MINISTRY OF HEALTH OF UKRAINE

ODESA NATIONAL MEDICAL UNIVERSITY

Faculty: medical №1
Department of propaedeutics of internal diseases and therapy

APPROVED BY.

Vice-rector for scientific and pedagogical work

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_____ 2023

METHODOLOGICAL DEVELOPMENT
FOR A LECTURE ON THE DISCIPLINE

Faculty, course: dentistry, 3
Discipline: Internal medicine

Approved:
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Lecture No. 1 «Arterial hypertension. Hypertensive disease (essential arterial hypertension). Symptomatic hypertension. Etiology. Pathogenesis. Hypertensive crises. Principles of prevention and treatment. Changes in the oral cavity in hypertension. »

Actuality of theme. Among cardiovascular diseases, arterial hypertension (AH) ranks first in prevalence. It belongs to the "diseases of civilization". Its prevalence among the adult population is within 20-25%. Hypertension is a leading risk factor for coronary heart disease, stroke and kidney failure. According to the data of the statistical department of the Ministry of Health of Ukraine, in 1997, an elevated blood pressure level was registered in 13.4% of Ukrainian residents, which in absolute terms amounts to almost 5.5 million men. This indicator does not correspond to the true prevalence of hypertension (V.N. Kovalenko and co-authors), which in Ukraine is 20-24% of the adult population. Therefore, hypertension remains undiagnosed in almost half of patients.

The "rule of half" is typical for AG. About 50% of people do not know about their blood pressure increase. Of those who know, half are not treated. Therefore, only about 25% of patients take drugs to lower blood pressure. Only 12-13% receive effective hypotensive therapy. A similar picture is observed in Ukraine.

The purpose of the lecture (goals):

1. Master the basics of identifying characteristic symptoms and syndromes in patients with hypertension.
2. Get acquainted with modern research methods, as well as with changes in indicators of laboratory and instrumental research methods for these diseases.
3. Get acquainted with the general principles of treatment of this category of patients.
4. To learn the basics of deontology and medical ethics when examining patients with arterial hypertension and hypertensive disease.

Basic concepts: Arterial hypertension, micro- and macroangiopathy, hypertensive crisis, blood pressure, pulse.

Determine the main tasks for applicants at the department of propaedeutics of internal diseases, which are:

1) method of clinical examination of patients;

2) symptomatology of diseases;

3) basics of laboratory and instrumental diagnostic studies for diseases of internal organs;

4) when acquainting applicants with the main nosological units (diseases) and syndromes, teach the ability to use, for example, the data obtained during the examination of the patient for the diagnosis of specific diseases.

Basic concepts: patient examination, patient complaints, propaedeutics, palpation, percussion, auscultation,

Plan and organizational structure of the lecture.
Determination of the educational goal.
Providing positive motivation.
Presentation of the lecture material according to the plan:
Summary of the lecture. General conclusions.
The lecturer's answer to possible questions.
Tasks for self-training.

Content of the lecture material
Arterial hypertensionthere is an increase in SBP up to 140 mm Hg and above or DBP up to 90 mm Hg. Art. and higher, if such an increase is stable, that is, it is confirmed by repeated blood pressure measurements (at least 2+3 times on different days for 4 weeks).
According to the latest recommendations of the European Society of Hypertension and the European Society of Cardiology (2007), several BP levels are distinguished (Table 1).

Classification of arterial hypertension according to the level of blood pressure

Categories	**SAT, mmHg**	**DAT, mm Hg**
Optimal	< 120	< 80
Normal	< 130	< 85
High normal	130-139	85-89
Hypertension 1 degree 2 degree 3 degree		 59 and/or 90-99 79 and/or/100-109 and/or ≥ 110

Isolated systolic hypertension	≥ 140	≤ 90

To establish the stage of hypertension, a classification based on target organ damage is used (Table 2).

Classification of arterial hypertension according to target organ damage

Stage I	Objective signs of organic damage to organs- there are no targets
Stage II	There are objective signs of damage to target organs without symptoms on their part or dysfunction. Hypertrophy of the left ventricle (according to the ECG, Echocardiography, X-rays) or generalized narrowing retinal arteries, or microalbuminuria and/or a small increase in the concentration of creatinine in plasma (in men 115-133 mmol/l, in women 107-124 mmol/l) Damage to the carotid arteries - thickening of the intima media0.9 mm or the presence of an atherosclerotic plaque
Stage III	There are objective signs of damage to target organs their symptoms and dysfunction
Heart	Myocardial infarction Heart failure of IIA-III century.
Brain	A stroke Transient ischemic attack Acute hypertensive encephalopathy Vascular dementia
Fundus	Retinal hemorrhages and exudates with disc swelling optic nerve or without
Kidneys	Concentration of creatinine in plasma in men > 133 μmol/l, in women > 124 μmol/l
Vessels	Dissection of the aorta Occlusive lesion of peripheral arteries

Risk factors:

The occurrence and course of hypertension are closely related to the presence of risk factors.

Age. There is a positive relationship between blood pressure and age. In general, the level of DBP increases until the age of 55, after which it changes little. SBP constantly increases with age.

Sex. Average blood pressure levels and the prevalence of hypertension in young and middle-aged women are somewhat lower than in men. Later, this dependence changes up to reversion.

Heredity is one of the most influential factors in the future development of hypertension. A close correlation was found between blood pressure of the closest relatives (parents, brothers, sisters). Body weight. The correlation between body weight and blood pressure level is direct, significant and stable. Excess weight is associated with a 2- to 6-fold increase in the risk of hypertension.

Alimentary factors. Table salt. Its use beyond the physiological norm is positively correlated with the blood pressure level.

Other trace elements. There is an inverse relationship between the use of K^+, Ca^{2+} and Mg^{2+} and the blood pressure level.

Macronutrients: proteins, fats, carbohydrates, dietary fibers. Predominance in the diet of vegetables and fruits, fish, white chicken meat, limiting the use of animal fats, cholesterol and sweets helps to reduce blood pressure.
Coffee and caffeine. Recovery of the pressor effect of caffeine occurs a few hours after drinking coffee. Hypertension is three times more common among those who drink 1 to 5 cups of coffee per day compared to those who do not drink coffee at all.

Smoking. Nicotine sharply increases blood pressure even in heavy smokers. The effect of each cigarette lasts about 30 minutes. Already in the 1st minute after its firing, SBP increases by 15 mmHg. Art., and on the 4th - by 25 mmrt. Art. At the same blood pressure levels, stroke and coronary heart disease occur in smokers 2-3 times more

often than in non-smokers.

Psychosocial factors. Stress contributes to an increase in blood pressure. However, it is not yet known whether long-term stress leads to a long-term increase in blood pressure.

Socio-economic status. In countries with a developed economy, there is an inverse relationship between JSC and the level of education, income and professional status. At the same time, in the countries of the transition and pre-transition period, hypertension is more common among the well-off strata of the population.

Physical activity. People who lead a sedentary lifestyle have a 20-50% higher risk of hypertension than physically active people. Physical exertion during the performance of professional duties contributes to an increase in blood pressure, and physical activity during leisure time does the opposite. Regular aerobic exercise is a fairly effective means of non-pharmacological treatment of hypertension.

Risk stratification.

A strategy based on determining the overall risk is recognized as the most useful for the patient. The latter refers to the risk of complications that this patient has due to increased blood pressure, as well as the presence of concomitant cardiovascular diseases, damage to target organs and the main risk factors listed in the table. 3.
There are several risk groups (Table 4).
People with blood pressure less than 140/90 mm Hg belong to the normal risk group. Art., without additional risk factors. A group of people who have an additional (to the usual) risk of complications, but it is relatively low, is selected as a moderate risk group. It consists of patients with hypertension of the 1st and 2nd degree, who have no more than 2 risk factors for cardiovascular diseases. Blood pressure increase to 180/110 mm Hg. and more increases the likelihood of complications, and such patients are already a high-risk group. The presence of damage to target organs or concomitant cardiovascular diseases indicates a high or very high risk of complications.

Indicators used to assess the total risk of complications

Main risk factors

Age (for men > 55 years, for women > 65 years)

High pulse pressure in the elderly (60 mm Hg)

Smoking

Dyslipidemia (total cholesterol >5.0 mmol/L or low-density lipoprotein cholesterol >3.0 mmol/L or high-density lipoprotein cholesterol <1.0 mmol/L in men and <1.2 mmol/L in women, or triglycerides 1.7 mmol/l
Fasting plasma glucose is 5.6 - 6.9 mmol/l

Violation of glucose tolerance

Abdominal obesity (waist circumference >102 cm in men and >88 cm in women)

Cardiovascular diseases in the family history (up to 55 years in men, up to 65 years in women)

Damage to target organs

🚌 Hypertrophy of the left ventricle. ECG criteria: Sokolov-Lyon index > 38 mm, Kornelsky>2440 mm/ms; echocardiographic criteria: left ventricular mass index for men > 125 g/m2, for women > 110 g/m^2

Ultrasound signs of vessel wall thickening (carotid artery intima-media thickness >0.9 mm) or the presence of an atherosclerotic plaque

The speed of the pulse wave is 12 m/s

Index of blood pressure leg/brachial artery < 0.9

A slight increase in creatinine concentration (in men 115-

133 μmol/l, in women – 107-124 μmol/l)

Decrease in estimated glomerular filtration rate (<60 ml/min/1.73 m2) or estimated creatinine clearance (<60 ml/min)

Microalbuminuria (30-300 mg/day)

Associated diseases

Diabetes

Fasting plasma glucose > 7.0 mmol/l

Blood plasma glucose 2 hours after exercise > 11.0 mmol/l

Cerebrovascular diseases (ischemic stroke, cerebral hemorrhage, transient ischemic attack)

Heart diseases (MI, angina pectoris, revascularization surgery, CHF IIA-III)

Kidney diseases (diabetic nephropathy, renal failure - serum creatinine in the blood in men >133 μmol/l, in women >124 μmol/l), proteinuria 300 mg/day
Occlusive lesions of peripheral arteries

Severe retinopathy (hemorrhages, exudates, swelling of the discus nerve)

Risk stratification for assessing prognosis in patients with hypertension.

Factors stratification	Blood pressure level, mm Hg				
	Normal SAT 120- 129, DATE 80-84	Vis. normal SAT 130- 139 DATE 85-89	AG 1 st. SAT 140- 159 DATE 90-99	AG 2 st. SAT 160-179 DATE 100-109	AG 3 st. SAT ≥ 180 DAT ≥ 110
There is none factors risk	Average risk in the population		low	moderate	moderate
1-2 factors risk	low	low	moderate	moderate	high

Plural factors risk, injury bodies targets, MS, CD	moderate	high	high	high	very high
cardiac vascular disease	very high	very high	very high	very high	very high

According to*Framingham criteria*, the terms "low", "moderate", "high" and "very high" risk mean the 10-year probability of cardiovascular complications (fatal and non-fatal) - < 15%, 15-20%, 20-30% and >30% , respectively.

*Preventive measures for hypertension*aimed at the introduction of a healthy lifestyle and the correction of identified risk factors.
They provide for:

limiting the use of table salt; decrease in body weight with its excess;

limiting the use of alcoholic beverages; reducing the use of saturated fats, sweets and cholesterol; smoking cessation;

increasing physical activity during leisure hours; psycho-emotional relief and relaxation.

Mandatory examination of all patients with elevated blood pressure:

1) anamnesis,

2) physical examination,

3) laboratory-instrumental examination:

4) blood pressure measurement on both arms;

5) blood pressure measurement on the legs,

6) auscultation of the heart, vessels of the neck, projection points of the renal arteries;

7) general blood test;

8) general urinalysis;

9) creatinine level in blood plasma with calculation of creatinine clearance or glomerular filtration rate;

10) the level of potassium and sodium in blood plasma;

11) blood plasma sugar level;

12) the level of cholesterol and triglycerides in blood plasma;

13) ECG registration;

14) fundus ophthalmoscopy;

15) ultrasound examination of the heart and kidneys.

Hypertensive crises

Hypertensive crisis- this is a sudden significant increase in blood pressure from a normal or elevated level, which is almost always accompanied by the appearance or strengthening of disorders on the part of target organs or the autonomic nervous system.

The criteria for a hypertensive crisis are::

sudden onset; significant increase
in blood pressure;

the appearance or increase of symptoms from the target organs.

Classification of crises of the working group of the Ukrainian Society of Cardiologists

(1999).

Depending on the presence or absence of damage to the target organs and the need for urgent blood pressure reduction, the following are distinguished:

- *complicated crises*(with acute or progressive damage to target organs, pose a direct threat to the patient's life, require an immediate, within one hour, blood pressure reduction);
- *uncomplicated crises*(without acute or progressive damage to target organs, pose a potential threat to the patient's life, require rapid

- within a few hours - a decrease in blood pressure).

Complicated hypertensive crises.

The course is characterized by clinical signs of acute or progressive damage to the target organs. The latter can be irreversible (myocardial infarction, stroke, aortic dissection) or reversible (Table 5). Such crises are always accompanied by the appearance or intensification of symptoms from the target organs. They are dangerous for the patient's life and require pressure reduction for a period of several minutes to one hour. Treatment is carried out in the conditions of the intensive care ward with the use of parenteral administration of antihypertensive drugs.

This category also includes those cases of a significant increase in blood pressure, when the threat to life does not occur due to damage to the target organs, but due to bleeding, most often - in the postoperative period.

Complicated hypertensive crises.

Myocardial
infarction Stroke
Acute dissecting aortic aneurysm Acute left

ventricular failure Unstable angina

Arrhythmias (tachycardia paroxysms, atrial fibrillation and flutter, ventricular extrasystole of high gradations)

Transient ischemic attack Eclampsia
Acute hypertensive encephalopathy
Bleeding (including nasal bleeding)

Uncomplicated hypertensive crises are characterized by the absence of clinical signs of acute or progressive damage to target organs, but they pose a potential threat to the patient's life, since untimely assistance can lead to complications and death. Such crises are accompanied, as a rule, by the appearance or intensification of symptoms from the target organs (intense headache, heart pain, extrasystole) or from the autonomic nervous system (autonomic-vascular disorders, tremors, frequent urination).

Increase in blood pressure to 240 mmHg. Art. or DBP up to 140 mmHt. Art. should also be considered as a hypertensive crisis, regardless of whether symptoms from the target organs have appeared or not, since it is dangerous for every patient. A significant increase in pressure in the early postoperative period due to the risk of bleeding is also dangerous.

All these clinical manifestations require pressure reduction for several hours. Hospitalization is not mandatory. Treatment is carried out by taking antihypertensive drugs by mouth or intramuscular (subcutaneous) injections.

Treatment of patients with arterial hypertension.

The goal of treatment-decrease in mortality from cardiovascular diseases. The higher the blood pressure, the higher the risk of stroke, coronary heart disease and premature death. Prolonged hypertension leads to damage to target organs, including left ventricular hypertrophy, heart failure (HF), kidney damage up to the development of kidney failure, etc. All associated risk factors are also subject to treatment: obesity, dyslipidemia, and others. Treatment (non-medicinal and medicinal) should be started as early as possible and should be carried out continuously, as a rule, throughout life.

Non-drug therapy:

decrease in body weight in the presence of obesity;
reducing alcohol consumption;

regular performance of dynamic physical exercises; limiting the use of table salt to 5.0 g per day (1/2 teaspoon of salt); sufficient intake of potassium, calcium and magnesium;

reducing the consumption of saturated fats and cholesterol;
smoking cessation.

Non-drug treatment is also called lifestyle modification, because its basis is the elimination of bad habits (smoking, excessive alcohol consumption), increasing physical activity, limiting salt in food, etc.

Drug therapy:

First-line drugs:

diuretics; ACE inhibitors;

long-acting calcium antagonists; angiotensin II
receptor antagonists; β-blockers;

First-line drugs, when used in equivalent doses, lead to the same reduction in blood pressure and a significant reduction in the risk of cardiovascular complications.

Second-line drugs:

a1-adrenoblockers; rauwolfia
alkaloids;

central a2-agonists (clonidine, guanfacine, methyldopa); agonists of imidazoline receptors (moxonidine).

Evidence of an effective reduction in the risk of cardiovascular disease with the use of

second-line drugs is much smaller compared to first-line drugs.

Recommended combinations of antihypertensive drugs.

Diuretic	ACE inhibitor
Diuretic	Angiotensin II receptor blocker
Beta blocker	Dihydropyridine antagonist calcium
ACE inhibitor	Calcium antagonist
Angiotensin II receptor blocker	Calcium antagonist

WHO experts (1999) formulated recommendations for the use of acetylsalicylic acid. It is believed that acetylsalicylic acid in small doses (75–100 mg per day) is advisable to be used in patients with hypertension, in whom BP is well controlled by medication and who have a high risk of coronary heart disease, but at the same time there is no high risk of bleeding from the gastrointestinal tract tract or other hemorrhages.
Treatment of crises.

