (ovaries, uterus). $AT_{2\ receptors}$ perform physiological functions such as vasodilation, healing, repair and regeneration processes, antiproliferative action, differentiation and development of embryonic tissues. The number of $AT_{2\ receptors}$ in tissues is not constant: their number increases sharply with tissue damage and the need for reparative processes.

The action of ACE inhibitors is not specific. It is mediated through ACE, which blocks the formation of AT II, on the one hand, and on the other hand, is a kininase that plays a key role in the kinin system. As a result, the destruction of bradykinin is blocked and the release of vasodilating prostaglandins (Pg E , PgI) and nitric oxide (NO) - a modulator of endothelial function - increases. It is with this mechanism of action of ACE inhibitors that the development of the most

clinically significant side effects is associated - cough, rash, angioedema, excessive vasodilation and a sharp decrease in blood pressure. This can lead to poor tolerance of ACE inhibitors and refusal of patients to take them. AT II receptor blockers have a specific effect and block only the biological effects of AT II without interfering with the kinin system, which improves the tolerability of these drugs.

ACE inhibitors, blocking the formation of AT II, inhibit the effects of stimulation of both AT_1 and $AT_{2\ receptors}$. At the same time, not only undesirable, but also physiological effects of AT II, mediated through $AT_{2\ receptors}$, are blocked, in particular, repair, regeneration, antiproliferative action and additional vasodilation. AT II receptor blockers are selective only for $AT_{1\ receptors}$, thereby blocking the harmful effects of AT II. Due to the increase in the level of AT II and other degradation products of AT (AT III, AT IV, AT 1-7) due to the blocking of the negative feedback mechanism, $AT_{2\ receptors\ are\ stimulated}$.

Currently, non-peptide blockers of AT II receptors have been created. According to the chemical structure, AT II receptor blockers belong to 4 groups:

- biphenyl derivatives of tetrazole (losartan, candesartan, irbesartan);
- non-biphenyl derivatives of tetrazole (telmisartan);
- non-biphenyl netetrazoles (eprosartan);
- non-heterocyclic derivatives (valsartan).

Some AT II receptor blockers are pharmacologically active (telmisartan, irbesartan, eprosartan); others are prodrugs (losartan, candesartan).

AT II receptor blockers are distinguished by a high degree of selectivity for AT_1 receptors (the ratio of AT_1 and AT_2 selectivity is 10,000–30,000:1). Pharmacologically, $AT_{1\ receptor\ blockers}$ differ in the strength of binding to the receptors (affinity) and the nature of the relationship (competitive or non-competitive). The AT_1 receptor blocker losartan is characterized by the lowest binding force to $AT_{1\ receptors}$, its active metabolite binds 10 times stronger than losartan. The affinity of new AT_1 receptor blockers is 10 times greater, which is characterized by a more pronounced clinical effect. Differences in the strength of

binding to receptors also affect the strength of the bond, which characterizes the duration of action. Thus, for losartan, the duration of action is the shortest and is about 12 hours, for valsartan - about 24 hours, for telmisartan - more than 24 hours.

The vast majority of AT $_{1\ \text{receptor blockers}}$ are non-competitive AT II blockers, which, together with a high degree of binding to the receptor, makes their pharmacological kinetics irreversible (for example, irbesartan, candesartan, telmisartan). Losartan is a weak competitive blocker, but due to the presence of an active metabolite that non-competitively inhibits AT II, it also belongs to the group of non-competitive blockers. Eprosartan is the only competitive blocker whose action is overcome by high concentrations of AT II.

$_1$ receptor blockers have a complex neurohumoral mechanism of vasodilating action, including the effect on the two most important body systems - RAAS and SAS, involved in the pathogenesis of many cardiovascular diseases. AT $_{1\ \text{receptor}}$ blockers block the effects of AT II mediated through AT $_1$ receptors of blood vessels and adrenal glands, such as arteriolar spasm, sodium and water retention, remodeling of the vascular wall and myocardium. In addition, these drugs interact with presynaptic receptors of noradrenergic neurons, which prevents the release of norepinephrine into the synaptic cleft, and thereby prevents the vasoconstrictive effect of the sympathetic nervous system. As a result, AT $_1$ receptor blockers cause systemic vasodilation and a decrease in total peripheral vascular resistance without an increase in heart rate; natriuretic and diuretic effects. In addition, AT $_{1\ \text{receptor blockers}}$ have an antiproliferative effect, primarily in the cardiovascular system. Hemodynamic and neurohumoral pharmacodynamic effects of AT $_1$ receptor blockers determine the expediency of their use in arterial hypertension and heart failure.