*Uncomplicated crises*In the case of the development of an uncomplicated crisis, as a rule, there is no need for intravenous administration of drugs. They use drugs that have a rapid antihypertensive effect, or intramuscular injections. In such cases, the use of clonidine is effective. Clonidine should not be prescribed to patients with impaired cardiac conduction, especially those receiving cardiac glycosides. Nifedipine is also used, which has the ability to reduce total peripheral resistance, increase cardiac output and renal blood flow. A decrease in blood pressure is observed already 15–30 minutes after taking it, the antihypertensive effect persists for 4–6 hours. The ACE inhibitor captopril lowers blood pressure already 30–40 minutes after taking it due to rapid absorption in the stomach. Intramuscular injections of clonidine or dibazol can also be used. In the case of vegetative disorders, sedative drugs are effective, in particular benzodiazepine derivatives, which can be used peros or in the form of intramuscular injections, as well as pyroxan and droperidol.

Drugs for the treatment of uncomplicated crises

Preparation	**Doses and method of administration**	**Beginning action, min.**	**Side effects**
Clonidine	0.01% 0.5-2.0 v/m 0.075-0.3 mg buts	30-60	Dry mouth, drowsiness. Contraindicated with AV blockade
Nifedipine	10-20 mg peros or sublingually	15-30	Headache, tachycardia, redness, angina pectoris
Captropril	12.5-50 mg peros or sublingually	15-45	Hypotension in patients with renin-dependent hypertension
Prazosin	0.5-2 mg buts	30	Orthostatic hypotension
Propranolol l	20-80 mg buts	30-60	bradycardia, bronchoconstriction
Dibazole	1% 3.0-5.0 in/in or 4.0-8.0 in/m	10-30	More effective in combinations with others antihypertensive means
Pyroxan	1 % 2.0-3.0 in/m	15-30	Orthostatic hypotension
Diazepam	0.5% 1.0-2.0 in/m	15-30	Dizziness, drowsiness
Furosemide	40-120 mg reros or IV	5-30	Orthostatic hypotension, weakness
Torasemide	10-100 mg reros or IV	5-30	Orthostatic hypotension, weakness

Parenteral therapy of complicated crises

Preparation	Doses and method introduction	Beginning action, min.	Duration actions	Notes
Vasodilators				
Nitroprusside sodium	in/in drop by drop 0.25-10 μg/kg/min (50-10 mg in 0 250-50 ml 5% 0 glucose)	Immediately	1-3 min.	Suitable for urgent decrease in blood pressure at any crisis. Enter only for help special the dispenser at monitoring of JSC
Nitroglycerin	in/in drop by drop 50-100 μg/min	2-5 min.	3-5 min.	Especially effective at acute heart attack, heart attack myocardium
Verapamil	IV 5-10 mg, you can continue in/interspersed with 3-25 mg/year	1-5 min.	10-30 min.	Do not use in patients with HF and those who are being treated beta-blockers

Enalaprilat	IV 1.25-5 mg	15-30 min	6 years.	Effective at acute insufficiency of the left ventricle
Nimodipine	in/interspersed with, 15 mcg/kg/year., then 30 mg/kg/h	10-20 min.	2-4 years.	At subarachnoid hemorrhages
Antiadrenergic drugs				
Labetalol	intravenously 20-80 mg with speed 2 mg/min or IV fusion 50-300 mg	5-10 min.	5-10 min.	Effective at most crises. Not apply in patients with HF
Propranolol	in/interspersed with 2-5 mg with rapid at a rate of 0.1 mg/min.	10-20 min.	10-20 min.	Mostly with dissection of the aorta and coronary syndrome
Esmolol	80 mg bolus 250 µg/kg/min infusion	1-2 min.	1-2 min.	It is a drug choice at dissection of the aorta and postoperative hypertension

Preparation	**Doses and method introduction**	**Beginning action, min.**	**Duration actions**	**Notes**

Clonidine	IV 0.5-1.0 ml or in/m 0.5-2.0 ml 0.01 % cal.	5-15 min	5-15 min	It is undesirable to cerebral stroke
Phentolamine	IV or IV 5-15 mg (1-3 ml 0.5% solution)	1-2 min.	1-2 min.	Mostly with pheochromocytoma, withdrawal syndrome clofelin
Other drugs				
Furosemide	IV, 40-80 mg bolus	5-30 min.	6-8 years	Mostly with hypertensive acute crises cardiac or renal insufficiency
Torasemide	10-100 mg IV			
Magnesium sulfate	IV, bolus 5-20 ml of 25% solution	30-40 min	3-4 years	With convulsions, eclampsia

Changes in the oral cavity in patients with GC.

With GC with frequent crises in the oral cavity, changes in the form of vesicovascular syndrome are sometimes detected. It manifests itself in the appearance of hemorrhagic blisters on the mucous membranes of the soft palate, tongue, less often on the gums and the mucous membrane of the cheek, mainly due to its trauma (pathological bite, the main symptom of which is the destruction of teeth). In the pathogenesis of this syndrome, a change is important the permeability of capillary vessels and the condition of the basal membrane of the mucous membrane of the oral cavity. Patients have a tendency to bleeding. In the period of

exacerbation of the disease (hypertensive crisis), treatment, especially tooth extraction, is contraindicated.

General material and mass-methodological support
lectures:
work program of the academic discipline
synopsis (plan-summary) of the lecture
multimedia presentation of the lecture

Questions for self-control:

1. Determination of arterial hypertension.
2. Hypertensive disease (essential arterial hypertension). Definition
3. Symptomatic hypertension. Etiology. Pathogenesis.
4. Hypertensive crises.
5. Principles of prevention and treatment.
6. Changes in the oral cavity in hypertension

Main:

1. 1. Propaedeutic of internal medicine: textbook / Y.I. Sick of it, O.G. YavorSCy, E.M. Neiko, etc.; edited by O.G.Yavorscy. – 6th ed., ed. and reported – K.: VSV "Medicine", 2020. – 552 p. + 12 p. color.
2. Methods of objective examination in the clinic of internal diseases: textbook posib. / O.O. Yakymenko, O.E. Kravchuk, V.V. Klochko and others. – Odessa, 2013. – 154 p.
3. Diagnostic methods in the clinic of internal medicine: textbook / A.S.Svintsitscy. - K.: VSV "Medicine", 2019. – 1008 p. + 80 p. color.

Additional:

1. Methods of examination of a therapeutic patient: textbook. posib. / S.M. Andreichyn, N.A. Bilkevych, T. Yu. Chernets. – Ternopil: TSMU, 2016. – 260 p.
2. Inquiry and physical examination of the patient of therapeutic profile: Textbook for students of III-IV courses of medical universities / V.E. Neiko, I.V. Tymkiv, M.V. Bliznyuk [et al.]. – Iv.-FrankivSC : IFNMU, 2016. – 142 p.
3. Yepishyn A.V. Propaedeutic of internal diseases with care for therapeutic patients /AB. Yepishin K. - 2015. 768s.
4. Kovaleva O.M. Propaedeutic of internal medicine / OM. Kovaleva, NA Safargalin-Kornilova // K.: Medicine 2010 - 750s.
5. Macleod's Clinical Examination / Ed. G.Douglas, F.Nicol, C.Robertson.– 13th ed.– Elsevier. 2013. – 471 p.
6. Bates' Guide to Physical Examination and History Taking /Ed. Lynn S. Bickley, Peter G. Szilagyi. – Wolters Kluwer, 2017. – 1066 p.

Electronic information resources

1. http://moz.gov.ua – Ministry of Health of Ukraine
2. www.ama-assn.org – American Medical Association / American Medical Association
3. www.who.int – World Health Organization
4. www.dec.gov.ua/mtd/home/ - State Expert Center of the Ministry of Health of Ukraine
5. http://bma.org.uk – British Medical Association
6. www.gmc-uk.org - *General Medical Council* (*GMC*)
7. www.bundesaerztekammer.de – German Medical Association
8. https://onmedu.edu.ua/
9. https://onmedu.edu.ua/kafedra/propedevtiki-vnutrishnih-hvorob-ta-terapii/
10. http://pvb. odessa. ua/index. html

Lecture No. 2 «Gastritis Ulcer disease of the stomach and duodenum. Intestinal diseases (chronic enteritis, colitis, non-specific ulcerative colitis). Pancreatitis. Cholecystitis. Gallstone disease. Chronic hepatitis. Liver cirrhosis. The role of the dentist in prevention.»

Actuality of theme. I

The purpose of the lecture (goals):

Basic concepts:

Determine the main tasks for applicants at the department of propaedeutics of internal diseases, which are:

1) method of clinical examination of patients;

2) symptomatology of diseases;

3) basics of laboratory and instrumental diagnostic studies for diseases of internal organs;

4) when acquainting applicants with the main nosological units (diseases) and syndromes, teach the ability to use, for example, the data obtained during the examination of the patient for the diagnosis of specific diseases.

Basic concepts: patient examination, patient complaints, propaedeutics, palpation, percussion, auscultation,

Plan and organizational structure of the lecture.
Determination of the educational goal.
Providing positive motivation.
Presentation of the lecture material according to the plan:
Summary of the lecture. General conclusions.
The lecturer's answer to possible questions.
Tasks for self-training.

Content of the lecture material

The main clinical manifestations of peptic ulcer disease (UPC) are pain and dyspeptic syndromes (syndrome of gastric and intestinal dyspepsia). The pain is characterized by rhythmicity and is often associated with eating. Depending on the meal, early, late, as well as "hungry" and night pains are distinguished. Early pains (after 0.5-1 hour) are characteristic of ulcers located in the body and upper parts of the stomach, often with damage to the cardiac and subcardial parts, the pain appears immediately after eating. Antral stomach ulcers and duodenal ulcers are characterized by late (after 1.5-2 hours) and night pains, which can also be "hungry" because they decrease or even stop after eating. With peptic ulcer disease of the DPC, the pain occurs on an empty stomach (often at night) and is reduced or completely eliminated after taking food and antacid drugs, cholinolytics. The duration of pain depends on the speed of evacuation of food. The intensity of pain depends on the activity of the ulcer process, the involvement of the serous layer in it, the severity of the inflammatory process around the ulcer, and individual pain sensitivity. Irradiation of pain in uncomplicated VH is usually absent. The appearance of radiating pain indicates, as a rule, the complication of the ulcer process by penetration into 46 neighboring organs, the development of the inflammatory process (perigastritis, periduodenitis), the presence of accompanying diseases (cholecystitis, pancreatitis, etc.) and is accompanied by a violation or disappearance of the usual daily rhythm of pain. Exacerbation of VH, as a rule, continues from several days to 6-8 weeks (in some cases up to 3-4 months) and is replaced by a phase of remission. The seasonality of the disease is more often manifested by spring and autumn exacerbations (in recent years it is not so indicative). Thus, the distinguishing features of the pain syndrome in VH are as follows: - periodicity of periods of exacerbation and remission; - rhythmicity associated with eating; - reduction of pain after vomiting, taking food, alkalis, cholinolytics; - seasonality (spring and autumn exacerbations); - increasing nature of pain, as the disease progresses. Pain in HC is often combined with heartburn, belching, nausea and vomiting.

The clinical picture of chronic pancreatitis (CP) is characterized by pain, signs of pancreatic exocrine insufficiency (dyspepsia, diarrhea, symptoms of impaired absorption, weight loss), symptoms of diabetes and a number of complications. Pain syndrome: pain in the left hypochondrium is more common, but it can also be ulcerative, according to the type of left-sided renal colic, "right hypochondrium" syndrome with jaundice syndrome, dysmotor in combination with a feeling of heaviness after eating and vomiting, common - without a clear localization. Sometimes patients complain of "high pains", interpreting them as "pain in the ribs", in the lower parts of the left half of the chest. Given that the head of the pancreas is located to the right of the midline, pain in the epigastrium is possible, including in its right half. With the progression of exocrine insufficiency of PP in patients with CP, secondary enteritis (enteropancreatic syndrome) is added. At the same time, the pains in the epigastrium and the left hypochondrium subside slightly and the cramping pain around the navel dominates. Patients with alcoholic pancreatitis often experience pain in the right hypochondrium due to the presence of hepatopathies,

cholecystopathies, and duodenitis. Irradiation of pain. The most characteristic radiation of pain is in the left half of the chest from the back, in the left half of the lower back according to the "left half belt" type, or according to the "full belt" type. Patients often emphasize the girdling nature of pain with figurative expressions - "sawing in half", "pulling with a rope", etc. Sometimes patients note only lower back pain. Irradiation to the left and up is also possible - to the left arm, collarbone, under the left shoulder blade, behind the sternum, in the precardial area, in the left half of the lower jaw. Duration of pain. Pain can be paroxysmal with the duration of attacks from several hours to two or three 48 days, constant with paroxysmal intensification or constant. In the latter case, they talk about the so-called painful form of pancreatitis, the pain of which is probably related to the involvement of nerve endings in the inflammatory process. At the same time, it is necessary to differentiate pancreatitis from pancreatic cancer. With pancreatic necrosis, pain decreases due to "deadening" of nerve endings, their loss of sensitivity. Intensity and nature of pain. With hyperenzymatic (that is, with the phenomenon of enzymes "getting into the blood") pancreatitis, the pain is usually very intense, as in these variants there is pronounced swelling of the pancreas with stretching of its capsule. According to the hypoenzymatic variant, acute pancreatitis (AP) and CP occur in the early stages (before the development of severe exocrine insufficiency). Pains are often so intense that they lead to the development of various mental changes in patients with CP. With HP, painful shock is possible. With secondary pancreatitis (which developed as a result of biliary or gastroduodenal pathology), the intensity of pancreatic pain often "overshadows the pain" associated with the main, i.e., primary disease. Less pronounced pain in alcoholic CP due to the analgesic effect of alcohol, euphoria in some patients. With hypoenzymatic pancreatitis, the size of the pancreas decreases, and the capsule tension also decreases. This leads to a weakening of the pain syndrome until it disappears (previously, these variants of pancreatitis were called latent). The nature of the pain can be different - from aching to cutting, "burning", "burning", etc. Time of onset of pain. Pain occurs or worsens after eating - after 30-40 minutes. It is at this time that the food lump is evacuated from the stomach, and the gastrointestinal tract actively produces enzymes and bicarbonates to neutralize and process the acidic content entering the gastrointestinal tract. During the period of functional ascent, there is a rush of blood to the PZ with stretching of its capsule. In addition, with an increase in the volume of pancreatic secretion at the height of digestion in patients with obstructive CP, the intraductal pressure increases, the walls of the ducts stretch, and the pain intensifies. Rarely, patients are bothered by night pains, which make the doctor think about peptic ulcer disease. These pains in pancreatitis are associated with a violation of the production of PP bicarbonates to "repay" the nocturnal peak of secretion of hydrochloric acid and its entry into the DPK. Pain is provoked by eating a large amount of food, fatty, smoked, spicy food, fresh vegetables and fruits, carbonated drinks. That is, the increase in pain is associated with the stimulating effects of PP, increased intestinal peristalsis (the latter is especially pronounced in hypofermentative pancreatitis). For differential diagnosis, it is important that pain in pancreatitis is provoked by taking alcohol, sweet, freshly baked food, which is not characteristic of other diseases of the digestive organs. With biliary pancreatitis, pain can be provoked by food with

choleretic properties (eggs, etc.), due to increased biliopancreatic reflux. Pain also increases after morphine injection due to spasm of the sphincter of Oddi.
According to the International Classification (Rome Consensus, 1999), the wording "dysfunctional disorders of the biliary tract" (DRBT) is proposed. Dysfunction of the gallbladder and dysfunction of the sphincter of Oddi are considered. In the International Classification of Diseases (ICD - 10), only "dyskinesia of the gall bladder and cystic duct" and "spasm of the sphincter of Oddi" are highlighted under the heading K83.4 under the rubric K82.8. Therefore, according to the Rome consensus, DRBT is defined as a complex of functional disorders observed for more than 3 months, the main clinical symptoms of which are recurrent attacks of severe or moderate pain lasting 20 minutes or more, localized in the epigastrium or right hypochondrium (biliary type); in the left hypochondrium, which decrease when leaning forward (pancreatic type); belted (combined type). Pain may be associated with eating, appear at night, be accompanied by nausea and/or vomiting. 51 Violations of synchronicity in the work of the HM and the sphincter apparatus are at the basis of dysfunctional disorders of the biliary tract and are the cause of the formation of clinical symptoms. The leading role in the emergence of dysfunctional disorders of the biliary tract belongs to psychogenic factors - psycho-emotional overload, stressful situations. Dysfunctions of MH and CO can be a manifestation of neurosis. DRBT occurs mainly in women. People of young age, undernourished, asthenic physique, with an emotionally unstable psyche are more often ill. With the hyperkinetic form of LV dysfunction and/or the hypertonic form of CO dysfunction, colicky pains appear periodically in the right hypochondrium with radiation to the back, under the right scapula, right shoulder, less often to the region of the epigastrium, the heart, and are aggravated by deep breathing. Pains are short-term and usually occur after mistakes in the diet, intake of cold drinks, physical exertion, stressful situations, sometimes at night. Irritability, increased fatigue, sweating, headaches, tachycardia and other symptoms of a neurotic nature are noted. With hypokinetic and hypotonic dysfunction of the biliary tract, dull pains in the right hypochondrium, a feeling of pressure, and distension are noted, which increase when the body is tilted. Frequent symptoms are nausea, bitterness in the mouth, bloating, constipation. When examining the skin, the skin is of normal color, excess body weight is often noted. On palpation, there is moderate pain in the projection of the liver (place of intersection of the outer edge of the right rectus abdominis muscle with the lower edge of the liver).
Diarrheal syndrome (from the Greek diarrhoia — "diarrhea") is a set of clinical signs characterizing pathologically accelerated release of the intestines in combination with changes in the consistency and quality of stool. Diarrhea is a pathological condition that is understood to mean a change in the shape of the stool (watery or mushy liquid masses) and the frequency of defecation (more than 3 times a day) with a volume of more than 200 ml. There are four pathogenetic variants of diarrhea: Secretory diarrhea caused by direct stimulation of the secretion of water and electrolytes into the intestinal lumen. This type of diarrhea is characterized by frequent loose stools with a volume of more than 1000 ml per day. It occurs first of all in bacterial and viral infections (cholera, salmonellosis, rotavirus and HIV infections), as well as in hormonally active tumors - apudoms

(gastrinoma, VIPoma secreted vasoactive intestinal peptide, carcinoid). Diarrheal syndrome is similar to that of cholera, however, it lasts for a long time, with persistent hypokalemia. Osmotic diarrhea is caused by an increase in osmotic pressure in the lumen of the intestine, which leads to the release of water into the lumen of the intestine. The volume of liquid stools is from 500 to 1000 ml per day. Osmotic diarrhea occurs in chronic pancreatitis with exocrine insufficiency, fermentopathies, gluten enteropathy, Whipple's disease, dumping syndrome, bacterial contamination of the small intestine, use of osmotic drugs (magnesium sulfate, lactulose). Exudative diarrhea is caused by exudation into the intestinal lumen of blood, mucus, pus against the background of inflammatory changes in the mucous membrane. The volume of liquid feces is 200–500 ml per day. This type of diarrhea develops in ulcerative colitis, Crohn's disease, ischemic and pseudomembranous colitis, colon tumors, radiation colitis, dysbacteriosis, diverticulosis of the large intestine with diverticulitis. Motor diarrhea is characterized by accelerated transit of a food lump against the background of active intestinal motor function. As a rule, with this form of diarrhea, polyfecality is not observed: the volume of liquid fecal masses per day is no more than 200–300 ml. Motor diarrhea is typical for irritable bowel syndrome (IBS), functional diarrhea, intestinal dysbiosis, observed in patients after vagotomy.

General characteristics of coprostasis. Coprostasis syndrome (constipation, constipation) is a frequent companion of diseases of the gastrointestinal tract. Constipation is a long (more than 48 hours) delay in emptying the bowels, which is accompanied by difficulty in the act of defecation, as well as a small amount (less than 100 g per day) or increased hardness of feces, a feeling of incomplete bowel emptying. Etiology and pathogenesis. The main reason for the development of coprostasis syndrome is a violation of the activity of the large intestine, which manifests itself mainly in the form of secretory and motor disorders. The phasing of the formation and advancement of fecal masses changes. Normally, the amount of stool should be adequate to the consumed diet, on average its weight is 200 g per day. However, with the consumption of a large amount of vegetable fiber, the weight of the stool can increase to 500 g per day, since the intake of 1 g of fiber with food causes an increase in the volume of fecal masses by 20 g. The main function of the large intestine is the formation of dense fecal masses from the liquid contents of the ileum and accumulating them to a certain amount with subsequent removal from the body during the act of defecation. Therefore, absorption of water and electrolytes (chlorine anions, sodium cations) continues in the large intestine, although its volume is much smaller compared to the small intestine — only 1-1.5 liters. Bicarbonates and potassium ions are actively secreted in the large intestine. Water makes up to 60-80% of the volume of normal stool, with an average liquid consumption of 2-2.5 liters per day, only about 100 ml of water per day is released with feces. The secretory and absorptive capabilities of the large intestine are much smaller than those of the small intestine, which is explained by the presence of an additional surface of the mucous membrane in the latter due to villi, microvilli and crypts. Therefore, constipation is characteristic of the pathology of the large intestine, while diarrhea is more characteristic of diseases of the small intestine. Coprostasis, caused by diseases of the organs of the gastrointestinal tract, is most often

associated with disorders of the motor function of the large intestine. Slowing down the passage of intestinal contents occurs according to the hypermotor (spastic) or hypomotor (atonic) mechanism. With hypermotor or spastic constipation, the peristalsis of the large intestine is increased due to non-propulsive contractions, a significant number of retrograde peristaltic waves are noted. At the same time, the lumen of the intestine narrows, deep and frequent haustration is pronounced. Hypomotor, or atonic, constipation occurs twice as often as hypermotor. However, it dominates among patients of the older age group. Atrophic processes of the intestinal wall, significant bacterial colonization of the mucous membrane, age-related atony of the muscles of the abdominal wall and pelvic floor are factors for the occurrence of constipation in the elderly. The cause of hypomotor constipation is a pronounced decrease in the motor function of the large intestine, which leads, in some cases, to its complete atony. Hypomotor and atonic disorders are observed in congenital anomalies of the development of the colon (megacolon, dolichosigma), chronic colitis, anorectal diseases, obstruction of the lumen of the intestine by a stone or tumor. At the same time, atonic and atrophic disorders are combined with each other. The cavity of the large intestine is stretched, haustration is reduced or absent, peristalsis is not determined. In addition to diseases of the large intestine, constipation is quite characteristic of the pathology of other organs of the gastrointestinal tract. The reflex effect on the intestines in organic damage to the stomach and hepatobiliary system often leads to coprostasis. In addition to diseases of the gastrointestinal tract, constipation can be associated with pathology of the endocrine system, female genital organs, pregnancy, toxic effects, the use of drugs, psychogenic reasons or irrational nutrition.

General material and mass-methodological support
lectures:
work program of the academic discipline
synopsis (plan-summary) of the lecture
multimedia presentation of the lecture

Questions for self-control:

1. Gastritis Definition.
2. Ulcer disease of the stomach and duodenum. Definition.
3. Intestinal diseases (chronic enteritis, colitis, non-specific ulcerative colitis).
4. Pancreatitis. Definition.
5. Cholecystitis. Definition.
6. Diseases of the biliary tract. Etiology.
7. Types of diarrhea.
8. General characteristics of coprostasis.

Used sources:

Lecture No. 3 « Rheumatic diseases. Rheumatic heart disease. Systemic vasculitis. Diffuse connective tissue diseases. Features of the dentist's tactics.**»**

Actuality of theme. To acquaint students with the etiology, pathogenesis and clinic of diffuse connective tissue diseases, systemic vasculitis. Consider the clinical features of rheumatoid arthritis, ankylosing spondylitis, systemic lupus erythematosus, idiopathic polymyositis, systemic scleroderma. Determine diagnostic standards, approaches to treatment and prevention of systemic connective tissue diseases and systemic vasculitis. To substantiate the role of the dentist in the prevention of complications and the choice of treatment tactics for diffuse connective tissue diseases, infectious endocarditis and heart defects.

The purpose of the lecture (goals):

1. Determine the preliminary clinical diagnosis of GRL and CRCS, which requires special patient management tactics,
2. to assess the impact of dental pathology and diseases of the maxillofacial system on the occurrence and course of GRL and CRHS.
3. to determine the role and place of the dentist in the prevention of GRL, CRHS and their complications;
4. to determine the previous syndromic diagnosis of GRL, CRCS, the dentist's tactics for GRL and CRCS.
5. to provide primary medical care for complications of GRL and CRHS.
6. main directive documents of the Ministry of Health of Ukraine regarding the standards of diagnosis, treatment and prevention of GRL and CRHS;
7. issues of classification, clinical diagnosis of GRL, CRHS and their complications;
8. principles of modern drug and non-drug therapy of GRL, CRHS and their complications;
9. the role of the dentist in the prevention of GRL, CRHS and their complications; issues of sanitary and educational work.

Determine the main tasks for applicants at the department of propaedeutics of internal diseases, which are:

Basic concepts: To determine the main tasks for applicants at the department of propaedeutics of internal diseases, which are:

1) method of clinical examination of patients;

2) symptomatology of diseases;

3) basics of laboratory and instrumental diagnostic studies for diseases of internal organs;

4) when acquainting applicants with the main nosological units (diseases) and syndromes, teach the ability to use, for example, the data obtained during the examination of the patient for the diagnosis of specific diseases.

Basic concepts: patient examination, patient complaints, propaedeutics, palpation, percussion, auscultation,

Plan and organizational structure of the lecture.
Determination of the educational goal.
Providing positive motivation.
Presentation of the lecture material according to the plan:
Summary of the lecture. General conclusions.
The lecturer's answer to possible questions.
Tasks for self-training.

Content of the lecture material

Acute rheumatic fever (ARF) –acute inflammatory disease connective tissue with the predominant localization of the process in the cardiovascular system, which develops in connection with an acute infection caused by β-hemolytic streptococcus of group A in susceptible persons, mainly in children and adolescents aged 7-15 years.

Classification.

I. Rheumatic fever without involvement of the heart

II. Rheumatic fever involving the heart

III. Rheumatic chorea

Diagnostic criteria.

(T.D. Jones, 1944, revised by the American Heart Association and recommended by the WHO, 1992) :

*Big criteria:*cardite, polyarthritis, small chorea, erythema annulare, subcutaneous rheumatic nodules

Small criteria:

a)clinical: previous rheumatism or rheumatic heart disease, arthralgia, fever.

b)paraclinical: indicators of the acute phase of inflammation, erythrocyte sedimentation rate; C-reactive protein, leukocytosis; prolongation of the P-R interval on the ECG;

*Data confirming streptococcal infection:*increasing titers anti-streptococcal antibodies, group A streptococci hanging from the pharynx, recently transferred scarlet fever.

The presence of 2 major criteria and signs of a previous streptococcal infection or 1 major, 2 minor and signs of a previous streptococcal infection allows a diagnosis to be maderheumatic fever.

Treatment.

1st stage - inpatient.

All patients with acute rheumatic fever are indicated for hospitalization with bed rest during the first 2-3 weeks of the disease, followed by a gradual expansion of the movement regime, the appointment of a diet containing a sufficient amount of complete proteins with a restriction of sodium chloride intake, fluid intake, an increase in the content of potassium, magnesium and vitamins in the diet

Etiotropic therapy is carried out with benzylpenicillin in a daily dose of 1,500,000 - 4,000,000 IU in older children and adolescents and 600,000 - 1,000,000 IU in younger children for 10 - 14 days with the subsequent transition to the use of durant forms of drugs - bicillin-5 or benzathine benzylpenicillin. Bicillin-5 is prescribed in doses of 1500000 IU for teenagers and 400000-600000 IU for children once every 2 weeks, and benzathine benzylpenicillin 600000-800000 IU for children and 1500000-2400000 IU for teenagers intramuscularly every 2 weeks. In cases of allergic reactions to penicillin preparations, the appointment of macrolides is indicated.

Pathogenetic treatment – nonsteroidal anti-inflammatory drugs (acetylsalicylic acid, indomethacin, sodium diclofenac, nimesulide, etc.). Acetylsalicylic acid (aspirin) is prescribed in medium doses (for children under 12 years of age, 0.2 g/kg/day, no more than 1-2 g in 3-4 doses, for teenagers - up to 3-4 g per day). With severe carditis - prednisolone 1-2 mg/kg/day in 3 doses for 2-4 weeks with gradual withdrawal and subsequent transition to aspirin.

In the presence of symptoms of insufficient blood circulation - appropriate therapy. In the treatment of chorea - calmness, silence, as indicated by phenobarbital, bromine preparations, other means prescribed by a pediatric neurologist.

*2nd stage*curation of the patient involves referral to a specialist rheumatological sanatorium or polyclinic to continue the treatment started in the hospital.

3rd stage- dispensary observation is carried out and carried out preventive measures.

Secondary prevention– prevention of relapses and progression diseases with the formation of new vices - carried out under dispensary supervision by regular administration of prolonged penicillins - bicillin-5 or benzathine benzylpenicillin. If the patient is allergic to penicillins, secondary prevention is carried out with macrolides in cycles of 10 days each month.

Children who suffered rheumatism without carditis receive secondary prevention until the age of 18, in the presence of carditis - until the age of 25 or more.

With a formed heart defect, secondary prevention of rheumatism is carried out for life.

Heart defectsuch an organic lesion of the heart valves is called him partitions, large vessels and myocardium, which leads to heart failure, blood stagnation in veins, tissues and organs, depletion of arterial blood. There are simple, combined and combined heart defects.

All patients with heart defects are subject to referral for surgical treatment in appropriate specialized institutions. In cases of impossibility or postponement of surgical treatment, such patients are subject to outpatient examination and treatment at their place of residence. The examination can be carried out in district polyclinics, and if necessary, additional examinations can be carried out with the help of city

cardiology dispensaries and diagnostic centers. In cases of HF progression, patients are sent to cardiology hospitals at their place of residence. Outpatient control and inpatient treatment are carried out before surgical treatment, or if the latter is impossible.

Diagnostics.

Mandatory studies: collection of complaints and history, clinical examination, blood pressure measurement, laboratory examination (general blood and urine tests, ALT, AST, bilirubin, creatinine, cholesterol, blood glucose, potassium, sodium, SRP; titers ASLO, AH, RF), 12-lead ECG, echocardiography, Doppler study, X-ray of OGK.*Additional studies:* cardiac catheterization and/or coronary ventriculography, daily ECG monitoring.

Treatment.

Mandatory- surgical treatment of heart disease; penicillin prophylaxis during the year, treatment of HF depending on the type (systolic or diastolic), anticoagulants - in patients with a permanent form of atrial fibrillation, thromboembolic complications in the anamnesis, with mitral stenosis and prosthetic heart valves. Mandatory control of the international normalized ratio (INR).

If it is impossible to determine the INR, determine the prothrombin index. Patients need constant dispensary supervision with examination at least 1-2 times a year. In the presence of HF, they are subject to dispensary examination at least once every 2 months, or more often, if such a need is determined by the clinical situation.

Requirements for dietary prescriptions and restrictions.

When overweight, the energy value of food is limited. Refusal of smoking, restriction of alcohol consumption. In the presence of CHF - limit the daily intake of sodium chloride: less than 3 g per day with preclinical and moderate CHF (do not use salty foods, do not add salt to food during consumption, less than 1.5 g per day with significant CHF (III-IVFC) A diet enriched with ω-3 polyunsaturated fatty acids is recommended.

Requirements for the regime of work, rest, rehabilitation.

In the presence of HF, it is recommended to limit physical activity according to the degree of HF. Regular physical activity (slow walking, low-intensity exercise) according to the patient's functional capabilities ("comfortable" but regular movement mode). Hypothermia and night work are not recommended.

Changes in the oral cavity in rheumatic disease.

The course of GRL and CRHS can be complicated by impaired blood circulation (stage II, III according to M.D. Strazhesko and V.Kh. Vasylenko). In this case, hyperemia of the mucous membrane, or cyanosis of varying degrees of expression, periodontal disease, the development of ulcers that do not heal for a long time, bleeding are determined in the oral cavity. This is due to blood microcirculation disorders and oral tissue hypoxia.

Patients have a burning sensation, pressure, swelling of the mucous membrane of the oral cavity, neuralgic toothache. Gingivostomatitis, desquamative glossitis, candidamycosis of the mucous membrane of the oral cavity, ischemic necrosis with sequestration of bone structures develop.

B in milder cases, there is an exacerbation of chronic stomatitis with a permanent nature of their course, especially in people with an untreated oral cavity and chronic tonsillitis.

B stages of blood circulation decompensation, the mucous membrane of the mouth is pale with a cyanotic tint in the area of the palatal arches and the gum margin. Significant cyanosis of the lips and the nearest areas of the skin. The mucous membrane of the cheeks, the tongue is swollen, the soft tissues are pasty. Ulcers appear, especially in areas of increased traumatization (pathological bite, prostheses, overhanging edges of fillings). Ulcers can be filled with necrotic detritus, a sharp putrid smell is detected

3 the mouth Mucous membrane around ulcers without reactive inflammatory changes. Changes in the epithelium of the tongue are also signs of cardiovascular insufficiency.

Desquamation of filiform papillae can be seen on the back of the tongue. They

become smooth and shiny ("polished tongue"). These changes in the tongue can be the reason for the burning of the tongue and the patient's visits to the dentist.

A dentist at his workplace should remember the above-mentioned features of the occurrence and course of GER and CRHS in order to prevent serious complications, as well as to provide emergency care in a timely manner.

Vasculitis is a heterogeneous group of diseases in which inflammation of the blood vessel wall causes its damage, which can lead to bleeding and restriction of blood flow, and, as a result, to ischemia and necrosis of the tissues supplied by the affected vessels. In some categories of vasculitis, there is also characteristic tissue damage that is not associated with vascular inflammation.

Vasculitis generally divided into 2 groups:

- **infectious**(caused directly by the invasion and reproduction of a pathogenic microorganism in the vessel wall)

-non-infectious

In actuality**classification of non-infectious vasculitis**in addition to the main categories, which primarily take into account the diameter of the affected vessels (large, medium, small and of different caliber) or organ specificity (single-organ vasculitis), vasculitis, which until now was called secondary, is distinguished.