$_1$ receptor blockers is complex and consists of the elimination of vasoconstriction caused by AT II, a decrease in the tone of the CAS, and a natriuretic effect. Almost all AT II receptor blockers show a hypotensive effect when taken once a day and provide control of blood pressure for 24 hours.

1 receptor blockers causes organoprotective effects: cardioprotective - due to reversal of myocardial hypertrophy and hyperplasia of the musculature of the vascular wall; improvement of vascular endothelial function; renoprotective.

The most important characteristic of AT1 receptor blockers is the lack of influence on the level of bradykinin, which is a powerful factor affecting the renal microcirculation. It has been shown that the accumulation of bradykinin as a result of the action of ACE inhibitors leads to a more pronounced decrease in the tone of the efferent renal arterioles. This may be the reason for the decrease in intraglomerular pressure, filtration fraction and glomerular filtration rate in the treatment of patients with ACE inhibitors, which is undesirable.

1 receptor blockers , unlike ACE inhibitors, have a less pronounced effect on the tone of the efferent arterioles, increase effective renal blood flow and do not significantly change the glomerular filtration rate. As a result, there is a decrease in intraglomerular pressure and filtration fraction, and a renoprotective effect is achieved. Compliance with a diet low in sodium chloride potentiates the renal and neurohumoral effects of AT 1 receptor blockers : the level of aldosterone decreases more pronounced, plasma renin activity increases and natriuresis is stimulated, while the glomerular filtration rate does not change. These effects are due to the blockade of AT 1 receptors that regulate sodium reabsorption in the distal tubules of the kidneys. With an increased intake of salt in the body, these effects weaken.

In patients with hypertension and chronic renal failure (CRF), AT1 receptor blockers maintain efficient renal blood flow and do not significantly alter the reduced glomerular filtration rate.

The renoprotective effect of AT 1 receptor blockers is also manifested by a decrease in microalbuminuria in patients with hypertension and diabetic nephropathy.

1 receptor blockers appear when they are used in lower doses than the doses that give a hypotensive effect. This may have additional clinical significance in patients with severe CKD or CHF, while ACE inhibitors, even at reduced doses, lead to increased azotemia and severe arterial hypotension.

of AT1 receptor blockers from those of ACE inhibitors are as follows:

- elimination of the biological effects of AT II in tissues, mediated through the blocking of AT $_{1\ receptors}$ (more complete blocking of the adverse effects of AT II);
- strengthening the effect of AT II on AT $_{2\ receptors}$, which complements the vasodilating and antiproliferative effect;
- milder effect on renal hemodynamics;
- the absence of undesirable effects associated with the activation of the kinin system

Pharmacokinetics

$_1$ receptor blockers is determined by lipophilicity, which characterizes not only stable pharmacokinetics, but also determines the degree of tissue distribution and effect on tissue RAAS. Losartan is the most hydrophilic drug, telmisartan is the most lipophilic.

$_1$ receptor blockers differ in their pharmacokinetic characteristics in terms of bioavailability, half-life ($T_{1/2}$), and metabolism. The first AT $_1$ receptor blockers are characterized by low and variable bioavailability (10-35%); new drugs are characterized by improved stable bioavailability (50-80%). After oral administration, the maximum plasma concentration (T_{max}) is reached after 2 hours; at long-term regular use stationary, or equilibrium, the concentration is established after 5-7 days. AT $_1$ receptor blockers are characterized by a high degree of binding to plasma proteins (more than 90%), mainly to albumins, partly to α_1 -acid glycoprotein, γ -globulin and lipoproteins. However, strong protein binding does not limit plasma clearance and volume of distribution of drugs, and the potential risk of interaction at the level of protein binding is low. The volume of distribution $_{of}$ AT1 receptor blockers varies according to their lipophilicity: telmisartan has the largest volume of distribution, which characterizes rapid membrane permeability and high tissue distribution.

$_1$ receptor blockers are characterized by a large $T_{1/2}$ - from 9 to 24 hours. However, $T_{1/2\ of\ AT\ 1}$ receptor blockers only approximately reflects the duration of action: their pharmacodynamic $T_{1/2}$ exceeds the pharmacokinetic $T_{1/2}$; the duration of action is also affected by the nature and strength of interaction with

receptors. Due to these features, the frequency of taking AT $_{1}$ receptor blockers is 1 time per day. The route of elimination of AT $_{1}$ receptor blockers is predominantly extrarenal: more than 70% is eliminated through the liver and less than 30% by the kidneys.