Nomenclature of vasculitis:

1) vasculitis of large vessels(Takayasu's arteritis, giant cell arteritis)

2) vasculitis of vessels of medium caliber(polyarteritis nodosa, Kawasaki disease)

3) vasculitis of small vessels:

-vasculitis associated with antibodies to the cytoplasm of neutrophils (ANCA): microscopic polyangiitis, granulomatous polyangiitis (Wegener's) , eosinophilic granulomatosis with polyangiitis (Cherzha-Strosc),

- vasculitis associated with immune complexes: disease associated with antibodies to the basement membrane, cryoglobulinemic vasculitis of small vessels of the skin, IgA-associated vasculitis (Schönlein-Henoch), hypocomplementemic urticarial vasculitis (anti-C1q-associated vasculitis)

4) vasculitis of vessels of various caliber(vasculitis in Behcet's disease, vasculitis in Kogan's syndrome)

5) single-organ vasculitis(cutaneous leukocytoclastic vasculitis, cutaneous vasculitis, primary vasculitis of the central nervous system, isolated aortitis)

6) vasculitis in systemic disease (vasculitis in SLE (lupus vasculitis), rheumatoid vasculitis, sarcoid vasculitis)

7) **vasculitis of probable etiology**(HCV-associated cryoglobulinemic vasculitis

Vasculitis of small vessels:mainly small interstitial arteries, arterioles, capillaries and venules are affected. There are 2 forms:

1) **vasculitis associated with antibodies to the cytoplasm of neutrophils**(ANCA) — immune deposits in small amounts or absent, and ANCAs directed against myeloperoxidase (MPO-ANCA) or proteinase-3 (PR3-ANCA) are present ("ANCA-negative" cases are also present);

2) **immune complex vasculitis**— moderate or significant deposits of immunoglobulins and/or complement components are present in the vascular wall (glomerulonephritis is common).

Hemorrhagic vasculitis(Schönlein-Henoch's disease) is a systemic vascular disease with predominant damage to capillaries, arterioles and veins, mainly skin, joints, kidneys, abdominal cavity.

Etiology and pathogenesis. The disease mainly occurs in children and adolescents, less often in adults, after an infection, the administration of vaccines and serums, as well as in connection with medical intolerance, cooling. The most likely autoimmune genesis is damage to the epithelium of vessels circulating with immune complexes.

Clinic. The triad of symptoms includes:

1) *Purple*(symmetric rashes on the buttocks, extremities)

The skin (simple) variant is the most common, which is characterized by skin hemorrhages with a symmetrical rash on the limbs, buttocks, and less often on the trunk. A papular-hemorrhagic rash appears. When pressed, the elements of the rash disappear.

2) Arthralgia or arthritis

The articular variant occurs together with the skin variant or a few days after it and is manifested by pain in large joints. After a few days, the pain goes away, but with a new wave it may appear again.

3) *Abdominal syndrome*(characteristic hemorrhagic rashes on the mucous membrane of the gastrointestinal tract, mesentery, peritoneum, which leads to perforation with the development of peritonitis). It is clinically manifested by intestinal colic-type pains, vomiting and bloody stools. It passes after a few days. It can often be observed with proteinuria, macrohematuria, as well as microhematuria.

Diagnostics. It is based on the presence of a characteristic triad of symptoms or hemorrhagic rashes on the skin.

Treatment. It is carried out with heparin, which is injected subcutaneously after 4 hours under the control of the number of platelets. For abdominal syndrome, glucocorticoids.

Essential cryoglobulinemic vasculitis

Essential cryoglobulinemic vasculitis is an immunocomplex disorder of small vessels with cryoglobulinemic deposits with skin and renal glomeruli damage.

Etiology and pathogenesis. The cause of this disease can be hepatitis B and C viruses, prolonged hypothermia. Cryoglobulins-immunoglobulins or immunoglobulin-containing complexes, which at low temperatures precipitate, forming a gel; when the temperature rises, they become soluble again.

Clinic. The patients are mainly women over 50. The main symptom is a rash on the skin of the shins and feet, which is accompanied by itching. Skin changes can be initiated by exposure to cold, pressure on the skin. The rash is accompanied by arthralgias and myalgias. At the site of skin purpura, narcosis and trophic ulcer may develop. Kidney dysfunction such as glomerulonephritis and pulmonary vasculitis is possible.

Diagnostics. The diagnosis is confirmed by the presence of cryoglobulins in the serum.

Churg-Strauss syndrome

Allergic vasculitis or Cherja-Strauss granulomatous angiitis is a granulomatous inflammation of small and medium vessels, mainly of the skin, peripheral nerves, and lungs. People in their 30s and 40s are sick.

Clinic. It is characterized by the clinical picture of bronchial asthma and high eosinophilia. In the prodromal period (may last up to 10 years), patients may have various allergic manifestations, which include rhinitis, bronchial asthma, and hay fever.

Diagnostics. It is based on clinical and morphological data. The diagnosis is confirmed in a hospital using the results of a biopsy of damaged tissues.

Microscopic polyangiitis (polyarteritis)

Microscopic polyangiitis (polyarteritis) is a systemic necrotizing vasculitis affecting the capillaries, venules and arterioles of the lungs, kidneys, and skin.

Clinic and diagnosis. Microscopic polyangiitis is mainly observed in middle-aged men. The appearance of fever, resistant to antibiotic therapy, weakness, weight loss, arthralgia is noted. A petechial rash with ulcerative-necrotic changes may appear on the skin. Necrotizing pulmonary capillaries develops with shortness of breath, hemoptysis and possible severe pulmonary bleeding. In contrast to Wegener's granulomatosis, radiologically, infiltrates without disintegration are detected in the lungs. Development of hemorrhagic or rapidly progressive fibrosing alveolitis is possible. Damage to the glomeruli is manifested by proteinuria and hematuria, the development of nephrotic syndrome is possible. Persistent hypertension is uncharacteristic. In the case of rapidly progressing glomerulonephritis after 3-6 months. a picture of kidney failure develops.

Wegener's granulomatosis

Wegener's granulomatosis is a giant cell granulomatous-necrotic vasculitis with predominant damage to the upper and lower respiratory tract, lungs, and kidneys.

Clinic and diagnosis

The disease begins at any age, but more often in 40-45 years. The upper respiratory tract is affected - ulcers, necrosis appear; lungs - infiltrates with decay; kidneys - glomerulonephritis.

Symptomatology: general symptoms of respiratory tract damage: cough, rhinitis, sinusitis, nosebleeds. X-ray of the lungs reveals bilateral rounded infiltrates with disintegration and formation of cavities.

Treatment. Etiotropic therapy is considered the most promising direction in the treatment of vasculitis. It is especially important for those diseases, the development of which is associated with certain infectious agents. Antimicrobial drugs, antivirals and intravenous immunoglobulin can contribute to the elimination of infectious agents that participate in the development of vasculitis or induce exacerbation of the pathological process. Instead, the appointment of specific etiotropic drugs for systemic vasculitis is limited due to the lack of clear etiological agents of the main nosological forms. Therefore, pathogenetic therapy is mostly carried out. The latter is currently aggressive and resembles immunosuppressive polychemotherapy of hematological diseases, which is clearly followed abroad, but has not yet spread in our country. The aggressiveness of therapy is determined not so much by the nosological form, but by the speed of progression of destructive changes in the vascular wall, the presence of visceritis, primarily kidney damage, and the activity of immune inflammation.

Currently, there are several stages in the treatment of systemic vasculitis:

1. Rapid and effective suppression of the immune response at the onset of the disease - induction of remission.
2. Long-term (at least 0.5-2 years) supportive therapy with immunosuppressants in doses sufficient to achieve clinical (vasculitis activity indices) and laboratory (ESR, C-RB, ANCA, Willebrand factor antigen) remission of the disease. Rapid suppression of the immune response in case of exacerbation of the disease.
3. Achieving stable, complete remission of vasculitis, determining the degree of damage to organs or systems of the body for the purpose of their correction, carrying out rehabilitation measures.

General material and mass-methodological support
lectures:
work program of the academic discipline

synopsis (plan-summary) of the lecture
multimedia presentation of the lecture

Questions for self-control:

1. Classification: rheumatic diseases.
2. Rheumatic heart disease.
3. Approach to the treatment of rheumatism.
4. Definition of acute rheumatic fever
5. Systemic vasculitis. Classification.
6. Systemic vasculitis. Etiology.
7. Diffuse connective tissue diseases.
8. Features of the dentist's tactics

Used sources:

Lecture No. 4 « Violation of hemostasis. Hemophilia. Thrombocytopenic syndromes. Pathogenesis. Diagnostics. Clinic. Complication. Principles of treatment. The role of the dentist in early diagnosis and prevention. Emergencies in the dentist's practice.**»**

Actuality of theme. Idiopathic thrombocytopenic purpura is one of the most common causes of acquired thrombocytopenia. The incidence of idiopathic thrombocytopenic purpura ranges from 1 to 13 per 100,000 population. Almost half of the patients are children. Among the adult population, women get sick more often. Among boys and girls, the disease occurs with the same frequency. Among pregnant women, idiopathic thrombocytopenic purpura occurs in 1-2 cases for every 1000 pregnancies, affecting both the body of the pregnant woman and the fetus.

Hemophilia is the most common hereditary hemorrhagic diathesis. Hemophilia A and hemophilia B are almost exclusively men. The inheritance of hemophilia C is not linked to gender. The incidence of hemophilia A is 1 case per 10,000 men, the incidence of hemophilia B is 1 per 50,000 men, and the incidence of hemophilia C is 1 per 1,000,000 population. Hemophilia is spread evenly among different races and ethnic groups.

Given the high prevalence of idiopathic purpura and hemophilia, as well as the danger posed by the characteristic hemorrhagic syndrome to the lives of patients, careful study of these diseases is an urgent medical task.

The purpose of the lecture (goals):

1. Master the basics of identifying characteristic symptoms and syndromes in patients suffering from hemophilia and thrombocytopenic syndrome.
2. Get acquainted with modern research methods, as well as with changes in indicators of laboratory and instrumental research methods for these diseases.
3. Get acquainted with the general principles of treatment of this category of patients.
4. Learn the basics of deontology and medical ethics when examining patients with hemophilia and thrombocytopenic syndrome

Basic concepts: Hemostasis, hemorrhagic diseases, hemophilia, thrombocytopenia, thrombocytopenia.

Determine the main tasks for applicants at the department of propaedeutics of internal diseases, which are:

1) method of clinical examination of patients;

2) symptomatology of diseases;

3) basics of laboratory and instrumental diagnostic studies for diseases of internal organs;

4) when acquainting applicants with the main nosological units (diseases) and syndromes, teach the ability to use, for example, the data obtained during the examination of the patient for the diagnosis of specific diseases.

Basic concepts: patient examination, patient complaints, propaedeutics, palpation, percussion, auscultation,

Plan and organizational structure of the lecture.

1. Determination of the educational goal.
2. Providing positive motivation.
3. Presentation of the lecture material according to the plan:
4. Summary of the lecture. General conclusions.
5. The lecturer's answer to possible questions.
6. Tasks for self-training.

Content of the lecture material

A common feature of the diseases and syndromes included in this group are manifestations of bleeding: from light "visual" forms to fatal bleeding that requires urgent measures.
Hemorrhagic manifestations can appear both as the main symptoms of the disease, and can be the result of hemostasis disorders in numerous diseases: cardiovascular, pulmonary, infectious, immune, neoplastic, during surgical interventions, injuries, transfusion therapy, drug intolerance, etc.

In the X revision of the International Classification of Diseases, hemorrhagic diseases and syndromes are distinguished in the rubric D65-D69

D65 disseminated intravascular coagulation
D66 hereditary deficiency of factor VIII
D67 hereditary factor IX deficiency
D68 other disorders of blood coagulation
D68.0 Willebrand's disease
D68.1 – hereditary factor XI deficiency
D68.2 – hereditary deficiency of other blood coagulation factors
D68.3 – hemorrhagic disorder caused by anticoagulants circulating in the blood
D68.4 – acquired deficiency of clotting factor
D68.8 - other specified disorders of blood coagulation
D68.9 – disorder of blood coagulation, unspecified
Purpura and other hemorrhagic conditions (D69)
D69.0 - allergic purpura
D69.1 – quality defects of platelets
D69.2 - other non-thrombotopenic purpura
D69.3 – idiopathic thrombocytopenic purpura
D69.4 - other primary thrombocytopenia
D69.5 – secondary thrombocytopenia
D69.6 – thrombocytopenia, unspecified
D69.8 - other specified hemorrhagic conditions
D69.9 – hemorrhagic condition, unspecified

Diagnosis of the main forms of hemorrhagic diseases is possible thanks to the method of complex differential analysis of the clinical picture of the disease and laboratory research of the structural and functional links of hemostasis.

Working pathogenetic classification of hemorrhagic diseases and syndromes.

1. Caused by a violation of vascular and platelet hemostasis:
1.1. Thrombocytopenia
1.2. Thrombocytopathies.
2 Caused by a violation of plasma (coagulation) hemostasis:
2.1. Lack of coagulation factors
2.1.1. Hereditary coagulation defects: (VIII - hemophilia A; IX - hemophilia B; XI - hemophilia C and others).
2.1.2. Acquired disorders of coagulation hemostasis (phylloquinovitaminosis and other dysprothrombinemias, hemorrhagic disease of newborns, when treated with anticoagulants of indirect (4-osikumarin derivatives) and direct (heparin, hirudin) action, fibrinolytics, DVZ - syndrome).
2.2. Excess or deficiency of anticoagulants:
- hyperheparinemia;
- hyperantithrombinemia;
- antiphospholipid syndrome (primary, secondary - with SLE);
- thrombophilia (AT III deficiency)

3. Caused by vascular disorders:
3.1. Congenital and hereditary forms:
- Randu-Weber-Osler disease;
- Kasabach-Merritt syndrome;
- Ellers-Danlo syndrome;
- Marfan's syndrome, etc.
3.2. Acquired: hemorrhagic microthrombovasculature, vascular purpura, idiopathic, Schamberg's disease, congestive with hemosiderosis, senile (Bateman's disease), steroid in systemic scleroderma (CRST - syndrome), etc.

Algorithm of clinical diagnosis of hemorrhagic diatheses.

The basis of the diagnosis algorithm of GD is the recognition of the type of bleeding in a given patient based on the analysis of anamnestic data and clinical examination. There are 5 main types of bleeding (Barkagan Z.S., 1988).

I. Hematoma type

It is characterized by massive, intense, deep and very painful hemorrhages in the joints, muscles, subcutaneous and retroperitoneal tissue, peritoneum and subserous membrane of the intestine, which is accompanied by a clinical picture of abdominal disaster (appendicitis, intestinal obstruction, peritonitis, colic, etc.). Hematomas easily occur at injection sites, especially intramuscular ones. Upon examination, large joints are deformed, their contours are smoothed, mobility is limited. Hematoma syndrome is often combined with profuse spontaneous, post-traumatic and postoperative bleeding, which can be late: several hours after injury or surgery. Umbilical bleeding in newborns, nosebleeds, bleeding from the gums, gastrointestinal bleeding, hematuria are characteristic symptoms of this type.

II.Petechial-ecchymotic (bruising) type.

It is manifested by numerous point (petechiae) and spotted hemorrhages on the skin in the form of bruises and "hemorrhages" (ecchymoses). Their size and color are varied (from crimson-blue to green and yellow), which is associated with different times of occurrence of hemorrhages, giving the skin the appearance of "leopard skin". Petechiae and ecchymoses do not disappear when pressed, they easily occur when the microvessels of the skin are injured when squeezed by tight clothing ("printing"), with a cuff when measuring blood pressure ("cuff"), superficial cuts and scratches are accompanied by prolonged bleeding. Bleeding from the gums, gastrointestinal bleeding, menorrhagia and metrorrhagia are common.

III.Mixed (bruise-hematoma) type.

It differs from the second type in the prevalence of bruising and thickening of the skin in places of hemorrhagic penetration, which is accompanied by pain. It differs from the first type in the predominance of hematomas in the subcutaneous and retroperitoneal tissue, in the mesentery, subserous membrane of the intestine with liquid involvement in the joint process.

IV.<u>Vasculitic purple type</u>
It is characterized by hemorrhages in the form of a rash in combination with elements of erythema. Hemorrhages occur against the background of exudative-inflammatory changes, rise above the skin level, are compacted, often surrounded by a rim of pigmentation, sometimes necrotized, covered with a crust. Reverse development is slow, with long-term preservation of infiltration and pigmentation. Often there is a combination with immune and allergic manifestations: fever, arthralgias, erythema nodosum, urticaria, Quincke's edema, damage to the kidneys, intestines, lungs, enlargement of the spleen, etc.
IN.<u>Angiomatous type</u> - characterized by stubborn bleeding that often recurs with a certain localization (from vascular dysplasia). At the same time, there are no hemorrhages in the skin, subcutaneous tissue, and other tissues. Profuse nosebleeds are the most frequent. Rarely, the source of profuse bleeding is in the vessels of the stomach, intestines, and lungs. The detection of one or another type of bleeding in combination with the anamnesis data makes it possible to make a preliminary diagnosis of GD and outline an appropriate program of paraclinical studies. Thus, the hematoma type of bleeding is characteristic of coagulopathy (inherited or acquired disorders of coagulation hemostasis), the petechial-ecchymous type - for disorders of vascular and platelet hemostasis (thrombocytopenia, thrombocytopenia). A mixed type of bleeding from hereditary diseases is characteristic of Willebrand's disease, while the acquired genesis of these disorders is most often found in DVZ - syndrome. The vasculitic-purpuric type of bleeding is manifested by hemorrhagic microthrombovasculitis (Schönlein-Henoch disease), angiomatous-telangiectasia (Randyu-Weber-Osler disease), hemangiomas, mesenchymal dysplasia, etc.

Diagnostic criteria for various types of bleeding and their laboratory identification

Type of bleeding	The most likely diseases and syndromes		Tests that detect violations	Tests that give normal or close to normal indicators
	hereditary	acquired		
Hematoma	Hemophilia A and B (severe forms)	Immune inhibition of factors VIII and IX	Blood clotting time, prothrombin consumption, activated partial thromboplastin time, autocoagulation test (ACT),	Prothrombin time, thrombin time, bleeding time, vascular tests. Normal levels of factors I and XIII, adhesive and aggregation function of

			thromboplastin generation test	platelets are revealed
	I. Medium and easy forms:		Autocoagulation test, activated partial thromboplastin time, quantitative determination of the level of factors VIII and IX	The same, as well as blood clotting time, prothrombin consumption
II. Petechial-spotted	a) thrombocytopenia and thrombocytopenia	Thrombocytopenia and symptomatic thrombocytopenia	Counting the number of platelets, studying the adhesive-aggregation function of platelets and the reaction of release from them, bleeding time, vascular tests	Blood clotting time, autocoagulation test, activated partial thromboplastin time (APT), prothrombin time, thrombin time
	b) a mild form of Willebrand's disease	Immune inhibition of the Willebrand factor	Bleeding time, ristomycin-platelet aggregation, activated partial thromboplastin time, autocoagulation test	Platelet count, study of the adhesive and aggregation function of platelets, prothrombin time, thrombin time
	c) shortage of factors: VII (mild form)	Deficiency of the same factors in different combinations	Prothrombin time	All other tests

III. Mixed X, V, II	X, U, II		Prothrombin time, autocoagulation test, APTC.	Thrombin time, study of adhesive and aggregation function of platelets, etc. Functions
	I	Factor I deficiency in liver pathology	The same, as well as thrombin time, reduction of factor I, violation of the adhesive and aggregation function of platelets.	
	a) Willebrand's disease	Willebrand syndrome	Bleeding time, adhesiveness and ristocetin-platelet aggregation, APTC, autocoagulation test, thromboplastin generation test.	Thrombin time, prothrombin time, study of adhesive and aggregation function of platelets, factor UIII level
	b) severe deficiency of UII factor		Prothrombin time	All other tests
	c) deficiency of UIII factor	Inhibition of UIII factor, overdose with anticoagulants	Solubility of the clot in urea (complete) APTC, autocoagulation test, thrombin time, prothrombin time, blood coagulation time	All other tests Studies of I and XIII factors, thrombin time during treatment with indirect anticoagulants

		Overdose with fibrinolysis activators	Decreased level of factor I, APTC, ACT, thrombin time, blood coagulation time, increased fibrinogen degradation products, positive paracoagulation tests.	
		DVZ-syndrome (thrombohemorrhagia)	The number of platelets, all coagulation tests, detection of paracoagulation products, adhesive properties of platelets, reduction of factor I and actithrombin III, impaired fibrinolytic activity of blood.	Unsystematic separate tests in the phase of transition from hypercoagulation to hypocoagulation.
IU. vasculitic-purpuric		Hemorrhagic microthrombovasculitis, hemorrhagic fevers and other diseases	Positive paracoagulation tests, an increase in the level of factor I, a shift in ACT, in severe cases, the changes resemble DVZ-syndrome	All other tests

U. Angiomatous	Telangiectasia, family angiomatosis	Postoperative microangiodysplasias	The hemostat parameters are initially not disturbed, thrombocytopenia is rare	

1. Randu-Osler disease(hereditary hemorrhagic telangiectasias).
Congenital hemorrhagic telangiectasia (Randu-Osler disease) is an autosomal dominant disease characterized by multiple telangiectasias of the skin and mucous membranes, as well as a hemorrhagic syndrome of various localization. The disease occurs with a frequency of 1 case per 50,000 population (Guttmacher).

Nowadays, a genetic defect has been established for this disease. McDonald et al. (1994) and Shovlin (1994) found in some families of patients the Randu-Osler disease gene in the region of the 9th chromosome 9q33-34 (locus OWR1). The mechanism of realization of genetic defects in Randu-Osler disease has not been definitively identified. The dominant view is the congenital insufficiency of the mesenchyme, which causes the appearance of telangiectasias. The vascular wall is devoid of muscle and elastic fibers, consists almost entirely of endothelium itself and is surrounded by loose connective tissue. Venules and capillaries that form telangiectasias are sharply thinned, post-capillary venules are expanded and anastomose with arterioles through capillary segments (arterial-venular anastomoses are a characteristic feature of the disease). Degenerative changes in the mesenchyme ("thinning" of connective tissue), accumulation of leukocytes and histiocytes around blood vessels, underdevelopment of skin papillae and weak development of sweat glands, and a decrease in the number of hair follicles are also noted. Bleeding in Randu-Osler disease is caused by extreme fragility of small blood vessels. Along with this, in some patients, a violation of platelet function is also determined (Endo, Mamiya, Niitsu, 1984), activation of fibrinolysis. However, these changes are rarely observed and are not considered characteristic of Randu-Osler disease.

Clinical picture

Symptoms of the disease in the form of bleeding of various localization are manifested already in early childhood, even in the newborn period and persist throughout life. Pathognomonic sign of the disease is telangiectasia. They are small bright red, purple spots or vascular "spiders" or bright red nodules with a diameter of 1-7 mm that protrude above the surface of the skin. When pressed, the nodules turn pale and thus differ from other hemorrhagic manifestations. According to the frequency of localization, telangiectasias in mucous membranes are distributed as follows: nose, lips, palate, throat, gums, cheeks, respiratory tract, gastrointestinal tract, genitourinary system (N. A. Alekseev, 1998). With microtraumas, infectious diseases (viral,

bacterial), especially with the development of rhinitis, with intense physical exertion and even with an acute psychoemotional stress situation, telangiectasias can bleed. 90% of patients have nosebleeds, they often recur. In 5-30% of patients, arterio-venous junctions in the lungs are observed, and more often in people who have mutations in the region of chromosome 9q. Shortness of breath, general weakness, reduced work capacity, cyanosis, hemoptysis, hypoxemic erythrocytosis are clinically noted. Approximately 20% of patients have bleeding from the gastrointestinal tract, but they appear mostly at the age of 40-50. Approximately 40% of all gastrointestinal bleeding originates from the upper parts, approximately 10% - from the large intestine, in half of patients it is not possible to verify the place of bleeding in the gastrointestinal tract.

The liver is rarely involved in the pathological process. Its increase and impairment of functions may be noted.

In some cases, a neurological syndrome may appear in the form of a clinic of intracerebral hemorrhages, local symptoms of impaired cerebral circulation. Neurological symptoms are caused by the development of telangiectasias, arterio-venous aneurysms or cavernous hemangiomas in the brain.

However, often the main clinical manifestations of Randu-Osler disease can be isolated gastrointestinal bleeding or bleeding from the urinary tract or hemoptysis in the complete absence of telangiectasias on the skin and visible mucous membranes. In this case, endoscopic research methods help in making a diagnosis.

Laboratory diagnostics

1. General blood test - with frequent recurrent bleeding, chronic posthemorrhagic hypsochromic anemia develops.
2. General analysis of urine - in the development of telangiectasias in the urinary tract and bleeding, macro- or microhematuria is determined.
3. Biochemical blood analysis - when the liver is involved in a pathological process, an increase in the levels of bilirubin, ALT, and AST in the blood is noted.
4. Coagulogram - usually there are no changes.
5. Ultrasound of the liver and spleen - reveals their increase.
6. X-ray of the lungs - rarely - small focal shadows during the formation of arterio-venous shunts in the lungs.
7. FGDS – telangiectasias are detected on the mucous membrane of the esophagus, stomach, and duodenum.

So, the diagnosis is based on the following main signs:

- detection of telangiectasias on the skin and mucous membranes;
- family nature of the disease;
- absence of pathology in the hemostasis system.

Treatment

Local means are used to stop bleeding. Locally, the mucous membrane is irrigated with thromboplastin, thrombin, lebetox, hydrogen peroxide solution. The best effect is given by irrigation of the nasal cavity with a cooled 5-8% solution of aminocaproic acid.

The primary stop of bleeding is provided by the introduction of a hemostatic tampon or compressed foam sponge soaked in liquid nitrogen into the nasal cavity. Next, destruction of telangiectasia is carried out using a cryoapplicator with nitrogen circulation (the time of each freezing is 30-90 s). At the third stage, 4-8 sessions (with intervals of 1-2 days) of one-second sprays of liquid nitrogen are carried out in the nasal cavity, which eliminates the dryness of the mucous membrane and the formation of crusts on it. The duration of the effect of such treatment ranges from several months to a year or more.

Vikasol, calcium chloride, gelatin, hemophobin, dizinon do not reduce the frequency and duration of bleeding.

Surgical treatment is used in case of frequent and abundant gastrointestinal, bronchopulmonary, renal and other bleeding. But due to the formation of new telangiectasias, after some time these bleedings may resume. Arteriovenous aneurysms should be surgically removed as early as possible, before the development of irreversible circulatory and dystrophic changes in the organs.

2. Schönlein-Henoch disease(hemorrhagic microthrombovasculitis)**.**

Hemorrhagic vasculitis is a disease from the group of hypersensitive vasculitis, the basis of which is aseptic immune inflammation and disorganization of the walls of vessels of the microcirculatory channel, multiple microthrombosis.

The etiology is unknown. Provocative factors are infections, vaccination, food and drug allergies, hypothermia.

Pathogenesis. Refers to immune complex diseases. Microvessels are subject to aseptic inflammation, destruction of walls, thrombosis, formation of extravasates.

Classification

1. Clinical forms:
a) skin
b) skin-joint
c) renal
d) abdominal
e) mixed
2. Course options:
a) lightning
b) acute
c) protracted
d) recurrent
e) chronic
3. Degree of activity:
a) low
b) moderate
c) tall
d) very high
4. Complications
a) DIC syndrome

b) intestinal obstruction, intestinal perforation
c) posthemorrhagic anemia
d) thrombosis and heart attacks in organs.

Clinical picture

1. Skin syndrome: symmetrical papular-hemorrhagic rashes, sometimes with urticarial elements, on the limbs, buttocks, less often the trunk. The rash is monomorphic, with a clear inflammatory basis at the beginning of the disease. When pressed, the elements of the rash do not disappear, it is often palpated as a seal or elevation above the skin level. In severe cases, central necrosis appears, the rash is covered with scabs. In the future, pigmentation persists for a long time (hemosiderosis), which indicates the destruction of erythrocytes in the extravasate and their capture by macrophages
2. Joint syndrome: usually occurs together with the skin syndrome or after several hours or days. Pain of varying intensity occurs in large joints (knee, ankle). Pain is characterized by volatility, its appearance again during a new wave of rash. Swelling of the joints, hyperthermia of the skin over them is possible.
3. Abdominal syndrome: more often observed in children, sometimes precedes skin changes. The main symptom is severe pain in the abdomen, constant or spasmodic, caused by hemorrhages in the intestinal wall and mesentery. Areas of necrosis with the occurrence of intestinal bleeding and perforations are possible. From the first days, fever and leukocytosis in the blood test are characteristic.
4. Renal syndrome: occurs in 30-50% of patients. It takes the form of acute or chronic glomerulonephritis, less often subacute, with hematuria, proteinuria. Sometimes nephrotic syndrome develops. Arterial hypertension occurs rarely. Kidney damage usually occurs immediately, and 1-4 weeks after the onset of the disease.

Diagnostics. In the general blood analysis, there is a moderate non-permanent leukocytosis, an increase in ESR. In the coagulogram, there is an increase in the level of the Willebrand factor, hyperfibrinogenemia.
The level of CIC, CRP increases, hyperglobulinemia, cryoglobulinemia occurs (with a cryoglobulinemic form of the disease).

Treatment. Mandatory hospitalization and bed rest for up to 3 weeks. Hypothermia, additional sensitization of the patient with medicinal substances and food products should be avoided. Coffee, chocolate, citrus fruits, fresh berries, seafood are excluded from the diet. Antibiotics, sulfonamides, and vitamins should be avoided. Antihistamines do not improve the well-being of patients. Short courses of glucocorticosteroids in medium doses, heparinotherapy (low-molecular-weight heparins are preferred — fraxiparin, clexan), plasmapheresis are prescribed.

3. Werlhof's disease(Idiopathic thrombocytopenic purpura, autoimmune thrombocytopenia) **(D 69.3)**

Autoimmune thrombocytopenic purpura (ITP) characterized as acute or chronic hemorrhagic diathesis with isolated platelet deficiency and microcirculatory type of bleeding. The disease is caused by increased and accelerated destruction of platelets as a result of the action of autoantibodies directed against one's own platelets. Chronic forms of autoimmune thrombocytopenia (lasting more than 6 months), in which the

cause of autoaggression cannot be determined, are called idiopathic thrombocytopenic purpura (ITP).**Clinic.**The main clinical symptoms of thrombocytopenia are bleeding from the mucous membranes, petechial rashes on the skin and small bruises that occur mainly without specific reasons - microcirculatory type of bleeding, a positive symptom of the harness. ITP is characterized by profuse bleeding from the nose, bleeding from the gums, and in women - long and heavy menstruation. In severe forms, renal hemorrhages, hemorrhages in the sclera or retina, hemorrhages in the ovary (apoplexia ovarii), which clinically simulates an ectopic pregnancy, may occur. The most dangerous complication is hemorrhage in the brain and subarachnoid space. Bleeding may occur after tooth extraction. Difficult surgical interventions and childbirth are accompanied by slightly increased bleeding, but, as a rule, do not lead to significant bleeding. The course of ITP is chronic - recurrent.

Organization of medical assistance

Medical assistance to patients can be provided in outpatient and inpatient conditions of specialized medical institutions of the III accreditation level, as well as in highly specialized medical institutions.

Diagnostic program:

• peripheral blood analysis: reduced number of platelets (<100 G/l, bleeding develops, of course, with the number of platelets <30 G/l). Morphological changes in platelets are revealed in the blood smear - large, small-grained platelets predominate. Other indicators of peripheral blood depend on the presence of bleeding: after profuse bleeding, acute posthemorrhagic anemia occurs, with frequent repeated bleedings - chronic posthemorrhagic anemia with characteristic changes in the hemogram;
• bleeding time - prolonged (more than 10 minutes when the norm is 3 - 5 minutes);
• blood clot retraction - broken;
• blood clotting time is normal;
• puncture biopsy of the bone marrow - hyperplasia of the megakaryocyte apparatus, less often - a normal content of megakaryocytes. A characteristic increase in the young forms of megakaryocytes with a predominance of megakaryoblasts and promegakaryocytes, a visual phenomenon - the absence of unlacing of platelets around them. After bleeding, there may be irritation of the red germ of the bone marrow;
• determination of anti-platelet antibodies - in 50-70% of ITPs, anti-platelet antibodies are found, bound mainly on glycoprotein complexes of platelet membranes. In 20% of cases, free antiplatelet antibodies are detected in blood serum.

Differential diagnosis

For the differential diagnosis of ITP and symptomatic thrombocytopenia, a detailed anamnesis is important: the first manifestations of the disease, its course, the presence of other diseases, taking medications, possible intoxications. For the diagnosis of symptomatic thrombocytopenia caused by an organic lesion of the megakaryocytic apparatus (aplastic anemia, hemoblastosis), a sternal puncture is crucial. ITP should be differentiated from other forms of immune thrombocytopenia, in particular, symptomatic autoimmune (systemic lupus, other collagenoses).

Diagnostic result criteria:

- duration - 10 days;
- share of performed diagnostic procedures;
- availability of morphological verification of the diagnosis.

Treatment program

Forms of the disease that are not accompanied by hemorrhages and with the number of platelets above the critical number are subject to observation by a hematologist.
Treatment of patients with ITP should be carried out in specialized hematological institutions and institutions - regional (city) hematology office, regional (city) hematology department, clinics of scientific institutions.

Indications for inpatient treatment

1. The presence of pronounced hemorrhagic syndrome, which requires the appointment of high and medium doses of steroid hormones or other methods of treatment.
2. Presence of acute posthemorrhagic anemia.
3. Carrying out splenectomy.
4. The need for other surgical interventions (ovarian apoplexy, etc.).