$_{1}$ receptor blockers undergo partial (less than 20%) metabolism in the liver, their excretion is carried out mainly in the active form. Metabolism is carried out by glucuronyl transferase or the microsomal system of the liver with the participation of cytochrome P450. Thus, cytochrome P450 is involved in the metabolism of losartan, irbesartan and candesartan, which is the cause of interactions with other drugs. In patients with severe hepatic insufficiency, there may be an increase in bioavailability, maximum concentration (C_{max}) and area under the concentration-time curve (AUC) of losartan, valsartan and telmisartan, as well as a decrease in clearance and biliary excretion of drugs. Therefore, they are contraindicated in patients with biliary obstruction or severe hepatic impairment, but may be used with caution in patients with mild to moderate hepatic impairment. In patients with mild or moderate renal insufficiency, correction of the dosing regimen of AT $_{1}$ receptor blockers is not required; however, in severe chronic renal failure, an increase in C_{max} and AUC may be observed, which necessitates caution when using these drugs.

In elderly patients, there may be an increase in bioavailability, leading to an increase in the maximum plasma concentration of drugs, and a slowdown in the rate of absorption, leading to an increase in T_{max} and $T_{1/2}$. However, due to the broad therapeutic index of drugs, there is no need to reduce doses in the elderly.

Place in therapy

In cardiology

In **cardiology** , AT II receptor blockers are used as the main groups of **antihypertensive** drugs. Under the influence of sartans, blood pressure decreases "physiologically", that is, while maintaining its natural circadian biorhythms, while the maximum hypotensive effect of sartans manifests itself after a fairly long time of use, which ranges from 2 to 5 weeks, depending on the drug chosen. At the same time, the achieved decrease in blood pressure is persistent, and the

escape of the effect of sartans and the development of tolerance to them are observed very rarely. The essence of this phenomenon lies in the blockade of both circulating and tissue RAAS, in which a longer conversion (about 60% of the total) of angiotensin I to angiotensin II occurs with the help of chymases, and not with the participation of ACE.

It should be remembered that the effectiveness of double blockade of the RAAS with the simultaneous administration of ACE inhibitors and sartans does not justify itself clinically and the only indication is the malignant renovascular form of AH. However, one of the clinical niches of sartans should be new-onset hypertension in young somatically uncomplicated patients, which requires the appointment of antihypertensive drugs in monotherapy. It is in this mode that the hypotensive effect of sartans exceeds the effectiveness of other known classes of antihypertensive drugs.

With long-term treatment with sartans, a decrease in myocardial mass index and regression of left ventricular myocardial hypertrophy (cardioprotective effect) are observed. The ability of AT II receptor antagonists to prevent atrial fibrillation is of particular importance in patient groups at high risk of this heart rhythm disorder, in particular at any stage of chronic kidney disease.

Valsartan is the only drug from the sartans group, which is included in the National guidelines for the diagnosis and treatment of acute myocardial infarction . myocardial infarction (AMI) with an increase in the ST segment on the ECG along with ACE inhibitors, which showed a decrease in mortality by 25% in the post-infarction period. Sartans have demonstrated their effectiveness in patients with chronic heart failure (CHF), which is associated with selective suppression of the RAAS without affecting the kallikrein-kinin and other neurohumoral systems that play a role in the pathogenesis of CHF, however, in terms of cardioprotective properties, sartans are inferior to ACE inhibitors. Therefore, AT receptor blockers in the treatment of chronic CHF are used as auxiliary drugs that are prescribed if ACE inhibitors are not possible due to side effects. Inferior in cardioprotection, sartans are leaders among all antihypertensive drugs in terms of their cerebral and nephroprotective capabilities.

In Nephrology

In **nephrology** , nephroprotection due to the influence of sartans is associated with targeted dilatation, persistently spasmodic in hypertension and diabetic nephropathy, efferent arterioles of the renal glomerulus, subsequent restoration of outflow, resolution of intraglomerular hypertension, and restoration of kidney function. At the same time, the nephroprotective effect does not depend on the degree of BP reduction. The glomerular filtration rate, which is a real reflection of the state of renal function, increases immediately with the appointment of sartans and deteriorates just as quickly when they are canceled. However, this fact is rarely taken into account by practitioners, and therefore the percentage of patients who are prescribed sartans for reasons of nephroprotection is extremely small.

In neurology

In **neurology** , sartans play an important role in providing brain protection in hypertension by directly acting on angiotensin AT receptors in neurons and endothelium of cerebral vessels, improving cognitive functions in elderly patients.