Increased bleeding is an indication for treatment. Treatment begins with the appointment**steroid hormones**. The initial dose of prednisolone is usually equal to 1 mg/kg of weight/day (if there is no effect, the dose is increased to 2-3 mg/kg of weight/day). In such doses, prednisone is prescribed for no longer than 2 - 3 weeks, after which the dose of the drug is gradually reduced to a maintenance dose (10 - 15 mg/day) or to complete withdrawal. Steroid hormones can be prescribed in short courses, in particular dexamethasone 40 mg/day for 4 days, repeating courses every 28 days, for a total of 6 cycles. In refractory forms of ITP, methylprednisolone is used in high doses parenterally (30 mg/kg/day - 3 days, 20 mg/kg/day - 4 days, later 5, 2 and 1 mg/kg/day for 1 week).
When treating with steroid hormones, it is necessary to prescribe potassium preparations, and when using oral prednisolone - antacid preparations.
In patients who need longer treatment, a weakened androgen - danazol can be used. The standard dose of the drug is 10 - 15 mg/kg/day for 2 - 4 months.
In case of ineffectiveness of conservative treatment after 3-6 months from the onset of the disease, it is recommended**splenectomy**. In particularly severe forms of the disease, the course of which is accompanied by a pronounced hemorrhagic syndrome, operative treatment should be carried out sooner. Practical recovery occurs in 70% of ITP patients after splenectomy. Operative intervention and the postoperative period are carried out under the protection of steroid hormones (prevention of adrenal insufficiency). With stable hemodynamics, starting from the 3rd day after surgery, the dose of prednisolone is gradually reduced until complete withdrawal.
A remote complication of splenectomy is the so-called OPSI syndrome (overwhelming post splenectomy infection). This syndrome is characterized by severe infections with massive bacteremia. In order to prevent these complications, patients are vaccinated 2 weeks before splenectomy. Patients receive polyvalent pneumococcal vaccine, Haemophilus influenzae b (Hib) and meningococcal C vaccine.

In patients refractory to corticosteroid hormones, who have contraindications for splenectomy, as well as when splenectomy is ineffective, use**immunosuppressive therapy**: vincristine at a dose of 0.02 mg/kg (1 - 2 mg) orally once a week for 1 - 2 months; azathioprine 1 - 4 mg/kg body weight/day for 2 months or cyclophosphamide 1 - 2 mg/kg/day. These drugs are prescribed in combination with small doses of steroid hormones. Recently, for the purpose of immunosuppression, cyclosporine has been used at a dose of 5 mg/kg of body weight/day for several months, as well as monoclonal antibodies - anti-CD20 (rituximab), anti-CD52 (alemtuzumab) and others. It is prescribed in urgent cases**polyvalent immunoglobulins** for long-term use. Immunoglobulin is administered intravenously at a dose of 0.4 g/kg of weight/day for 5 days or at a dose of 1 g/kg of weight/day for 2 days. In 70% of patients with ITP, a rapid increase in the number of platelets is observed, but after 2-3 weeks the number of platelets returns to previous values. Given the high cost of the drug and the short duration of the effect, the administration of immunoglobulins is carried out only in urgent cases: in case of life-threatening bleeding, brain hemorrhage, childbirth, surgical interventions in patients with severe hemorrhagic syndrome.
In case of ineffectiveness of the indicated methods of treatment, in order to quickly stop bleeding, in urgent cases, recombinant activated factor VII (VII a) is administered at a dose of 60 - 90 mg/kg daily every 2 hours. until the bleeding stops. In immune forms of thrombocytopenia (ITP), platelet concentrate transfusions are not indicated due to the fact that antibodies to allogeneic platelets may be formed. In patients with significant anemia, if blood transfusions are necessary, washed erythrocytes are administered. Patients with post-hemorrhagic anemia are prescribed iron preparations. E-AKK, protease inhibitors, and etamsylate are prescribed as auxiliary therapy for hemorrhages.

Treatment outcome criteria:

- the proportion of completed treatment measures;
- presence of complications;
- degree of normalization of laboratory indicators;
- assessment of the patient's quality of life;
- duration of the period of incapacity for work;
- disability group;
- the duration of the relapse-free period of the disease.

Control of the patient's condition

After discharge from the hospital, patients should be under the supervision of a hematologist. Supportive therapy with steroid hormones or immunosuppressants is carried out on an outpatient basis under the supervision of a hematologist. Control examinations are carried out depending on the presence of hemorrhagic syndrome

4. **Von Willebrand disease (D68.0)**

Von Willebrand disease is a disease caused by impaired synthesis or quality abnormalities of the autosomal components of factor VIII - Willebrand factor (VIII: v.WF) and its related antigen (v.WF: Ag). The disease is inherited according to the

autosomal dominant type, there are variants of the disease which are inherited according to the autosomal recessive type. Both men and women are sick.
The disease is not a uniform hemorrhagic diathesis, there are several variants of this disease.

Classification of Willebrand's disease

subtype)	cteristic
	erate quantitative deficiency of the Willebrand factor
2	tative defect of the Willebrand factor
	ssive proteolysis, release defect
	ased affinity of the Willebrand factor to GP Ib
	ced affinity of the Willebrand factor to GP Ib
	ced affinity of Willebrand factor multimers to factor VIII
3	re quantitative deficiency of the Willebrand factor

Differential diagnosis of certain types of the disease is important for the choice of treatment tactics.

Clinic. Willebrand's disease is characterized by a microcirculatory hematoma type of bleeding. Depending on the variant of the disease, the microcirculatory or hematoma nature of hemorrhagic manifestations may prevail in individual patients. Taking into account the autosomal dominant type of inheritance, the genetic risk for the offspring is 50%, regardless of the sex of the fetus.
With a mild course of the disease in patients with type 1 Willebrand's disease (70% of patients), the course of the disease is manifested by an increased tendency to bruises, nosebleeds, in women - abundant and prolonged menstruation. Excessive bleeding can occur after tooth extraction and after surgery, rarely - increased bleeding after childbirth.
Severe forms of the disease, in particular type III, appear already in the first years of life. Bleeding from the mucous membranes is characteristic, and in women - abundant, long menstruation. Skin hemorrhages are more often manifested by small bruises. Rarely, the disease is complicated by gastrointestinal bleeding, hematuria. One of the characteristic manifestations of the disease is bleeding from wounds after even minor injuries, surgery and childbirth. Hemorrhages in the joints are rarely observed, only with a significant decrease in the activity of factor VIII: C (type III, 2A and 2N). Unlike hemophilia, with Willebrand's disease, further progression of the pathological process and the development of deforming osteoarthritis, as a rule, is not observed. In such patients, the hematoma type of bleeding prevails.
Hemorrhages in the spinal cord and their membranes in Willebrand's disease are associated with trauma. In some cases, the cause of hemorrhage can be a hypertensive crisis or taking drugs that disrupt the function of platelets (acetylsalicylic acid, butadione, etc.).

Diagnostic program:

• Collection of anamnesis and complaints in diseases of hematopoietic organs and blood:

- the presence of an increased tendency to bleeding in relatives;
- complicated obstetric anamnesis (were there complications in the form of hemorrhagic syndrome during childbirth and in the early postpartum period, hypermenorrhea, ovarian apoplexy);
- performed surgical interventions (in particular, tooth extraction) in the past, were there any bleedings;
- burdened hereditary anamnesis regarding Willebrand's disease;
- therapy with plasma preparations containing factor VIII (if so, its dosage, effectiveness, whether there were allergic reactions).

• Visual examination of blood and hematopoietic organs (examine the skin and visible mucous membranes; pay attention to the presence of hematomas, hemarthroses).
• Palpation in diseases of the blood and hematopoietic organs. It is performed for hemarthroses and hematomas. Assess the surface, density, presence/absence of tenderness, presence of compaction or muscle tension, local hyperthermia. In the case of hematomas, the size, consistency, presence of signs of compression of surrounding organs and tissues are evaluated.
• Consultation of an otolaryngologist is carried out in case of epistaxis.
• Consultation of a gynecologist is carried out in case of hypermenorrhea with dysfunctional uterine bleeding, suspected gynecological pathology - ovarian apoplexy, cysts, ovarian cysts, uterine fibroids, endometriosis, etc. According to indications, hysteroscopy is prescribed, which allows detecting pathological changes (myomatous nodes, synechiae, endometrial polyps).
• Ultrasound of the uterus and appendages is performed in patients with gynecological diseases to determine its size and localization of the pathological process.
• Blood sampling from a peripheral vein is performed on an empty stomach.
• Activated partial thromboplastin time (APT) is determined for differential diagnosis with coagulopathies. It shows a deficiency of factors XII, XI, IX (at a factor level of 20% and below) or VIII (30% and below), as well as the presence of their inhibitors in the blood. In these cases, APTC is prolonged.
• Determination of prothrombin (thromboplastin) time in plasma is carried out for differential diagnosis. Its elongation indicates a deficiency of coagulation factors VII, V, X, II.
• Determination of factor VIII activity.
• Determination of factor IX activity is carried out for differential diagnosis with hemophilia B or carrier of the hemophilia B gene, in which case a decrease in the level of factor IX is noted. In Willebrand's disease, the level of factor IX remains normal.
• Determination of the activity and properties of the Willebrand factor (ristocetin-cofactor activity vWF:RCo) in the blood is carried out to diagnose the type of Willebrand's disease.
• Willebrand factor antigen is determined in patients with reduced ristocetin cofactor activity. With type I, the ratio of ristocetin-cofactor activity and Willebrand factor antigen is 0.7, and with the ratio of ristocetin-cofactor activity and Willebrand factor antigen less than 0.7, type II Willebrand disease is diagnosed. With type III

Willebrand's disease, determination is impossible due to the small amount of Willebrand's factor.
• Investigation of platelet aggregation induced by ristocetin.
• Studies of platelet aggregation induced by ADP, collagen, and adrenaline are performed for differential diagnosis with thrombocytopathies.
• Determining the activity of inhibitors to factor VIII and to Willebrand factor is performed in those cases when the level of the deficient factor is 1-2% and there is no clinical effect from prescribing drugs that contain human coagulation factor VIII and human von Willebrand factor, or other blood coagulation factor drugs VIII, which also contain the von Willebrand factor.
• Examination of the level of total hemoglobin, the number of erythrocytes, leukocytes, blood platelets, the calculation of the leukocyte formula and the sedimentation rate of erythrocytes are performed in the case of prolonged bleeding to rule out anemia, thrombocytopenia in the patient, as well as in the case of suspected purulent complications.
Organization of medical assistance Patients with Willebrand's disease are treated by hematologists.
Outpatient polyclinic assistance includes diagnosis, treatment and further dispensary observation of patients. Administration of human coagulation factor VIII and human von Willebrand factor, or in the absence of other blood coagulation factors VIII, which also contain von Willebrand factor, is carried out in outpatient polyclinic institutions and institutions by medical workers, emergency medical care specialists, and at home by the patient himself or by other persons after educating the patient and his parents (guardians).
Inpatient treatment of patients is carried out in hematological surgical departments, departments of hematological centers and multidisciplinary hospitals, as well as in specialized departments of medical and preventive institutions and institutions, depending on the type of clinical manifestations of Willebrand's disease.
Hospitalization patients with hemorrhages in vital organs (head injuries, hemorrhages in the brain and spinal cord, injuries in the back, neck, gastrointestinal bleeding, intra-abdominal hematomas, gynecological pathology: ovarian apoplexy, massive menorrhagia, ectopic pregnancy; acute surgical pathology: acute appendicitis, perforated ulcer, peritonitis, rupture of the spleen, etc.; otolaryngological pathologies: profuse bleeding from the nose, hemorrhages in the larynx) is carried out in specialized departments of medical institutions and institutions that have the opportunity to provide a hematologist's consultation, replacement therapy and a complex of necessary examinations.
When focal symptoms appear in patients with Willebrand's disease, with a head injury, it is necessary to immediately administer human coagulation factor VIII and human von Willebrand factor, or in their absence, other blood coagulation factors VIII, which also contain von Willebrand factor, further treatment in hospital conditions under under the supervision of a neurologist. A patient who has symptoms suggestive of a

possible brain or spinal cord hemorrhage, including drowsiness or an unusual headache, requires emergency hospitalization.
The main principle of treatment of patients with Willebrand disease is timely and adequate replacement hemostatic therapy with human coagulation factor VIII and human von Willebrand factor, or in their absence with other coagulation factors VIII, which also contain von Willebrand factor, which allows to increase the level of the factor in plasma and increase adhesive and aggregate properties of platelets.
The formula for calculating a single dose of the drug in Willebrand's disease:
X = M x (L - P) x 0.5,
where X is the dose of von Willebrand blood coagulation factor for a single administration (MO);
M - patient's body weight, kg;
L - the percentage of the desired level of von Willebrand factor in the patient's blood plasma;
P - the initial level of the factor in the patient before the introduction of the drug.
All surgical interventions in patients with Willebrand disease, including diagnostic invasive procedures (puncture for biopsy) are performed with the use of hemostatic therapy with human coagulation factor VIII and human von Willebrand factor, or in their absence with other blood coagulation factors VIII, which also contain von Willebrand factor.
Removal of teeth, except for molars, is performed on an outpatient basis against the background of hemostatic therapy. Technically difficult tooth extraction is carried out in stationary conditions. In patients with Willebrand's disease, complicated by the presence of an inhibitor, tooth extraction is performed in hospital conditions, no more than one tooth is removed at a time. Due to the increased risk of local anesthesia, the use of general anesthesia is recommended.
Taking into account that the peculiarity of Willebrand's disease is that there is variability in the activity of the Willebrand factor at different time intervals, therefore, in the event of bleeding, patients are prescribed human coagulation factor VIII and human von Willebrand factor, or in their absence, other blood coagulation factors VIII, regardless of laboratory data , which also contain von Willebrand factor at a dose of 25 IU/kg.
In mild and moderate (factor VIII level >5%) forms of Willebrand's disease type I, effective use of desmopressin is mainly in the form of intravenous, subcutaneous injections and intranasal spray.
In the absence of human coagulation factor VIII and human von Willebrand factor, or other blood coagulation factors VIII, which also contain von Willebrand factor, treatment of Willebrand disease can be carried out with fresh frozen plasma.
Treatment at home patients with a severe and moderate form of Willebrand's disease can be carried out after training and instruction from a hematologist (taking a course of study at a school for a patient with hemophilia and other coagulopathy). Patients are taught to recognize the early signs of bleeding and inject the necessary amount of concentrates of human coagulation factor VIII and human von Willebrand factor, or in

their absence, other coagulation factors VIII that also contain von Willebrand factor at home to stop the bleeding. Treatment at home can be carried out both for preventive purposes and when bleeding occurs.
Treatment at home is the most effective, because the time interval between the occurrence of a hemorrhage and the beginning of its treatment is significantly shortened, which for a patient with Willebrand's disease plays a decisive role.
Treatment at home allows you to reduce both the duration of treatment and the amount of drug administered and improves the quality of life of patients.
Preventive treatment consists in the intravenous administration of preparations of human coagulation factor VIII and human von Willebrand factor, or in the absence of other blood coagulation factors VIII, which also contain von Willebrand factor to prevent bleeding. The goal of prevention: to convert a severe form into a moderate one, reaching a minimum level of von Willebrand deficiency factor up to 10%, which allows to reduce the frequency of exacerbations and the risk of developing severe complications.
With Willebrand's disease, secondary prevention is carried out if the frequency of spontaneous bleeding occurs more than twice a month.
Treatment program
The main principle of treatment of Willebrand's disease with agents that affect the blood is replacement therapy, for which human coagulation factor VIII and human von Willebrand factor are used, or in their absence, other blood coagulation factors VIII, which also contain von Willebrand factor. The formula for calculating the amount of the drug is presented in the previous section.
With bleeding from the nose, gums, menorrhagia, hemarthrosis, minor surgical interventions, the level of the coagulation factor should be increased to 50%, with abundant and prolonged bleeding from the nasal cavity, mouth, internal organs, gastrointestinal bleeding, invasive surgical interventions (including dental) - up to 60 - 80%, with hemorrhages in the brain and spinal cord - up to 80 - 100%.
For bleeding from the nose, gums, menorrhagia, hemarthrosis, minor surgical interventions, human coagulation factor VIII and human von Willebrand factor, or in their absence, other blood coagulation factors VIII, which also contain von Willebrand factor, are administered during the first two days every 12 hours. It is possible to continue therapy with human coagulation factor VIII and human von Willebrand factor, or in their absence with other blood coagulation factors VIII, which also contain von Willebrand factor, every 24 hours. until the bleeding stops within 3-5 days.
With prolonged menorrhagia, maintenance of hemostasis in Willebrand's disease is carried out by introducing human coagulation factor VIII and human von Willebrand factor, or in the absence of other blood coagulation factors VIII, which also contain von Willebrand factor, every 12 hours. (the level of factor VIII should not be lower than 40-50%) until the bleeding stops completely, and then - supportive therapy for 5 days with an interval of 24 hours.

When bleeding from the mucous membranes of the mouth and nose, the use of local hemostatic agents, as well as the appointment of antifibrinolytic drugs, is the method of choice in case of activation of fibrinolysis. For this purpose, the following can be used: epsilon-aminocaproic acid in a dose of 3.0 g four times a day, aminomethylbenzoic acid in a dose of 0.25 g twice a day, tranexamic acid in a dose of 0.25 g twice a day for 5 days.

It should be noted that women of reproductive age who take hormonal contraceptives should not be prescribed antifibrinolytic drugs due to the risk of developing DVZ-syndrome.

Taking into account the variability of the activity of factor VIII in the event of active bleeding, patients with Willebrand disease, regardless of laboratory data, are prescribed human coagulation factor VIII and human von Willebrand factor, or in their absence, other blood coagulation factors VIII, which also contain von Willebrand factor in a dose of 25 IU/ kg

For minimally invasive surgical and dental interventions (removal of 1 to 3 teeth), human coagulation factor VIII and human von Willebrand factor, or in their absence, other blood coagulation factors VIII, which also contain von Willebrand factor, are administered in 1 hour. before surgery, and after 12 and 24 hours. after her It is possible to continue therapy with human coagulation factor VIII and human von Willebrand factor, or in their absence with other blood coagulation factors VIII, which also contain von Willebrand factor every 24 hours. until the bleeding stops for up to 3 days. Longer hemostatic therapy is prescribed individually depending on the clinical situation. A collagen sponge can be used as a tamponing material.

Emergency therapy for gastrointestinal bleeding (GI) should be started immediately with human coagulation factor VIII and human von Willebrand factor or, in their absence, other coagulation factors VIII that also contain von Willebrand factor every 12 hours. (the level of the factor before re-injection should not be less than 80%) until complete cessation of bleeding, later - maintenance therapy for 7 days with an interval of 24 hours.

Emergency care for suspected hemorrhage in the brain and spinal cord should be started immediately with preparations of human coagulation factor VIII and human von Willebrand factor, or in their absence with other blood coagulation factors VIII, which also contain von Willebrand factor, with subsequent hospitalization of the patient. Maintaining the level of hemostasis indicators in Willebrand disease is carried out by introducing human coagulation factor VIII and human von Willebrand factor, or in the absence of other blood coagulation factors VIII, which also contain von Willebrand factor every 8 hours. (the level of the factor before re-injection should not be less than 80%) until complete cessation of bleeding, later - supportive therapy for 15 days with an interval of 24 - 48 hours.

During surgical interventions and in the first 2 days after surgery, maintaining the level of hemostasis indicators is carried out by ensuring the level of the von Willebrand factor from 80 to 100%, and in the postoperative period - 50% until the wound heals.

In all conditions that threaten the patient's life, hemostatic therapy should be started on an outpatient basis and continued in the hospital.
During hemostatic therapy of life-threatening bleeding, it is necessary to pay attention to the fact that the level of the von Willebrand factor in the patient against the background of treatment should not exceed 150%.
Treatment of children is carried out according to the scheme of treatment of adults.
Treatment outcome criteria:
- the proportion of completed treatment measures;
- presence of complications;
- assessment of the patient's quality of life;
- duration of the period of incapacity for work;
- disability group;
- the duration of the period without hemorrhagic manifestations (bleeding, hematomas).

Control of the patient's condition
All patients with Willebrand's disease must be registered with a hematologist at the dispensary, and always have documents with them that indicate the exact diagnosis, blood group, Rh type, and specific recommendations in case of bleeding.
Rehabilitation and spa treatmentof complications of Willebrand's disease allows to significantly suspend and, sometimes, prevent the process of invalidation of patients. Its specific types should be prescribed by a hematologist together with a physiotherapist. In some cases, physiotherapeutic procedures are carried out under the guise of hemostatic drugs. Physical therapy, massage, and swimming are indicated for strengthening the muscular system.
Prevention
In childhood - providing the patient with conditions that would minimize the possibility of injury. Later - the right choice of profession (not related to physical exertion). Do not prescribe anti-aggregation drugs (acetylsalicylic acid, etc.), and limit intramuscular injections.
5. Hemophilia (D66, D67, D68.1)
Hemophilia is a hereditary disease caused by a deficiency or molecular abnormalities of one of the procoagulants involved in the activation of blood clotting.
Allocate:
• **hemophilia A** - deficiency of blood coagulation factor VIII (87 - 94% of cases);
• **hemophilia B** - deficiency of blood clotting factor IX (6 - 13% of patients from the total number of patients with hemophilia);
• **hemophilia C**- blood coagulation factor XI deficiency.
Hemophilia A and B is inherited in a recessive X-linked type, which is why only men are affected. Women who inherit an X-chromosome from a hemophiliac father and one X-chromosome from a healthy mother are carriers of hemophilia.
Genetically determined factor XI deficiency is also conventionally classified as hemophilia C or Rosenthal's disease, which affects both men and women.
Depending on the level of the deficiency factor, the following are distinguished:

• severe form of the disease - factor level <2.0%;
• medium severity form - factor level - 2.1 - 5.0%;
• a mild form of the disease - factor level >5.0%.
Some authors additionally distinguish a "hidden" form with a factor level of 15 - 50%.
Clinic. Hemophilia, as a rule, is manifested in childhood by increased bleeding with minor injuries. Sometimes the disease is detected in youth or adulthood (with mild forms of hemophilia). When collecting anamnesis, attention should be paid to the presence of hemorrhages in the patient's family. Hemophilia is characterized by the so-called "hematoma" type of bleeding - profuse and prolonged bleeding from cuts and injuries, hemorrhages in the joints, the occurrence of intermuscular and intramuscular hematomas.

Fig. Arthropathy of knee joints

The course of the disease is characterized by periods of increased bleeding, which alternate with periods of relative clinical remission. One of the characteristic manifestations of hemophilia is hemorrhage in the large joints of the limbs (most often in the knee, less often - hip, elbow, shoulder). Hemorrhages are often associated with a minor injury, inadequate to the size of the hemorrhage.
As a result of recurrent acute hemarthroses, chronic hemorrhagic-destructive osteoarthritis develops: the joint increases in volume, deforms, its mobility is limited), which becomes a cause of disability.
Hemophilia is also characterized by the formation of large subcutaneous, intramuscular hematomas that can simulate phlegmon. Compression of blood vessels by a hematoma can lead to tissue necrosis, destruction of large areas of bones, and the formation of so-called hemophilic pseudotumors. Retroperitoneal hematomas, which can simulate acute appendicitis, are severe. Subserosal hematomas of the intestine can be the cause of partial obstruction, inhibit the wall and break into the lumen of the intestine. 14-30% of hemophiliacs have long-term renal bleeding. Gastrointestinal bleeding in hemophilia is rarely observed, mainly in patients with concomitant peptic ulcer disease. A severe complication of hemophilia is hemorrhage into the brain or spinal cord and their membranes, which occurs after an injury. The severity of the hemorrhage is inadequate to the injury, and the hemorrhage clinic appears some time after the injury (up to a day).
One of the characteristic manifestations of hemophilia is prolonged recurrent bleeding after injuries and operations, cuts, and significant bleeding can begin several hours after the operation or injury.

Diagnostic program

• Collection of anamnesis and complaints in diseases of the blood and hematopoietic system:
Find out:
- hereditary history of hemophilia;
- conducting therapy with antihemophilic drugs, its dosage, effectiveness;

- in the case of hemarthroses and hemorrhages, their antiquity, the circumstances under which they arose, the presence and intensity of the pain syndrome at the present time are established.
• Visual examination for diseases of the blood and hematopoietic system:
• Skin and visible mucous membranes are examined. Pay attention to the presence of hematomas, hemarthroses; on the symmetry of the joints, their sizes, possible deformations, the volume of movements in the joints.
• Palpation is performed for hemarthroses and hematomas. Assess the surface, density, presence/absence of tenderness, presence of compaction or muscle tension, local hyperthermia). In the case of hematomas, the size, consistency, presence of signs of compression of surrounding organs and tissues are evaluated.
• Measurement of the volume of movements in the joints is performed in the presence of flexion-extension contractures using goniometry.
• X-ray and computer tomography of the joints is performed for hemarthrosis in order to determine organic changes in the bone structures of the joint, the presence or absence of fluid in the joint.
• Ultrasound of the joints is performed in hemarthrosis in order to determine the volume of blood, the condition of the synovial membrane, signs of compression of the surrounding tissues.
• Magnetic resonance imaging of the joints is used to determine the degree of damage to the joint surfaces and cartilage tissue.
• X-ray of the skull in one or two projections is performed when a fracture of the bones of the skull is suspected after a craniocerebral injury.
• Ultrasound of soft tissues is performed in case of hemorrhage in soft tissues in order to determine the spread of the hematoma, its density, signs of compression of the surrounding tissues.
• Examination (consultation) of a doctor - dentist, surgeon is performed in case of bleeding from the mucous membrane of the mouth.
• An examination (consultation) of a urologist is performed in case of hematuria and suspicion of pathology of the urinary system. To confirm hematuria, a general urinalysis is performed.
• A survey image of the abdominal cavity and pelvic organs and ultrasound of the kidneys and bladder are performed in patients with hematuria in order to rule out pathology of the urinary system.
• Ultrasonography of the retroperitoneal space, a survey image of the organs of the abdominal cavity and pelvis is performed in patients with a retroperitoneal hematoma in order to determine its size and localization, as well as the presence of signs of compression of the organs of the abdominal cavity and pelvis.
• Blood sampling from a peripheral vein is performed on an empty stomach.
• Activated partial thromboplastin time (APT) is determined to diagnose hemophilia. It shows a deficiency of factors XII, XI, IX (at a factor level of 20% and below) or VIII (30% and below), as well as the presence of their inhibitors in the blood. In these cases, the APTT is prolonged.

• Determination of the activity of factors VIII and IX is carried out in those patients in whom prolongation of the AChT was detected. At a factor level of <2.0%, a severe form of hemophilia is diagnosed, 2.1 - 5.0% - moderate, >5.1% - a mild form of hemophilia.
• Determination of Willebrand factor activity in the blood is performed for differential diagnosis with Willebrand's disease in those patients in whom a decrease in factor VIII is detected;
• Determining the activity of inhibitors to factor VIII and IX is performed in cases where the level of the deficient factor is <1% and the clinical manifestations of hemophilia occurred in adulthood;
• Examination of the level of total hemoglobin, the number of erythrocytes, leukocytes, platelets, the calculation of the leukocyte formula and the rate of sedimentation of erythrocytes are performed during prolonged bleeding to rule out anemia, thrombocytopenia in the patient, as well as when purulent complications are suspected.
• Examination (consultation) of a surgeon is performed for all patients with clinical manifestations of gastrointestinal bleeding and retroperitoneal hematoma.
• Examination (consultation) of an orthopedic doctor is performed in case of extensive hemarthroses, which are accompanied by signs of impaired joint mobility, in case of suspicion of intra-articular fractures.
• Examination (consultation) of a neuropathologist is performed in the presence of clinical signs of hemorrhage in the brain and spinal cord.
• Esophagoduodenoscopy is performed for all patients with gastrointestinal bleeding.
• Computed tomography of the head or magnetic resonance imaging is performed when a hemorrhage in the brain and spinal cord is suspected.

Organization of medical assistance

Organization of medical care for hemophilia patients is carried out by hematologists.

Outpatient polyclinic assistance includes detection, diagnosis, treatment and further dispensary observation of patients, as well as medical and genetic counseling to prevent new cases of the disease in the families of patients. Intravenous administration of clotting factors VIII or IX is carried out in outpatient polyclinic institutions and institutions by medical workers, emergency medical care specialists, and at home by the patient himself or other persons after training the patient and his parents (guardians).

Inpatient treatment patients are treated in surgical and specialized orthopedic departments of hematology centers and multidisciplinary hospitals, as well as in specialized departments of medical institutions and institutions, depending on the type of clinical manifestations of hemophilia.

Urgent hospitalization patients with hemorrhages in vital organs: head injuries, hemorrhages in the brain and spinal cord, injuries in the back, neck, gastrointestinal bleeding, retroperitoneal hematomas, massive hematuria; acute surgical pathology: acute appendicitis, perforated ulcer, peritonitis, rupture of the spleen, etc. is carried out in specialized departments of medical institutions and institutions that have the

possibility of hematologist consultation, replacement therapy and a complex of necessary examinations.
Instrumental methods of examination are carried out when ensuring the level of clotting factors VIII or IX of the patient is not lower than 50%.
Inpatient planned treatment includes reconstructive and restorative operations, orthopedic and surgical rehabilitation of patients with recurrent hemarthroses and severe arthropathy, treatment of inhibitory forms of hemophilia.
Operative treatment of joints
The clinical picture in hemophilia is characterized by the hematoma type of bleeding - the occurrence of hematomas and bleeding. The most severe and specific symptom of hemorrhagic manifestations of hemophilia is hemorrhage in large joints - hemarthrosis. They appear in patients with hereditary coagulopathy, the sooner the more severe the form of hemophilia. Acute hemarthrosis is accompanied by a pain syndrome caused by an increase in intra-articular pressure. The affected joint is enlarged, the skin over it is hyperemic, with a positive symptom of fluctuation and restriction of movement in it. Early replacement therapy and systematic prophylactic administration of concentrates of coagulation factors VIII (IX) can prevent the progression of hemophilic arthropathies and preserve the function of the musculoskeletal system in patients with hemophilia. However, the untimeliness and inadequacy of replacement therapy inevitably leads to the progression of hemophilic arthropathies. Early occurrence of hemarthroses and formation of synovitis in patients with hemophilia - acute, recurrent and chronically progressive - leads to permanent damage to joint surfaces and periarticular tissues, cartilage destruction, deforming osteoarthritis and osteoporosis.
In the course of the pathological process in hemophilic arthropathy, the following forms are distinguished:
1. Acute hemarthrosis (primary, recurrent).
2. Posthemorrhagic synovitis:
- acute;
- subacute;
- chronic (exudative and adhesive form);
- rheumatoid syndrome.
3. Deforming osteoarthritis.
4. Ankylosis (fibrous, bone).
Indications for synovectomy (open or arthroscopic) in patients with hemophilia are the presence of chronic synovitis with a frequency of hemarthrosis from 4-5 per year to 2-3 per month. In the case of chronic synovitis, pain in the joint may be absent due to the destruction of the joint capsule, but the joint is constantly increased in size and gradually loses its function. As the pathological process progresses, fibrous degeneration of the synovial membrane occurs and deforming osteoarthritis gradually forms. The frequency of hemarthroses decreases, the destruction of cartilage tissue, destruction of joint surfaces and axial deformation of the limb occurs. At this stage, planned reconstructive and restorative surgical interventions (arthroplasty, corrective

osteotomy, etc.) are shown to patients. There is no exudate in the immobilized joints, hemorrhages in the form of separate fibrous cysts, narrowing of the joint space and violation of the congruence of the joint surfaces. This leads to a decrease in the range of motion in the joint and the development of persistent flexion-extension contractures and axial deformation. At the current level, at this stage of hemophilic arthropathy, joint replacement is indicated for patients. In the late stages of hemorrhagic-destructive osteoarthritis, the joint space is sharply narrowed, the joint is deformed, the supporting function is often lost, the movements in the joint are extremely "wobbly", bone ankylosis is gradually formed. Orthopedic care is reduced to arthrodesis of the affected joint.

Highly specialized surgical care for hemophilia patients should be provided in hemophilia centers with specially trained staff, modern equipment and a sufficient supply of antihemophilic drugs. In patients with hemophilia, all operative interventions are divided into planned and urgent. All surgical operations, depending on the volume of blood loss and the degree of risk, can be divided into small, medium and bulky. According to their nature, they can be divided into 3 types:

- reconstructive and restorative (synovectomy (open or arthroscopic), arthroplasty, osteosynthesis, corrective osteotomy, joint replacement, etc.);
- general surgery (surgery of the abdominal cavity, purulent surgery, extirpation of pseudotumors, laparoscopic surgery, amputations, etc.);
- dental.

Extensive surgical interventions in patients with hemophilia should be performed under general anesthesia (endotracheal anesthesia with artificial lung ventilation) against the background of appropriate replacement therapy with concentrated coagulation factors VIII (IX) and full preoperative preparation.

Estimated amount of antihemophilic drugs during surgical interventions

N pp	Operative interventions	Type of coagulopathy	Required factor dose (MO)
1	Volumetric	Hemophilia A	8000 - 100000
		Hemophilia B	60000 - 72000
2	Average	Hemophilia A	40000 - 50000
		Hemophilia B	30000 - 36000
3	Small	Hemophilia A	20000 - 30000
		Hemophilia B	12000 - 18000
4	Tooth extraction	Hemophilia A	10000 - 12000
		Hemophilia B	6000 - 9000

Hemostatic therapy prescribed to a patient with hemophilia after the diagnosis has been established and for hemorrhagic manifestations (with the exception of prophylactic treatment). The main principle of treatment of patients with hemophilia is timely and adequate replacement hemostatic therapy with drugs of blood coagulation factors VIII or IX (plasma and recombinant), which are used to increase its concentrations in the blood plasma to a level that will ensure effective hemostasis.