The cerebroprotective properties of sartans were noted not only in relation to the prevention of ischemic strokes, but also in the prevention of new cases of hemorrhagic strokes during sartans therapy. Sartans block receptors for angiotensin II and the subsequent increase in its titer in tissues. This provides a constant tone of large cerebral vessels and protects small distal resistive vessels (Charcot-Bouchard aneurysms) from pressure drops, rupture and diapedetic bleeding from which are the morphological substrate of hemorrhagic stroke, the prognosis after which is incomparable in severity with the outcomes of ischemic stroke. Sartans can prevent **stroke and** cardioemblic stroke (episodes of atrial fibrillation (AF), including in patients taking antiarrhythmic drugs. .

In endocrinology

In **endocrinology,** sartans have a regulatory effect on carbohydrate and fat metabolism. In patients with type 2 **diabetes mellitus** , while taking sartans, there

is a decrease in insulin resistance due to stimulation of nuclear PPAR receptors in adipose and muscle cells, as well as hepatocytes. Moreover, the positive metabolic and hypoglycemic effect of sartans in some cases is comparable to the effect of oral hypoglycemic drugs. It has been proven that in patients receiving sartans as an antihypertensive agent or in the complex therapy of chronic heart failure, the incidence of new cases of type 2 diabetes mellitus decreases by 33%.

Also associated with stimulation of PPAR receptors hypolipidemic the effects of sartans and the emergence of a formula for the additivity of their effects with the effects of statins. It has been proven that in patients with dyslipidemia, sartans prescribed in addition to statins reduce the risk of cardiovascular events by almost half (synergism of sartans with statins). Sartans also have a distinct hypouricemic effect. Losartan (50–100 mg/day) has the best effect on uric acid levels, followed by valsartan (80–160 mg/day), irbesartan (150–300 mg/day) and candesartan (8–16 mg/day).).

The uricosuric effect of sartans is accompanied by an increase in the excretion of oxypurinol. The drugs of this group increase the excretion of urates in the urine by reducing their reabsorption in the proximal tubules of the kidneys. The uricosuric effect is also preserved when they are combined with diuretics, due to which the increase in the level of uric acid in the blood caused by diuretics is prevented. Angiotensin II-induced superoxide production is the result of direct stimulation by nicotinamide adenine nucleotide-phosphate oxidase through AT1 receptors, and in patients with gout it is blocked by losartan. It is important that the uricosuric effect is preserved even when they are combined with diuretics, due to which the increase in the level of uric acid in the blood caused by diuretics is prevented. Therefore, sartans are recommended for use in patients with hypertension on the background of metabolic syndrome .

Tolerability and side effects

1 receptor blockers , the development of cough associated with the effect of bradykinin on the lungs has the greatest clinical significance. AT 1 receptor blockers do not affect the metabolism of kinins and therefore cause cough much less frequently than ACE inhibitors. The incidence of cough ranges from 1%

(valsartan, eprosartan, telmisartan) to 4.6% (losartan, irbesartan, candesartan), and in patients with the development of cough on ACE inhibitors, the incidence of cough reached 15.6% (telmisartan) - 19% (valsartan).

The incidence of other PEs associated with the activity of the kinin system (angioneurotic edema, rash) does not exceed 1%. The effect of the "first dose" (dizziness, weakness, postural hypotension, fainting), which occurs when taking ACE inhibitors and is due to a sharp hemodynamic effect, is slightly pronounced in AT 1 receptor blockers. Unlike ACE inhibitors, AT1 receptor blockers do not cause a clinically significant retention of potassium in the body (the incidence of hyperkalemia is less than 1.5%). AT 1 receptor blockers have a neutral metabolic profile: they do not affect the metabolism of lipids and carbohydrates.

Withdrawal syndrome in AT 1 receptor blockers was not noted.

Contraindications and warnings

$_1$ receptor blockers are:

- $_1$ receptor blockers ;
- arterial hypotension;
- hyperkalemia;
- dehydration;
- stenosis of the renal arteries;
- pregnancy and lactation;
- childhood.

$_1$ receptor blockers, it is necessary to monitor the level of blood pressure and heart rate (especially in elderly patients and with impaired renal function) and monitor kidney function (potassium, creatinine levels).

6. Agonists of imidazoline receptors and agonists of alpha-2-adrenergic receptors in the brain

Not included in international recommendations. Regardless of this, they are used for the treatment of hypertension, often with self-medication. Imidazoline receptor agonists can be used in the metabolic syndrome. There is a side effect (in 2% of cases) - dry mouth, which does not require discontinuation of the drug and disappears during treatment. The most dangerous side effect of long-term use of

all vasodilator drugs, including cerebral alpha-2 adrenoreceptor agonists and imidazoline receptor agonists, is an increase in intracranial pressure, even if it is accompanied by a decrease in central arterial pressure. There are significant CNS side effects. Resistance and addiction may develop.

5.3 Prevention of arterial hypertension

Arterial hypertension is understood as an increase in blood pressure over 140 and 90 mmHg. Art. If left untreated, hypertension leads to an increased risk of coronary heart disease, stroke, kidney damage, and an increase in overall mortality.

Hypertension, like any chronic progressive disease, is easier to prevent than to treat. Therefore, the prevention of hypertension, especially for people with aggravated heredity, is a matter of prime necessity.

First of all, it is worth thinking about the prevention of hypertension for everyone whose blood pressure is within the high or borderline norm, especially for young people and adolescents.

Prevention of arterial hypertension is primary and secondary.

Primary refers to *the* prevention of the onset of the disease. These prevention methods should be followed by healthy people who have a high risk of developing hypertension (heredity, work). But not only they, everyone should live in accordance with the principles of primary prevention of hypertension, because this disease often overtakes at the most unexpected moment even those who do not have unfavorable heredity and other risk factors.

Primary prevention of hypertension includes:

- Normalization of the function of the central nervous system (prevention of stress).
- A clear daily routine (constant time for getting up and going to bed).
- Outdoor exercise and physical therapy (long walks in the open air, cycling, moderate work in the garden).
- Daily loads in the gym and at home.
- Normalization of sleep (sleep lasting up to 8 hours).

- Balanced diet. Carefully count the kilocalories consumed with food, do not allow excessive consumption of fats. Fats can be consumed per day no more than 50-60 grams, and 2/3 of them should be vegetable fats: corn, sunflower oil. Limit foods containing a large amount of animal fats - whole milk, butter, sour cream. The diet should contain a sufficient amount of proteins: low-fat varieties of fish, poultry, skimmed milk, cottage cheese, kefir, etc. It is necessary to limit the intake of easily digestible carbohydrates: sugar, honey, pastry products, chocolate, semolina, rice cereal.
- Weight loss (obese). Without weight loss, there is no need to talk about the prevention of hypertension. You can not try to lose weight dramatically, you can reduce body weight by 5 - 10% per month.
- To give up smoking!!!
- Reduced salt intake (use no more than 6 grams per day).
- Consumption of foods high in potassium, calcium and magnesium salts (low-fat cottage cheese, parsley, beans, prunes, beets, baked potatoes, dried apricots, pitted raisins.)
- Limiting the consumption of alcoholic beverages.

Secondary prevention is carried out in patients in whom arterial hypertension is established as a diagnosis. Its purpose is to prevent the occurrence of complications. At the same time, this type of prevention includes two components: non-drug treatment of arterial hypertension and antihypertensive (drug) therapy. Non-drug treatment, in principle, corresponds to primary prevention, only with more stringent requirements. If each individual person is not able to change heredity and the environment, then the way of life and nutrition are completely. Drug therapy - drugs prescribed by a doctor that purposefully act on a high level of pressure, reducing it. Patients with arterial hypertension should strictly adhere to the doctor's recommendations and take drugs as prescribed, thereby preventing the risk of complications.

The prevention of arterial hypertension can be attributed to the systematic monitoring of the level of pressure in the morning and evening. Relentless adherence to the recommendations of the attending physician, timely appeal to him in case of deterioration.

Test tasks

1. Arterial hypertension is determined if:

A) SBP ≥ 140 mm Hg. with DBP ≥ 90 mm Hg.

B) SBP > 120 mm Hg. with DBP > 80 mm Hg.

C) SBP > 120 mm Hg. and/or DBP > 80 mmHg

D) SBP ≥ 140 mm Hg. and/or DBP ≥ 90 mmHg

2. Which of the following is not a link in pathogenesis

GB:

A) increased activity of the sympathoadrenal system

B) increased activity of the RAAS - system

B) endothelial dysfunction

D) a decrease in the content of Na + ions in the vascular wall

3. How many according to modern ideas exist

GB stages:

A) 2

B) 3

C) 4

D) 5

4. How would you rate the blood pressure equal to 166/94 mm Hg. :

A) high normal

B) AH 1 degree

C) AH 2 degrees

D) AG 3 c degree

5. How would you rate the blood pressure equal to 136/100 mm Hg:

A) high normal

B) AH 1 degree

C) AH 2 degrees

D) normal

6. How would you rate the blood pressure equal to 160/80 mm Hg:

A) AH 1 degree

B) high normal

C) 3 degree hypertension

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D) isolated systolic hypertension

7. How would you rate the blood pressure equal to 120/96 mm Hg:

A) high normal

B) AH 1 degree

B) normal

D) optimal

8. How would you rate the blood pressure equal to 170/105 mm Hg:

A) isolated systolic hypertension

B) AH 1 degree

C) AH 2 degrees

D) AH 3 degrees

9. What is mandatory for stage III GB:

A) disease e(s) of the cardiovascular system or

kidneys, directly or indirectly associated with elevated blood pressure

B) AH 3 degrees

C) history of GB over 30 years

D) left ventricular hypertrophy, microalbuminuria

10. Which of the domestic medical scientists proposed the term

"hypertonic disease":

A) Lang G.F.

B) Myasnikov A.L.

C) Tareev E.M.

D) Strazhesko N.D.

11. Which of the following conditions does not apply to

target organ damage in hypertension:

A) microalbuminuria

B) left ventricular hypertrophy

B) hypertensive retinopathy

D) slight increase in serum creatinine (115-133 µmol/l for men and 107-124 µmol/l for women)

12. Microalbuminuria is considered the level of protein excretion with urine, equal to :

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A) 0.1 - 0.3 mg / day

B) 0.3 - 30 mg / day

C) 30-300 mg/day

D) up to 1 g / day

13. What is meant by associated clinical conditions:

A) all diseases that aggravate the course of GB

B) diseases of the cardiovascular system and kidneys, pathogenetically associated with GB

C) target organ damage

D) any concomitant HD diseases

14. Which of the following is not associated clinical condition:

A) ischemic stroke

B) hypertrophic cardiomyopathy

B) diabetic nephropathy

D) myocardial infarction

15. Which of the pathologies of the heart is considered associated clinical condition in GB:

A) chronic heart failure

B) ischemic cardiomyopathy

B) mitral valve insufficiency

D) aortic valve insufficiency

16. Which of the conditions does not reflect kidney damage in HD and is not an associated clinical condition:

A) diabetic nephropathy

B) serum creatinine >133 μmol/l for men and

> 124 μmol/l for women

B) chronic kidney disease

D) bilateral stenosis of the renal arteries

17. Which of the following is associated

clinical condition in GB:

A) Alzheimer's disease

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B) diabetic retinopathy

B) vegetative-vascular dystonia

D) dissecting aortic aneurysm

18. How is pulse blood pressure calculated:

A) GARDEN - DBP

B) (SBP + DBP) / 2

C) (SBP - DBP) / heart rate

D) this is the SBP measured during the study of the pulse on

radial artery

19. What age is considered a risk factor

poor prognosis for GB:

A) over 65 years old

B) men over 55 years old, women over 65 years old

C) women over 55 years old, men over 665 years old

D) age has no prognostic value

20. What is the value of the content of total cholesterol

elevated in individuals without cardiovascular disease:

A) > 6.5 mmol/l

B) > 5.5 mmol/l

C) > 5.0 mmol/l

D) > 3.0 mmol/l

21. What level of LDL-C is elevated in persons without

cardiovascular diseases:

A) > 3.0 mmol/l

B) > 2.5 mmol/l

C) > 5.0 mmol/l

D) > 1.0 mmol/l

22. Which of the following values of HDL-C level in more in line with normal

A) 0.4-0.6 mmol / l

B) 0.6-0.8 mmol/l

C) 0.8-1.0 mmol/l

D) 1.0-1.2 mmol/l

78

23. What value of the level of triglycerides in the blood is considered upper limit of normal:

A) 1.5 mmol/l

B) 1.6 mmol/l

C) 1.7 mmol/l

D) 1.8 mmol/l

24. Which of the following options is the most corresponds to the normal state of metabolism:

A) TG 5.4 mmol/l; LDL cholesterol 2.9 mmol/l; blood glucose 7.9 mmol/l; waist 106 cm

B) TG 2.0 mmol/l; LDL cholesterol 4.0 mmol/l; blood glucose 5.0 mmol/l; waist 90 cm

C) TG 1.5 mmol/l; LDL cholesterol 2.3 mmol/l; blood glucose 5.5 mmol/l; waist 87 cm

D) TG 1.7 mmol/l; LDL cholesterol 3.4 mmol/l; blood glucose 3.8 mmol/l; waist 120 cm

25. Which of the criteria for metabolic syndrome is main:

A) dyslipidemia

B) violation of carbohydrate metabolism

B) abdominal obesity

D) AG

26. To which risk group would you classify the patient if him: AH 1 degree, the patient is a smoker, suffers obesity, type 2 diabetes, complicated by diabetic nephropathy:

A) I (low)

B) II (medium)

B) III (high)

D) IV (very high)

27. Patient V., 70 years old, had 2 heart attacks 20 and 10 years ago. On examination, no complaints, BP 150/92 mm Hg, TG 1.8 mmol/l,

79

LDL cholesterol 2.8 mmol/l, blood glucose 4.2 mmol/l. Sick regularly taking antihypertensives and lipid-lowering drugs. Which risk group would you it was taken:

A) I (low)

B) II (medium)

B) III (high)

D) IV (very high)

28. Patient M., 48 years old, has high normal blood pressure; five years ago, he was diagnosed with type 2 diabetes. Which risk group You will take this patient:

A) I (low)

B) II (medium)

B) III (high)

D) IV (very high)

29. What value of body mass index indicates the presence

overweight:

A) 22 kg / m 2

B) 26 kg / m 2

C) 31 kg / m 2

D) 36 kg / m 2

30. When should a patient be advised

lifestyle change:

A) all GB patients

B) with the ineffectiveness of drug therapy

C) in the presence of damage to target organs

D) if blood pressure does not exceed 150/90 mm Hg. Art.

31. Choose the wrong statement:

A) in all patients with hypertension, it is necessary to achieve

gradual decrease in blood pressure to target levels, starting

with minimal doses of drugs followed by

dose increase and/or addition of a new drug

B) you can not use more than two antihypertensive drugs

drugs to prevent unwanted

80

drug interactions and risk reduction

side effects

C) it is recommended to use rational

combinations of antihypertensive drugs

D) for patients with a slight increase in blood pressure and

low or moderate risk at the start of treatment

be selected as monotherapy

32. What class of antihypertensive drugs does not belong to

to the main group of medicines for the treatment

GB patients:

A) angiotensin- II receptor blockers

B) calcium antagonists

) α- blockers

D) β- blockers

33. The mechanism of action of drugs from the groups of inhibitors APF is that they:

A) prevent the conversion of renin to angiotensin- I

B) prevent the conversion of angiotensin-I to angiotensin II

B) block angiotensin receptors

D) prevent the breakdown of angiotensin- II

34. In what situation is the prescription contraindicated? ACE inhibitors:

A) chronic heart failure

B) diabetic nephropathy

B) bilateral stenosis of the renal arteries

D) atrial fibrillation

35. Which of the following drugs does not apply to class of ACE inhibitors:

A) enalapril

B) captopril

B) perindopril

D) ascoril

81

36. Advantage of angiotensin 1 receptor blockers type before ACE inhibitors is that the first of them:

A) not contraindicated during pregnancy

B) do not cause dry cough

C) more effective in lowering blood pressure

D) are more studied drugs

37. Which of the following drugs refers to class of angiotensin type 1 receptor blockers:

A) captopril

B) candesartan

B) carvedilol

D) xymelagatran

38. Increased risk of developing hyperkalemia when taking drugs that block the RAAS is associated with:

A) elimination of the influence of aldosterone on transport and excretion of ions in the nephron tubules

B) the effect of these drugs on Na + / K + - ATPase vascular endothelial cell membranes

C) a decrease in renal blood flow due to decrease in systemic blood pressure and, as a result, weakening ion release

D) the presence in the molecule of K + ions falling into blood flow during drug metabolism

39. Selectivity of β- blockers is determined by:

A) the ratio of the degrees of blockade β1-adrenergic receptors of the heart β1-adrenergic receptors of vessels

B) the ratio of the degrees of blockade of β1-adrenergic receptors and β2-adrenergic receptors

C) the ratio of the degrees of blockade of β - adrenergic receptors and α - adrenergic receptors

D) the ratio of the degrees of blockade of β1-adrenergic receptors in the cardiovascular system and β1-adrenergic receptors other organs and systems

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40. An absolute contraindication to the appointment of β-blockers is:

A) pregnancy

B) chronic heart failure

C) atrioventricular blockade of the 1st degree

D) bronchial asthma

41. Which of the following drugs is antihypertensive:

A) allohol

B) bisoprolol

B) formoterol

D) paracetamol

42. Diuretics of which group are most indicated for long-term management of patients with GB:

A) thiazide and thiazide-like

B) loop

B) aldosterone antagonists

D) vasopressin receptor blockers

43. Which of the following drugs is not diuretic:

A) amrinone

B) eplerenone

B) indapamide

D) hydrochlorothiazide

44. Choose a combination of antihypertensive drugs, which is not rational:

A) β -blocker + non-dihydropyridine AK

B) ACE inhibitor + diuretic

) α -blocker + β-blocker

D) ACE inhibitor + calcium antagonist

45. Choose a combination of antihypertensive drugs, Which one do you think is preferable?

A) lisinopril + valsartan + spironolactone

83

B) enalapril + propranolol + doxazosin

C) indapamine + perindopril + amlodipine

D) methyldopa + propranolol + amlodipine

46. Choose a statement that does not match participation kidneys in the pathogenesis of hypertension:

A) decreased renal perfusion reduces excretion salts and water, which leads to an increase in the basic vascular tone

B) decreased perfusion of the kidneys at the initial stage promotes hyperactivation of the renal RAAS system

C) in all patients with long-term GB, there is an increase in plasma renin concentration blood, which makes ACE inhibitors the drug of choice in treatment of elderly patients

D) activation of the renal RAAS system is due to hypertrophy of the juxtaglomerular apparatus, accompanied by increased production of renin

47. Choose the statement that is most correct characterizing GB:

A) HD is a multifactorial disease, in origin of which are involved genetic mechanisms and environmental factors

B) HD is a disease in which an increase in blood pressure due to pathology of internal organs (kidneys, heart, vessels)

C) HD is a hereditary disease

D) HD is a disease caused by age. involution of the cardiovascular system

48. Which disease is less often accompanied by the development of AG:

A) pheochromocytoma

B) Itsenko-Cushing's disease

B) severe chronic heart failure

D) diffuse toxic goiter

84

49. Below what values is it not recommended to reduce blood pressure:

A) SBP < 140 mm Hg, DBP < 90 mm Hg.

B) SBP < 130 mm Hg, DBP < 80 mm Hg.

C) SBP < 120 mm Hg, DBP < 75 mm Hg.

D) SBP < 110 mm Hg, DBP < 70 mm Hg.

50. How many main classes of antihypertensive drugs are there

drugs:

A) 4

B) 5

AT 6

D) 7

51. Which of the following options is the most

meets the definition of resistant hypertension:

A) AH, not amenable to correction by changing the image

life

B) if with the simultaneous appointment of three antihistamines

different classes fail to reduce blood pressure to the target

levels

C) the same as symptomatic hypertension

D) the same as uncontrolled hypertension

52. Choose an answer that is not characteristic

clinical feature of patients with resistant hypertension:

A) obesity

B) young age

B) SD

D) chronic kidney disease

53. Which of the following does not cause

pseudoresistance:

A) incorrect technique for measuring blood pressure

B) low patient adherence to treatment

B) white coat effect

D) initially higher blood pressure before the start of drug therapy

therapy

85

54. Regular intake of any of the following

drugs does not lead to poor BP control:

A) non-narcotic analgesics

B) oral contraceptives

B) erythropoietin

D) antacids

55. The most common cause of resistant hypertension is:

A) stenosis of the renal arteries

B) hyperparathyroidism

B) Cushing's syndrome

D) pheochromocytoma

56. Which of the following is not the most common

cause of resistant hypertension

A) obstructive sleep apnea

B) primary aldosteronism

B) coarctation of the aorta

D) diseases of the renal parenchyma

57. Hypertensive crisis is:

A) increase in SBP $\geq$ 40 mm Hg. for a period of 1 hour.

B) an acute pronounced increase in blood pressure,

accompanied by clinical symptoms

requiring an immediate controlled reduction

for the purpose of preventing or limiting POM

C) increase in SBP up to 180 mm Hg.

D) this is a temporary increase in SBP above 140 mm Hg. at

people without hypertension

58. What distinguishes complicated hypertensive crisis from uncomplicated:

A) higher blood pressure levels

B) development of acute clinically significant POM

C) the presence of clinical symptoms

D) occurs in patients with resistant hypertension

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59. What can complicate a hypertensive crisis:

A) brain stroke

B) dissecting aortic aneurysm

B) acute left ventricular failure

D) all of the above

60. Which of the drugs used for relief of hypertensive crisis, has both oral, and parenteral medicinal form:

A) enalaprilat

B) dibazol

B) captopril

D) nifedipine

Answers to test tasks

1-d 11-c 21-a 31-b 41-b 51-b
2-d 12-c 22-d 32-c 42-a 52-b
3-b 13-b 23-c 33-b 43-a 53-d
4-in 14-b 24-in 34-in 44-a 54-d
5-in 15-a 25-in 35-g 45-in 55-a
6-d 16-d 26-d 36-b 46-c 56-c
7-b 17-d 27-d 37-b 47-a 57-b
8-in 18-a 28-in 38-a 48-in 58-b
9-a 19-b 29-b 39-b 49-d 59-d
10-a 20-c 30-a 40-g 50-b 60-g