The formula for calculating a single dose of the drug for hemophilia A:
in severe form:
X = M x L x 0.5
with medium and mild form:
X = M x (L - P) x 0.5
The formula for calculating a single dose of the drug for hemophilia B:
in severe form:
X = M x L x 1.2
with medium and mild form:
X = M x (L - P) x 1.2
Where X is the dose of blood coagulation factor for single administration (MO);
M - patient's body weight, kg;
L - the percentage of the desired and necessary level of the factor in the patient's blood plasma;
P - the initial level of the blood plasma factor in the patient before the drug is administered.
At the same time, it should be taken into account that 1 MO of factor VIII administered per 1 kg of the patient's weight increases the content of factor VIII by 1.5 - 2.0%, and 1 MO of factor IX increases the content of factor IX by 0.8%.
With a mild form of hemophilia A, the use of desmopressin is effective, mainly in the form of intravenous, subcutaneous injections and intranasal spray.
The use of cryoprecipitate is extremely limited due to the low concentration of factor VIII in the preparation, which does not allow to achieve the required level of hemostasis, unreliable viral inactivation and possible post-transfusion reactions and is possible only in the conditions of the transfusion office of a medical institution. Cryoprecipitate should not be used for preventive and home treatment.
Home treatment: patients with severe and moderate with inhibitory forms of hemophilia after training and instruction from a hematologist learn to recognize the early signs of bleeding and administer the necessary amount of blood coagulation factor concentrates or anti-inhibitory drugs to stop bleeding at home, which has already started. Both prophylactic treatment and therapy in the event of bleeding can be carried out.
Home treatment is the most effective, because the time interval between the occurrence of hemorrhage and the beginning of its treatment is significantly shortened, which plays a decisive role for a patient with hemophilia. Home treatment allows you to reduce both the duration of treatment and the amount of antihemophilic drug administered. Its implementation significantly improves the quality of life of patients.
Preventive treatment consists in intravenous administration of concentrates of blood coagulation factors to prevent bleeding and hemorrhages. The goal of prevention: to convert a severe form of hemophilia into a moderate one, reaching a minimum level of a deficient factor >2.0%, and in some cases even a mild one - >5.0%, which allows to prevent the development of hemophilic arthropathy, reduce the frequency of exacerbations and the risk of developing serious complications .

Types of prevention: primary, secondary.
Primary prevention is a long-term treatment that is used in patients with a severe form of hemophilia A and B. It can be started at the age of 1 to 2 years before the manifestation of clinical symptoms of the disease (primary prevention, determined by age) or regardless of the age of the patient, who have no more than one joint hemorrhage (primary prevention, determined by the first bleeding).
In secondary prevention, long-term treatment is carried out in cases where the conditions of primary prevention are not met.
Ensuring hemostasis in the inhibitory form of hemophilia is carried out by anti-inhibitory drugs (one of the indicated), regardless of the titer of the inhibitor:
• Blood coagulation factors II, VII, IX, X in combination (anti-inhibitory coagulation complex).
• Eptakog alfa is activated
The simultaneous use of these drugs is unacceptable due to the possibility of developing thrombotic complications. It is allowed to use coagulation factors II, VII, IX, X in combination no earlier than after 4 hours. after the introduction of eptacog-alfa activated. Appointment of activated eptacog-alpha is possible only 48 hours after the use of blood coagulation factors II, VII, IX, X in combination.
Treatment program
The main principle of treatment of patients with hemophilia is replacement therapy, for which they use: coagulation factor VIII or coagulation factor IX. The formula for calculating the amount of the drug is presented in section 1.
In case of hemarthrosis, nosebleeds, small superficial hematomas, hematuria, minor surgical interventions, the level of the clotting factor should be increased to 40-50%, in case of extensive retroperitoneal hematomas, gastrointestinal bleeding, invasive surgical interventions (including dental) - up to 60 - 80%, with hemorrhages in the brain and spinal cord - up to 80-100%.
For hemarthrosis, nosebleeds, small superficial hematomas, hematuria, coagulation factor VIII is administered during the first two days every 12 hours, coagulation factor IX - every 18 hours. Later, clotting factors VIII and IX are administered every 24 hours. until the bleeding stops and the pain disappears. In the case of minimally invasive surgical and dental interventions (extraction of 1 to 3 teeth), loosening factors are administered 30 minutes before manipulation, every 12 hours. (with hemophilia A) and every 18 hours (with hemophilia B) during the postoperative period until the wound is completely healed.
If a retroperitoneal hematoma is suspected in hemophilia A, coagulation factor VIII is administered every 8 hours, in hemophilia B - coagulation factor IX is administered every 18 hours. within 3 days. Later - maintenance therapy for 14 days with blood coagulation factor VIII or IX every 24 hours.
In the presence of extensive hematomas with signs of compression of surrounding tissues, including retroperitoneal, long-term hematuria, correction of hemostasis in hemophilia A is carried out by introducing coagulation factor VIII every 8 hours, in hemophilia B - coagulation factor IX every 18 hours (the level of the factor before

repeated by injection should not be lower than 60%) until the complete stop of bleeding, later - supportive therapy for 14 days with an interval of 24 hours. clotting factor VIII or IX.
Emergency medical care for gastrointestinal bleeding (GI) should begin immediately with drugs of clotting factors VIII or IX, followed by hospitalization of the patient. Maintenance of hemostasis in hemophilia A is carried out by introducing blood coagulation factor VIII every 8 hours, in hemophilia B every 18 hours. by the introduction of factor IX (the level of the factor before re-injection should not be less than 80%) until complete cessation of bleeding, later - supportive therapy for 14 days with an interval of 24 hours. clotting factor VIII or IX.
Emergency medical care in case of suspected hemorrhage in the brain and spinal cord should be started immediately with drugs of clotting factors VIII or IX, followed by hospitalization of the patient. Maintenance of hemostasis in hemophilia A is carried out by the introduction of coagulation factor VIII every 8 hours, in hemophilia B every 18 hours. by the introduction of factor IX (the level of the factor before re-injection should not be less than 100%) until complete cessation of bleeding, later - supportive therapy for 14 days with an interval of 24 hours. clotting factor VIII or IX.
Data on administration of the drug eptacog-alpha (activated) during brain hemorrhages instead of administration of blood coagulation factors VIII or IX at a dose of 90 - 120 μg/kg of body weight indicate effectiveness. If necessary, the dose can be repeated after 2 hours.
In all conditions that threaten the patient's life, hemostatic therapy should be started on an outpatient basis and continued in the hospital.
During hemostatic therapy of life-threatening bleeding, it is necessary to pay attention to the fact that the level of factors VIII or IX in the patient against the background of treatment should not exceed 150%.
The most serious complication of hemophilia is damage to the musculoskeletal system. With frequent hemarthroses, damage to cartilage tissue gradually develops, which leads to the appearance of deforming arthrosis with persistent loss of function. Such patients are subject to expensive surgical intervention - joint endoprosthetics. When using the preparation of the sodium salt of hyaluronic acid in the form of intra-articular injections, the lubricating and shock-absorbing effect of the synovial fluid is restored, as well as joint friction, which causes pain, is eliminated. When conducting a course of treatment with the sodium salt of hyaluronic acid in patients with hemophilia, the functional activity of the joints increases and metabolic processes in the cartilage tissue improve.
During surgical interventions and in the first 2 days after surgery, maintenance of hemostasis is carried out by ensuring the level of factor VIII or IX is 100 - 120%, and later 60% until the wound heals.

Inhibitory form of hemophilia

The emergence of inhibitory antibodies to factors VIII or IX is one of the most serious complications of replacement therapy in hemophilia. Under the action of the inhibitor, exogenous factor VIII (IX) quickly loses its procoagulation activity, stimulates

additional production of antibodies - accordingly, the titer and activity of inhibitory antibodies in the patient's circulating blood increases. The prevalence of inhibitory forms in hemophilia A is 11-13% and about 5% in hemophilia B.
The presence of inhibitory antibodies aggravates the severity of the clinical course of hemophilia, bleeding becomes uncontrollable, and replacement therapy with VIII (IX) clotting drugs is ineffective.
Among patients with an inhibitory form of hemophilia, patients with a weak response (titer J5 Bethesda units (BO/ml)) and patients with a strong response (titer >5 BO) should be distinguished.
For 1 Bethesda unit, it is customary to count such a titer of inhibitory antibodies, at which 50% of the activity of factor VIII (IX) is inhibited.
Inhibitors in patients with a poor response can be neutralized by high doses of coagulation factor VIII (IX) drugs with satisfactory hemostasis. However, in patients with a high response, in order to eliminate the inhibitor and achieve stable hemostasis, treatment with hemostatic drugs should not be carried out according to the principle of replacement therapy, but anti-inhibitor "shunt" drugs should be used. For the treatment of inhibitory forms of hemophilia in Ukraine, it is possible to use one of two registered drugs:
- eptacog-alpha (activated)
- a complex of blood clotting factors (anti-inhibitory coagulation complex).
These drugs have different units of measurement of activity:
- for eptacog-alpha (activated) - in mg or CMU (1 CMU = 20 μg)
- for the complex of blood coagulation factors (anti-inhibitory coagulation complex) - in units/kg of body weight. A unit of the anti-inhibitory coagulation complex is taken as its amount in the solution, at which there is a reduction of APTC of the inhibitory plasma to factor VIII by up to 50% compared to the buffer solution.
The simultaneous use of drugs eptacog-alpha (activated) and a complex of blood coagulation factors (anti-inhibitory coagulation complex) is undesirable due to the possibility of the development of thrombotic complications, however, a transition during treatment from one anti-inhibitory drug to another is permissible if the time interval is observed.
When a poorly responsive inhibitor appears in the course of treatment in patients with hemophilia (inhibitory antibody titer J5 BO), the main principle of treatment is the introduction of neutralizing doses of factor VIII (IX) drugs and corticosteroids (prednisolone at a dose of 1 - 2 mg/kg).
Maintenance of hemostasis is carried out by introducing coagulation factors VIII every 8 hours. (the level of factor VIII before re-injection should not be lower than 60%), with hemophilia B - factor IX every 12 - 18 hours. (the level of factor IX before re-injection should not be lower than 60%) until complete cessation of bleeding, and later - maintenance therapy for 14 days with an interval of 24 hours. drugs of coagulation factors VIII or IX.
In hemarthroses, superficial wounds and cuts, nosebleeds, hematuria, minor surgical interventions in patients with a weakly responsive inhibitor (J5 BO), hemostatic

therapy is provided by the introduction of coagulation factors VIII (IX) until the concentration in the blood is 40 - 50%, factor VIII preparations are administered every 12 hours the first 2 days, and factor IX - every 18 hours, then factors VIII (IX) are administered every 24 hours. until the bleeding stops and the pain syndrome disappears.

In the case of large intermuscular hemorrhages with compression of nerves and vessels, hemorrhages in the retroperitoneal space, macrohematuria, planned surgical interventions, anti-inhibitor therapy in patients with a weakly responsive inhibitor should be carried out exclusively in hospital conditions. The condition of these patients is life-threatening and requires immediate and long-term administration of antihemophilic drugs in large doses, with the level of factor VIII (IX) not lower than 50%.

In patients with a weak response to trauma to the head, spine, hemorrhage in the brain and spinal cord, and other hemorrhages that threaten the patient's life, hemostatic therapy should be started immediately in an outpatient clinic and continued in a hospital.

With a weakly responsive inhibitor, when the level of the inhibitor is (5 IU) with hemorrhage in the brain and spinal cord, factor VIII is administered every 6-8 hours. (the level of factor VIII before re-injection should not be lower than 100%), in hemophilia B - factor IX should be administered every 12-18 hours. (the level of factor IX before re-injection should not be lower than 100%) until complete cessation of bleeding, then maintenance therapy for 14 days with an interval of 24 hours. coagulation factor VIII (IX).

With gastrointestinal bleeding, maintenance of hemostasis is carried out by the introduction of factor VIII concentrate every 6 - 8 hours, with hemophilia B - factor IX is administered every 12 - 18 hours. until the bleeding stops completely. The level of factor VIII (IX) before re-injection should not be lower than 80%. Maintenance therapy is carried out for 14 days with an interval of 24 hours. coagulation factor VIII (IX).

With a highly reactive inhibitor, when the level of the inhibitor is (>5 IU), eptacog-alpha (activated) is immediately administered at a dose of 120 μg/kg of body weight, which is repeated every 2 hours. within 2 days Then, maintenance hemostatic therapy is carried out with eptacog alfa (activated) at a dose of 90 μg/kg of body weight every 4 hours. or a preparation of a complex of blood coagulation factors (anti-inhibitory coagulation complex) at a dose of 50 - 100 units/kg of the patient's body weight every 12 hours.

In patients with a highly reactive inhibitor (>5 IU), hemostatic therapy (for gastrointestinal or renal bleeding) is carried out according to one of the schemes: Initially, eptacog-alpha (activated) is administered at a dose of 120 μg/kg of body weight every 2 hours. until the bleeding stops, later hemostasis is ensured by the preparation of a complex of blood clotting factors (anti-inhibitory coagulation complex) in a dose of 75 units/kg of the patient's body weight every 12 hours. within 2 weeks.

When using only one preparation of the blood coagulation factor complex (anti-inhibitory coagulation complex) it is administered in an initial dose of 100 units/kg. Subsequently, the drug is administered at a dose of 50 units/kg of the patient's body weight every 6 hours. until the bleeding stops completely, and then every 12 hours. within 2 weeks. In case of recurrence of bleeding, the dose of the drug is again increased to 100 units/kg per administration. The daily dose should not exceed 200 units/kg.
In patients with a strong response (titre of inhibitory antibodies > 5 BO) with acute hemarthrosis and hematomas (which have arisen recently and are progressing strongly), hemostatic therapy is carried out with one of two anti-inhibitory drugs (simultaneous administration of the drugs is inadmissible).
Eptakog-alpha (activated) is administered at a dose of 90 μg/kg of body weight from 2 to 4 injections every 2 hours. until there are clear signs of clinical improvement.
The preparation of the blood coagulation factor complex (anti-inhibitory coagulation complex) is administered in an initial dose of 75 units/kg every 12 hours. Treatment is continued until clear signs of clinical improvement: disappearance of pain, restoration of joint mobility, reduction of hematoma volume and its density, restoration of lost function.
In the case of planned surgical interventions, it is advisable to conduct plasmapheresis (once or twice) to reduce the inhibitor titer, followed by anti-inhibitor therapy according to one of the schemes.
Immediately before the operation, eptacog-alpha (activated) is administered at a dose of 120 μg/kg, and thereafter - every 2 hours. within 2 days until receiving clear signs of absence of bleeding. Further hemostasis is ensured by the administration of the drug eptacog-alpha (activated) in a dose of 90 μg/kg every 4 hours. or by the introduction of a preparation of a complex of blood coagulation factors (anti-inhibitory coagulation complex) at a dose of 75 units/kg of body weight every 12 hours. until complete healing of the postoperative wound.
When using the preparation of a complex of blood clotting factors (anti-inhibitory coagulation complex), it is administered immediately before surgery in a dose of 100 units/kg of body weight. Further hemostasis is ensured by the administration of the drug in a dose of 75 units/kg of the patient's body weight every 12 hours. until the surgical wound is completely healed.

Treatment outcome criteria:

- the proportion of completed treatment measures;
- presence of complications;
- assessment of the patient's quality of life;
- duration of the period of incapacity for work;
- disability group;
- the duration of the period without hemorrhagic manifestations (hematomas, hemarthroses).

Control of the patient's condition

All patients with hemophilia must be registered with a hematologist at the dispensary, always have documents with them indicating the exact diagnosis, the presence of an inhibitor, blood group, Rh type, and specific recommendations in case of bleeding.
Rehabilitation and spa treatmentcomplications of hemophilia can significantly suspend, and sometimes even prevent, the process of invalidation of patients. Its specific types should be prescribed by a hematologist together with a physiotherapist. In some cases, physiotherapeutic procedures are carried out under the guise of hemostatic drugs. Physical therapy, massage, swimming are recommended for strengthening the muscular system and musculoskeletal system.
Prevention
In childhood - providing the patient with conditions that would minimize the possibility of injury. Later - the right choice of profession (not related to physical exertion). Do not prescribe anti-aggregation drugs (acetylsalicylic acid, etc.), as well as intramuscular injections.
General material and mass-methodological support
lectures:
work program of the academic discipline
synopsis (plan-summary) of the lecture
multimedia presentation of the lecture

Questions for self-control:

1. Hemoblastosis. Definition of the concept. Clinical picture. Main syndromes. Changes in blood and oral cavity analysis in hemoblastosis (chronic myelo- and lymphocytic leukemia).
2. Thrombocytopenia and thrombocytopenia: etiology, classification, clinical data, main syndromes, complications, principles of treatment.
3. Hemophilia A, B, C: etiology, classification, clinical data, main syndromes, complications, principles of treatment.
4. Willebrand's disease: etiology, classification, clinical data, main syndromes, complications, principles of treatment.
5. Secondary immunodeficiencies: etiology, classification, clinical data, main syndromes, complications, principles of treatment. Dental aspects of diseases of the immune system

Used sources: