Ministry of health of the Republic of Belarus
Educational institution
«Gomel State Medical University»

Department of general and clinical pharmacology

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METHODOLOGICAL RECOMMENDATIONS

for a practical lesson on the discipline "Clinical pharmacology"
with six-year students of the Faculty of Foreign Students,
studying at the specialty 1-79 01 01 "General medicine"

TOPIC 7: «CLINICAL PHARMACOLOGY OF DRUGS AFFECTING THE HEMOSTASIS SYSTEM. CLINICAL PHARMACOLOGY OF ANTI-ANEMIC DRUGS. CLINICAL PHARMACOLOGY OF DRUGS USED FOR THE TREATMENT OF DIABETES MELLITUS TYPE 2 AND THYROID DISEASES»

Time: 7 hours

Approved at the meeting of the department of general and clinical pharmacology

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2023

LEARNING AND EDUCATIONAL GOALS, OBJECTIVES, MOTIVATION FOR LEARNING THE TOPIC

The problem of correction of hemostasis disorders as well as the problem of treatment of thyroid diseases and diabetes mellitus are among the most urgent issues of modern practical medicine. There are various pharmacological developments, international guidelines and recommendations on these problems. Their knowledge will lead to the competent use of the modern arsenal of drugs and, as a result, the prescription of adequate and timely treatment for patients with these diseases.

Learning objective:

– formation of scientific knowledge about the pharmacokinetics and pharmacodynamics of drugs on the topic of the class in order to master the rational differentiated pharmacotherapy of the relevant diseases and pathological conditions.

Educational purpose:

– to develop their value-personal, spiritual potential, to form the qualities of a patriot and citizen, ready for active participation in the economic, industrial, socio-cultural and public life of the country; to realize the social significance of their future professional activities, to learn to follow academic and work discipline, standards of medical ethics and deontology.

Tasks:

As a result of the study lesson, the student should

know:

– clinical and pharmacological classification of drugs used in the treatment of diseases on the topic of the lesson, their pharmacokinetic and pharmacodynamic features;

– indications and contraindications for the prescription of drugs on the theme of the class, the features of their use in different age groups and in various concomitant diseases; dosage regimen of drugs and their interaction with other pharmacological groups;

– principles of control over the effectiveness and safety of the respective drugs, possible side effects, ways to prevent and correct them;

be able to:

– choose the most effective and safe medications on the topic of the lesson, taking into account their basic pharmacokinetic and pharmacodynamic characteristics, possible side effects and drug interactions, on the one hand, the characteristics of the disease, age and gender of the patient, the presence of concomitant pathology and the degree of impairment of the basic functions of the body, on the other hand;

– conduct objective monitoring of the effectiveness and safety of the medicines on the study topic, analyze their pharmacokinetic parameters and use the data to calculate single and course doses;

– determine the optimal route of administration of the medicines on the theme of the class, prescribe them taking into account the time of day, intake and composition of food, predict, prevent and detect side effects of medicines, avoid polypragmasy and irrational combination of different medicines;

– prescribe medications on the topic of the class in the prescription;

– inform patients about the nature of the action of the medicines on the topic of the class, the rules of their administration and possible side effects;

– evaluate scientific information about the effectiveness of the studied drugs, work with reference and other literature on the topic of the class;

possess:

– skills ability and willingness to analyze the characteristics of absorption, distribution, biotransformation and excretion of drugs on the topic of the class;

– ability and readiness to rationally dose a medication on the topic of the class, including the choice of dosage form, routes of administration and dosing regimen;

– skills to use medicines on the topic of the class in the treatment, rehabilitation and prevention of relevant diseases and pathological conditions, taking into account the main pharmacodynamic parameters;

– skills to search, analyze and summarize information on the use and effects of various medicines on the topic of the class.

Motivation for learning the topic:

– the specifics of training doctors in this specialty determines the need for purposeful study of students' knowledge of the pharmacokinetics and pharmacodynamics of drugs on the topic of the class and the ability to justify and conduct a rational differentiated pharmacotherapy of the relevant diseases and pathological conditions.

MATERIAL EQUIPMENT

Reference and informational literature, charts, tables, presentations, patient histories, package of regulatory documents, collection of medications.

CONTROL QUESTIONS FROM RELATED DISCIPLINES

- biochemistry and physiology: physical properties and structure of cell membranes, transport of substances through biological membranes in norm and pathology;

- general and bioorganic chemistry: basics of chemical kinetics and catalysis, buffer solutions and systems, pH calculation;

- from biochemistry: kinetics of enzymatic reactions, Michaelis-Menten kinetics equation, the concept of enzyme inhibitors, types of enzyme inhibitors;

- from pathological physiology: cell damage, disorders of protein, fat, carbohydrate and mineral metabolism, disorders of local and general circulation, immunopathological processes, allergy, inflammation, pathophysiological mechanisms of formation of disorders of physiological functions, and homeo- and hemostasis in the human body;

- from Latin: basic rules for coordinating parts of speech and drawing up prescriptions when prescribing medicines;

- from pharmacology: general questions of pharmacology, pharmacokinetics and pharmacodynamics of drugs, general prescription and prescription rules;

- from internal diseases: peculiarities of clinical and anamnestic data in patients with disorders of physiological functions, as well as homeo- and hemostasis, etiopathogenesis and modern approaches to the diagnosis of major diseases accompanied by disorders of physiological functions, as well as homeo- and hemostasis.

CONTROL QUESTIONS ON THE TOPIC OF THE CLASS

1. The main causes leading to disorders of the coagulating and anticoagulant systems. Clinical and pharmacological characteristics of antiplatelet agents, direct and indirect anticoagulants, thrombolytic drugs.
2. The main drugs used in reducing the activity of the clotting system: proaggregants, procoagulants, fibrinolysis inhibitors. Indications and contraindications for use, methods of evaluation of effectiveness.
3. Classification of anemias. Iron-deficient, B12- and folic-deficient anemias: etiology, clinical manifestations and principles of pharmacotherapy.
4. Clinical and pharmacological characteristics of antianemic drugs. Indications and contraindications for the use of iron-containing drugs and cyanocobalamin. Criteria for the effectiveness of pharmacological therapy.
5. Clinical and pharmacological characteristics of sulfonylurea derivatives, biguanides, meglitinides, thiazolidinediones and incretins.
6. Insulin derivatives. Indications and contraindications, methods of monitoring the effectiveness and safety of insulin therapy.
7. Drugs for replacement therapy in hypothyroidism. 8.
8. Clinical and pharmacological characteristics of antithyroid drugs.

PROCESS OF THE STUDY

1.
2.
3.
4.
5.

Theoretical part

Theoretical questions are described in the appendix to the methodological recommendations.

Practical part

1. Take notes on theoretical material demonstrated by the teacher.
2. Master the methods of solving the tasks and writing out prescriptions on the topic of the class.

Theme learning control

Conducted in the form of independent written work (solution of practical problems and prescriptions for individual task).

METHODOLOGICAL RECOMMENDATIONS FOR ORGANIZATION AND EXECUTION OF STUDENTS' INDEPENDENT WORK (SIW)

The time given for independent work can be used by students for:

- preparing for the practical classes;
- completing the tasks on the topic of the class in the workbook;
- preparing thematic reports, essays and presentations;
- taking notes from academic literature.

The main methods of organizing independent work:

- completing tests and practical tasks of the electronic educational-methodical complex (EEMC) for self-monitoring and self-assessment;
- writing a case history.

The list of tasks of the SIW:

- solving practical problems in the EEMC;
- completing the test tasks of the EEMC;
- writing a case history.

Control of the SIW is carried out in the form of:

- assessment of an oral answer to a question, report, report, or solution of a task in a practical class;
- individual conversation;
- checking a case history.

METHODOLOGICAL RECOMMENDATIONS FOR ORGANIZATION AND EXECUTION OF CONTROLLED INDEPENDENT WORK OF STUDENTS (CIWS)

Recommended forms of CIWS organization:

- writing a case history;
- writing an essay on a given topic;
- preparing a report and a multimedia presentation on a given topic.

The list of tasks of the CIWS:

Topics of essays / multimedia presentations:

1. The use of adaptogens from the position of evidence-based medicine.
2. The specifics of the use of antiplatelet agents and anticoagulants in the elderly with regard to comorbidity.
3. Pharmacology of sports medicine.

Forms of control of CIWS realization:

- checking a case history;
- checking and grading an essay on a given topic;
- checking and grading a multimedia presentation on a given topic.

LIST OF REFERENCES

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2. Кратко о лекарственных средствах: учебно – методическое пособие для студентов 3 и 6 курсов факультета иностранных студентов, учреждений высшего мед. образования: в 2 ч.=Drugs in short: partical workbook for 3 and 6 year students Faculty for International Students of medical higher educational institutions: in 2 parts /

Е.И. Михайлова [и др.]. – Ч. 1. – Гомель: ГомГМУ, 2020. – 56с. – Режим доступа: http://elib.gsmu.by/xmlui/handle/GomSMU/7128 – Дата доступа: 23.05.2022.

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4. Rang and Dale's Pharmacology / J.M. Ritter [et al.]. - 9th ed. - Edinburg [et al.]: Elsevier, 2020. - xvi, 789 p.: ill., tab. + Student consult online.

DRUGS AFFECTING BLOOD

Agents **increasing** blood coagulation [1-4]

Classification	**Hemostatic agents**		**Inhibitors of fibrinolysis**
	Topical	**Resorptive**	
Drugs	1. Thrombin 2. Hemostatic sponge	3. Fibrinogen 4. Vitamin K1 (phytomenadione), K3 (vicasol) 5. Ethamylate (dicinone) 6. Anti hemophilic Factor VIII, Factor VIIa, IX	7. Aminocaproic acid 8. Tranexamic acid 9. Aminomethyl benzoic acid (ambene) Inhibitors of proteolytic enzymes: 10. Aprotinin (contrycal, gordox)
Mechanism of action	The natural components of the coagulation system – provide the formation of blood clot (1-4, 6), ↑ formation of thromboplastin (5).		Inhibition of activation of the plasminogen → plasmin formation inhibition. Brakekinin systems and the activity of fibrinolysis (7-9). Inhibit fibrinolysin (plasmin), heparin → inhibit fibrinolysis and ↑ activity of the coagulation system blood (10).
Pharmacological effects	1. Hemostatic 2. Anti allergic effect, ↑ liver detoxification (7) 3. Inhibition of proteolytic enzymes (trypsin, chymotrypsin, kallikrein, plasmin) (10)		
Indications	1. Bleeding: capillary (1, 2, 5) and parenchyma (1, 2, 5). 2. Hypofibrinogenemia: postpartum hemorrhage. DIC-syndrome (3) 3. Bleeding against liver diseases and vitamin K absorption disorders (4) 4. Congenital/acquired coagulation factors deficiency (6)		1. Local (nasal bleeding, tonsillectomy, extraction of teeth, etc.) and generalized (in thoracic and abdominal surgery) 2. Acute pancreatitis (contrycal), ↑ risk of bleeding (gordox) 3. Bleeding during an overdose of fibrinolytic agents
Side effects	1. Allergic reactions, nausea, headache (5)		1. Intra vascular thromboses 2. Hypotension, arrhythmia 3. Impairment of color vision (8) 4. Allergic reactions (8, 10)
Contraindications	1. Increased blood clotting 2. Thrombo embolism		1. DIC-Syndrome 2. Bleeding from the kidneys and ureters 3. Propensity for thrombosis and embolism 4. Pregnancy
NB!	**Not for i/m or i/v use → thrombosis**	Hemophilia A (VIII factor), haemophilia B (IX)	*Aprotinin*is is used for extra corporeal circulation of blood during heart operations and liver transplantation.
	Vegetable coagulant: Leaves of nettle, yarrow, corn bark, arnica flowers		

Drug interactions	1. Do not mix in the same syringe with other medicines (5). 2. Reopoliglyukin leads to inhibition of the action of both drugs (5). 3. Antibacterial agents with a wide spectrum of action ↓ the effectiveness of the drug (4). 4. When wetted by thrombin, hemostatic action is potentiated (2). 5. Colestipol ↓ absorption in the digestive tract (4). 6. Blocks the effect of indirect anticoagulants (4). 7. A combination with solutions of aminocaproic acid and vicasol is acceptable (5). 8. Pre-administration of reopoliglyukin blocks the hemostatic effect (5.)	1. The simultaneous use of drugs of this group is dangerous due to the risk of massive thrombosis 2. ↓ effectiveness while taking with anticoagulants and antiplatelet agents 3. Do not administer in mixed infusions (10) 4. Chemical incompatibility with glucocorticosteroids, nutrient solutions containing amino acids and fats (10) 5. Incompatible with penicillins, urokinase, norepinephrine, tetracyclines, dipyridamole, diazepam (8)

Blood thinners

Anti platelets are drugs decreasing platelet aggregation [1-4]

Classification	Cyclooxygenase (COX) inhibitors	Phosphodiesterase inhibitors	ADP receptor blockers	Glycoprotein IIb / IIIa receptors blockers
Drugs	1. Acetyl salicylic acid (aspirin) *in small doses*	2. Dipyridamole	3. Ticlopidine 4. Clopidogrel	5. Abciximab 6. Tirofiban
Mechanism of action	Their reversible blockade of COX of thrombocytes (an enzyme involved in the formation of thromboxane A2 and prostacyclin from arachidonic acid).	It blocks phosphodiesterase and adenosine uptake → ↑ cAMPlevel ↓ intracellularcontentof Ca2 + → ↓ platelet aggregation and has a vasodilating effect.	Block ADP receptors on the platelet membrane → interfere with the interaction of platelet receptors with fibrinogen.	Eliminate the activation of glycol protein receptors GP IIb / IIIa → disrupt platelet aggregation.
Pharmacological effects	1. Antiplatelet 2. Improve myocardial and cerebral microcirculation 3. Coronary vasodilatation (2)			
Indications	1. Angina pectoris 2. Prevention of MI (in the presence of risk factors) 3. Prevention of thrombosis and embolism after operations on the heart and vessels	1. Prophylaxis of ischemic trokein chronic cerebrovascularin sufficiency 2. Prevention of thrombo embolic complications after operations on peripheral vessels	1. Prophylaxis of thrombosis in patients with is chemic heart disease (after MI) 2. Atherosclerosis of cerebral and perioreric vessels 3. Intolerance to acetylsalicylic acid	1. Acute coronary syndrome 2. Atherectomy and angioplasty operations (in combination with aspirin and heparin).
Side effects	1. Dyspepsia 2. Risk of bleeding 3. Allergic reactions	1. Coronary steal when IHD. 2. Dyspepsia 3. ↓ AP, headache	1. Dyspeptic disorders 2. Thrombocytopenic purpura 3. Neutropenia, agranulocytosis (3)	1. Bleeding, thrombocytopenia 2. Allergic reactions
Contraindications	1. Exacerbation of erosion-ulcerative lesions of the gastrointestinal tract 2. Pregnancy 3. as an anti pyretic for viral infection in children	1. Acute myocardial infarction, unstable angina	1. Increased risk of bleeding 2. The gastro duodenal ulcer 3. Liver disease	1. Thrombocytopenia 2. Hemorrhagic diathesis 3. Aneurysm
NB!	The COX of the vascular wall restores its activity for several hours in contrast to the COX of platelets →anti trimboxane effect of prostacyclin. For ↓ irritating effect on the stomach → enteric-coated forms	Effective only in combination with aspirin or in direct anticoagulants	Antiplatelet effect → in 24-48 h. Peak action→ in 3-10 days, and for acetylsalicylic acid in 1 h.	In the congenital absence of this re-receptor complex, blood loss develops-Glanzmann's thrombasthenia

Drug interactions	1. NSAIDs, glucocorticosteroids ↑ risk of erosive and ulcerative lesions of the gastrointestinal tract with hidden bleeding. 2. Glucocorticosteroids, ibuprofen lead to ↓ antiplatelet activity of aspirin. 3. Warfarin, methotrexate, oral hypoglycemic drugs lead to ↑ toxicity. 4. Antihypertensive drugs lead to ↓ the effectiveness of these drugs. 5. Other antiplatelet agents and anticoagulants lead to a ↑ risk of bleeding. 6. Cardiac glycosides lead to ↑ plasma drug concentrations. 7. Alcohol ↑ risk of ulcerogenic effects and bleeding. 8. Hypoglycemic agents with acetylsalicylic acid ↑ risk of hypoglycemia. 9. Salicylates displace valproic acid from protein binding. 10. Selective serotonin reuptake inhibitors ↑ risk of gastrointestinal bleeding due to synergy effect. 11. The combination with deferoxamine lead to ↑ tissue toxicity of iron. 12. The combination with uricosuric agents is accompanied by a ↓ effect (exacerbation of gout).	1. NSAIDs, antiplatelet agents, anticoagulants ↑ risk of hemorrhagic complications. 2. Combination with antihypertensive drugs ↑ risk of collapse. 3. Proton pump inhibitors, antacids ↓ the effectiveness of dipyridamole. 4. Combination with beta-blockers ↑ risk of arrhythmia and asystole. 5. Cephalosporins ↑ effect of dipyridamole. 6. The combination with cholinesterase inhibitors leads to a ↓ effect (exacerbation of myasthenia gravis). 7. The combination with xanthine derivatives leads to ↓ coronary expansion effect (2). 8. Combination with digoxin ↑ its absorption.	1. NSAIDs, glucocorticosteroids ↑ risk of erosive and ulcerative lesions of the gastrointestinal tract with hidden bleeding. 2. Medicines that inhibit CYP2C19 (fluoxetine, fluconazole, ciprofloxacin, PPI, cimetidine) ↓ the effectiveness of these drugs. 3. Substrates CYP2C8 (repaglinide, paclitaxel) ↑ toxicity. 4. Aspirin potentiates an antiplatelet effect.	1. ↑ risk of bleeding when combined with other drugs, ↓ blood coagulation. 2. ↑ the risk of bleeding with the simultaneous use of dextrans (5). 3. The introduction of other monoclonal antibodies ↑ the risk of allergic reactions.

Blood thinners (continued)

Anticoagulants – drugs reducing blood coagulation and prolonging coagulation time [1-4]

Classification	**Direct anticoagulants**		**Indirect anticoagulants**	**Direct oral factor Xa inhibitors**
	***Indirect* thrombin inhibitors**	***Direct* thrombin inhibitors**		
Drugs	1. Heparin *Low molecular weight heparins (LMWHs):* 2. Nadroparin (Fraxiparine) 3. Enoxaparin (Clexane) 4. Dalteparin (Fragmin) *Synthetic LMWH:* 5. Fondaparinux	6. Lepirudin, 7. Bivalirudin 8. Argatroban	9. Warfarin 10. Fenindione, 11. Acenocoumarol (syncumar) 12. Ethyldicoumarol (Neodicum Marine)	13. Rivaroxaban 14. Apixaban
Mechanism of action	*1. Heparin* + Antithrombin III → blockage of thromb inactive center → *inactivation of thrombin* (factorIIa); *inhibition* of a number of activated c*oagulation factors* (XIIa, XIa, IXa and especially **Xa** (prothrombinase**)**). *2. LMWH* practically do not effect thrombin, mostly *effect X coagulation factor* (increase the effect of anti thrombin III on factor Xa).	Independently attach to the active center of thrombin and do not require binding to anti thrombin III.	Vitamin K antagonists: block the synthesis of vitamin K-dependent coagulation factors (II - prothrombin,VII,IX,X) in the liver.	Selectively inhibit pro thrombinase (factorXa) → the reisn convertion of prothrombin to thrombin.
Pharmacological effects	1. Anticoagulant 2. Anti platelet 3. ↓ plasma lipid level (1,6-8) 4. Hypoglycemic, diuretic, anti-inflammatory, antiallergic, vasodilating (1) 5. Cholagogue, relax the smooth musculature of the vessels, analgesic and sedative action (9-12)			
Indications	Prevention and therapy of thromboembolic diseases and their complications (prevention of thrombosis during surgery, unstable angina, acute myocardial infarction, thrombosis and embolism of peripheral arteries and deep veins)			
Side effects	1. Bleeding of various localization, thrombosis-mourning 2. Paradoxical thrombosis (antibodies to heparin) 3. Allergic reactions	1. Bleeding	1. Bleeding 2. Alopecia 3. ↑ level of liver enzymes	1. Bleeding 2. ↑ level of hepatic enzymes 3. Nausea
Contraindications	1. Hemophilia, thrombocytopenia, hemorrhagic diathesis, bleeding 2. Malignant neoplasm and ulcerative lesions of the digestive tract 3. Dysfunction of the liver and kidneys			
NB!	Heparin is given to increase PPT (activated partial thromboplast in time) twice (30-35 sec) – this is optimal dose. **Antidote for overdose – protamine sulfate.**	For the treatment or prevention of thromboses associated with heparin-induced thrombocytopenia.	INR (international normalized ratio) should be controlled (INR<2-3). **Antidote is vitamin K (phytomenadione).**	Do not require a regular study of blood clotting.

Drug interactions	1. Have pharmaceutical interactions with other drugs in infusion solutions (1-5). 2. Tetracyclines and antibiotics of the polypeptide structure lead to ↓ effect (1). 3. Propranolol, verapamil, quinidine lead to ↓ communication with blood plasma proteins. 4. NSAIDs, carbenicillin, glucocorticosteroids lead to a ↑ risk of ulceration and bleeding from the gastrointestinal tract (1-5). 5. Combined oral contraceptives lead to ↓ anticoagulant action (1-5). 6. Ergot alkaloids, thyroxine, antihistamines, nicotine lead to ↓ effect (1) 7. Potassium preparations, potassium-sparing diuretics, ACE inhibitors, angiotensin-II inhibitors lead to hyperkalemia (3).	1. ↑ the risk of bleeding when combined with other agents that reduce blood coagulation.	1. Avoid concurrent use with: antiplatelet agents, NSAIDs, cimetidine, chloramphenicol, sulfonamides, cimecidin, because they ↑ bleeding risk 2. Safety control (INR) is needed in case of combination with drugs such as allopurinol, amiodarone, macrolides, fluoroquinolones, cephalosporins, metronidazole, azoles, interferon, amitriptyline, glibenclamide, heparin, digoxin, statins, alpha and beta interferon, methotrexate, paracetamol, propranolol, sulfonamides, tamoxifen, ethanol, ginkgo biloba, garlic, angelica, papaya, sage. 3. Monitoring of INR is needed in case of combination with drugs such as barbiturates, valproic acid, carbamazepine, vitamin K and C, spironolactone, azathioprine, mercaptopurine, griseofulvin, coenzyme Q10, cyclosporine, herbal remedies containing ginseng. 4. When combined with sulfonylurea derivatives, ↑ risk of hypoglycemic effect.	1. ↑ the risk of bleeding when combined with other agents that reduce blood coagulation.

Fibrinolytics– drugs that disolve blood clots [1-4].

Classification	I generation	II generation
Drugs	1. Streptokinase 2. Urokinase 3. Antistreplase	1. The tissue activator of plasminogen (alteplase) 2. Recombinant plasminogen activator (reteplase) 3. Tenecteplase
Mechanism of action	Equally activate both plasminogen on the surface of the thrombus and plasminogenin the plasma → plasmin (fibrinolysin)	Activate predominantly plasminogen on the surface of the thrombus
Pharmacological effects	**1. Fibrinolytic** (dissolve the filaments of fibrin, destroy fresh thrombi in the arteries, veins and cavities)	
Indications	1. Thrombosis of veins and arteries 2. Acute myocardial infarction (1-2 days) 3. Pulmonary thrombo embolism	
Side effects	1. Bleeding 2. Allergic reactions (1-3)	
Contraindications	1. Acute bleeding 2. Recent (up to 10 days) surgery and trauma 3. Violations of the blood coagulation system 4. Recent hemorrhagic stroke 5. Dissecting aortic aneurysm	
NB!	1. Apart from streptokinase, all thrombolytic drugs are administered together with heparin (unfractionatedorLMWHs), usually for 24 to 48 hours. 2. Trombolysis shouldn't be done in patients with acute coronary syndrome but without ST-segment elevation.	

Anemia drugs *(erythropoiesis-stimulating agents)*

Anemia is a medical condition in which the red blood cell count or hemoglobin is less than normal.

Pathology	Drugs
Iron deficiency anemia (hypo chromic) **NB!** Ferrous iron (Fe^{2+}) c combination with vitamin C is absorbed better. An exception is preparations of iron (III)-hydroxyl deploy maltose complex (IPC, Maltofer)	Iron supplements: 1.**Ferrousfumarate(Ferrocite)** 2.**Ferrousgluconate (Fergon, Ferralet)** 3.**Ferroussulfate** (**Ferrousal, Ferosul**) 4.Maltofer Cobalt supplements: 5. Ionic cobalt Human recombinantery thropoietin: 6. Epoetin alfa – i/v, s/c
Megaloblasticanemia	Cyanocobalamin (B12), folicacid(B_c)

Rules for the prescribing of iron supplements:

1. Treatment begins with oral administration of drugs;
2. Iron preparations are taken in 1 hour before meals or 2 hours after meals;
3. Monitor the effectiveness of therapy (a week later an increase in the number of reticulocytes, a month later - hemoglobin);
4. If oral use has no effect the drugs should be given intravenously;
5. Treatment begins with parenteral administration of drugs (afirst a tolerance test). In impaired absorption (diseases of the stomach and intestines) and with the aim of achieving rapid effects in severe anemia;
6. Prevent the simultaneous intake of iron preparations by mouth and by injection;
7. The duration of the treatment is at least 2 months.
8. To avoid darkening of the teeth, you should thoroughly rinse your mouth after taking iron-Containing drugs.

Aid for poisoning: gastriclavage, ***antidote is deferoxamine,*** symptomatic treatment.

Preparations for parenteral nutrition [1-4]

I. Donators of plastic material

Standard solutions of crystalline amino acids with a high nitrogen content **1.Aminoven 10 and 15%,** **2. Aminosol - Neo 10% and 15%; 3. Aminosmazal E 10% and 15%** **4.Infezol 100**	Standard solutions of crystalline amino acids with a low nitrogen content, used, as a rule, for peripheral parenteral nutrition **5. Aminoven 5%,** **6. Aminoplazmal E 5%** **7. Infezol 40**	Metabolic solutions of crystalline amino acids **8.Aminoplasmal-Hepa 10%** **9. Hepa Aminosteril 5 and 8%** **10.Aminosteril-Nephro** **11.Neframin.**	Crystalline amino acid solutions for children **12. Aminoven Infant 6**

II. Donators of energy

1. A solution of concentrated glucose 10%, 20%, 30%	2. Fat emulsions: - based on soybean oil (only long-chain triglycerides) - Intralipid, Lipovenosis; - based on soybean and coconut oils, containing a mixture of long chain and medium chain triglycerides (50:50) - Lipofundin; - based on soybean (20%) and olive (80%) oils - Clinoleic; - containing a mixture of soybean (30), medium chain triglycerides (30), olive (25) oils and fish oil (15) - SmofLipid or soybean (40), medium chain triglycerides (50) and fish oil (10) - Lipoplus; - Based on fish oil only - Omegaven

III. Three in One Containers

1. Cabiven central and peripheral;
2. OliClinomel central and peripheral;
3. Nutriflex Lipid.

VI. Micronutrients

Vitamin complexes 1. Cernevit 2. Soluvit 3. Vitalipid	Micronutrients complexes 3. Addamel

Plasma Substitution Solutions

In accordance with the functions of the blood, several groups of plasma-replacing agents exist:

Group 1 includes hemodynamic drugs. They are prescribed for the treatment of blood loss, shocks of various origins, during operations to restore hemodynamics and microcirculation, as well as hemodilution (colloids, crystalloids).

2nd group - detoxification infusions. These drugs are used to treat diseases that are accompanied by intoxication (reopoliglyukin, albumin).

The 3rd group includes drugs used for parenteral nutrition: nitrogen-containing (protein hydrolysates, mixtures of amino acids), energy (fat emulsions, carbohydrate solutions), as well as vitamin and microelement mixtures for parenteral administration.

Group 4 consists of regulators of water-salt balance and acid-base balance. This group includes crystalloid saline solutions, as well as osmodiuretics.

Group 5 - these are infusions with an oxygen-transport function (perfluorane, gelenpole).

6th group - drugs of complex action, which combine the properties of several groups of plasma-replacing agents.

Thyroid and antithyroid drugs [1-4]

Thyroid drugs - preparations of thyroid hormones (TG).
Antithyroid drugs - drugs that exert a retarding effect on the biosynthesis of thyroid hormones.

Classification	Thyroid drugs		Antithyroid drugs
Drugs	**T4 drugs** **1. L-thyroxine (eutiroks, levothyroxine)** **2. Iodothyrox (levothyroxine sodium + potassium iodide)**	**T3 drugs** **3. Lyotyronin**	**4. Thiamazole (Mercazolil, tyrosol)** **5. Propylthiouracil**
Mechanism of action	Receptor binding to the genome, a change in oxidative metabolism in the mitochondria		Thyroid peroxidase is blocked and iodination of thyronine in T4 in T3 is inhibited.
Pharmacological effect	In small doses - anabolic, in moderate - ↑ activity of the cardiovascular system and tissues oxygen demand, in big - oppression of thyrotropin-releasing hormone and thyroid-stimulating hormone.		↓ T3 and T4 levels in the blood
Indications for use	**1**. Hypothyroidism 2. Euthyroid goiter 3. Autoimmune thyroiditis 4. Substitution therapy after surgical treatment of thyroid cancer 5. Микседема (3) 6. Cretynism (3) 7. Hypothyroid obesity		**1. Thyrotoxicosis** **2. Preparation for resection of thyroid gland or treatment** 3. Postoperative relapse of thyrotoxicosis (4) 4. Nodular goiter (4)
Side effects	1. Arrhythmia 2. Tachycardia 3. Angina pectoris 4. ↑ temperature 5. Anxiety, insomnia		1. Arthralgia 2. Allergic reactions 3. Suppression of myelopoiesis 4. Dysfunction of the liver 5. Vasculitis 6. Hypothyroidism
Contraindications	1. Uncompensated pituitary or adrenal insufficiency 2. Thyrotoxicosis 3. Acute myocardial infarction 4. Myocarditis 5. Pancarditis 6. Cachexia (3)		1. Hypersensitivity 2. Leukopenia, agranulocytosis 3. Hypothyroidism 4. Hepatic insufficiency 5. Cirrhosis of the liver 6. Active hepatitis 7. Cholestasis (4) 8. Pregnancy, lactation

Drug interactions	1. ↑ the effect of indirect anticoagulants (coumarin derivatives). 2. ↓ the effect of antidiabetic drugs. 3. ↓ the effect of cardiac glycosides (1,2). 4. ↑ the effect of tricyclic antidepressants (1,2). 5. Wwhen phenytoin is rapidly injected intravenously, free levothyroxine levels may increase (1,2). levothyroxine in plasma may increase, which may cause cardiac arrhythmias. 6. Protease inhibitors (e.g., ritonavir, indinavir, lopinavir) may affect the efficacy of levothyroxine. Close monitoring of thyroid hormone concentrations is recommended. The dose of levothyroxine sodium should be adjusted if necessary. 7. Ion-exchange resins such as cholestyramine and cholestipol inhibit the absorption of sodium levothyroxine. In this regard, levothyroxine sodium should be used 4-5 hours before taking these drugs. 8. Drugs containing aluminum, iron, calcium carbonate ↓ the effectiveness of drugs containing levothyroxine when taken simultaneously. 9. Salicylates, dicumarol, furosemide in high doses (250 mg), clofibrate and other drugs can displace levothyroxine sodium from binding to plasma proteins, which leads to increased concentration of fT4 fraction. 10. Oral contraceptives ↓ efficacy. 11. Co-containing products may contribute to ↓ intestinal absorption of levothyroxine sodium. 12. Phenytoin, salicylates, dicumarol, furosemide (in high doses), clofibrate, antidepressants, cardiac glycosides, ketamine ↑ the concentration and risk of side effects of liothyronine. 13. Concomitant use with potassium-saving diuretics may ↑ blood potassium levels (2). 14. Somatotropin when used concomitantly with Iodothyrox may accelerate the closure of epiphyseal growth zones.	1. Lack of iodine ↑ thyroid susceptibility to the drug (4), and excess iodine ↓ reduces it. Other direct interactions with other drugs are unknown. Note that the metabolism and excretion of other drugs may be increased in hyperthyroidism. These parameters are normalized when the thyroid function is restored. If necessary, the drug dosage should be adjusted. There is also evidence that correction of hyperthyroidism may normalize increased anticoagulant activity in patients with hyperthyroidism. 2. Thyreostatic effect is attenuated by iodine-containing drugs, including radiopaque agents (5). 3. Doses of propranolol or coumarin derivatives should be corrected if concomitantly taken with propranolol or coumarin derivatives (5). 4. Myelotoxic drugs ↑ manifestation of hematotoxicity of the drug (5)

Insulins and synthetic hypoglycemic agents [1-4]

Hypoglycemic agents are drugs used to normalize blood glucose levels in diabetes mellitus.

Classification	Insulins	Oral hypoglycemic agents
Drugs	*Rapid-acting* - **Lispro (Humalog)** - **Aspart (Novolog)** - **Glulisine (Apidra)** *Short-acting* - **Regular (R) or novolin** - **Velosulin (for insulin pump)** *Intermediate-acting* - **NPH (**neutral protamine Hagedorn) *Long-acting* **- insulin glargine (Lantus, Basaltag)** **- insulin determir (Levemir)** **- insulin deglutec (Tresiba)** *Pre-mixed* **- Humulin 70/30** **- Novolin 70/30** **- Novolog 70/30** **- Humulin 50/50**	*Sentesizers* ***Biguanides*** - **metformine** - **buformine** ***Thiazolidinedione (glitazones)*** - **rosiglitazone** - **pioglitazone** - **troglitazone** *Glucosurics(gliflozins***)** - **remogliflozin** - **sergliflozine** - *Alpha-glucosides inhibitors* - **acarbose** *Secretagogues* ***Sulphonilureas*** **- Ist generation (tolbutamide, tozalamide)** **- IInd generation (gliclazide, glipizide, gliquidone)** ***Non-sulphonilurea secretagogues (meglitinides)*** **- meglitinide** **- repaglinide** *Glucagon-like peptide analogues* **- exanatide** **- liraglutide** *Dipeptidyl peptidase-4 inhibitors(gliptins)* **- sitagliptin** **- alogliptin**
Mechanism of action	Binding to insulin receptors, inclusion in the cytoplasmic membrane of intracellular vesicles with glucose transfer proteins, transport of glucose to the cell.	*Sentesizers*: ↑ uptake of glucose by the periphery. *Secretagogues, gliptin, glucagon-like peptide analogues:* ↑ insulin output from the pancreas. *Glucosurics:* block the re-uptake of glucose in the renal tubules, promoting loss of glucose in the urine. *Alpha-glucosides inhibitors*: slow the digestion of starch in the small intestine.
Pharmacological effect	1. Hypoglycemic 2. Anabolic (enhancing the synthesis of proteins and fats) 3. Anticatabolic (↓ protein hydrolysis and lipolysis)	1. Hypoglycemic
Indications for use	1. Type 1 diabetes mellitus 2. Type 2 diabetes mellitus (resistance to oral hypoglycemic agents, intercurrent diseases, pregnancy)	1. Type 2 diabetes mellitus 2. Obesity
Side effects	1. Hypoglycemia 2. Visual impairment 3. Lipodystrophy in the injection site.	1. Hypoglycemia 2. Nausea, vomiting 3. Diarrhea
Contraindications	1. Hypoglycemia, 2. Hypersensitivity	1. Type 1 diabetes mellitus 2. Diabetic ketoacidosis 3. Dysfunction of the liver and kidneys

NB!	**Rules for insulin administration:** • Short-acting insulin: 30 minutes before meals. • intermediate-acting insulin: 45-60 minutes before meals. (Both types - to simulate stimulated secretion of insulin) • Long-acting insulin: once a day to simulate the basal secretion of insulin.

Drug interactions	Currently, there are about 1,500 drugs that can influence the hypoglycemic effect of insulin. The following examples may be given. 1. Drugs ↑ the effects of inulin: Oral antidiabetic drugs, salicylates and other NSAIDs, androgens and anabolic steroids, bromocriptine, anorexigenic drugs,fluoxetine and MAO inhibitors (including furazalidone), ACE inhibitors and angiotensin II receptor blockers, Carboanhydrase inhibitors, β-adrenoblockers, α-adrenoblockers, moxonidine, disopyramide, guanethidine, theophylline, pentoxifylline, pyridoxine, sulfonamides, tetracyclines, ampicillin, fibrates, cyclophosphamide. 2. Drugs, ↓ the effects of insulin: glucagon, adrenomimetics (epinephrine, dopamine), β2-adrenoreceptor agonists: terbutaline, salbutamol, etc.), glucocorticoids, ACTH, somatotropic hormone, somatostatin and its analogues or antagonists (octreotide/lanreotide), estrogen preparations (including hormonal contraceptives), thyroid hormones, Heparins and other anticoagulants, triamterene, loop, thiazide and thiazide-like diuretics, phenolphthalein, isoniazid, nifedipine, phenytoin, , neuroleptics (phenothiazine derivatives, chlorpromethoxine, etc.), morphine, morphine, amphetamines and other drugs.), morphine, amphetamine and other psychostimulants, baclofen, nicotinic acid. 3. Drugs that can both ↑ or ↓ the effects of insulin: clonidine and reserpine, lithium preparations; tricyclic and quadracyclic antidepressants, which, being synergistic with insulin, can increase the need for it by increasing appetite. 4. Biological activity of insulins ↓ as a result of contact with ethanol, other antiseptics, so the skin is not treated with disinfectants before injecting insulins. 5. Strong alcoholic beverages act as synergists of insulin, often causing hypoglycemia; weak ones first contribute to hyperglycemia, sometimes very prolonged, and later may cause delayed hypoglycemia.	1. Glucocorticoids, thiazide diuretics, oral contraceptives, thyroid hormones, phenothiazine derivatives ↓ efficiency of metformin. 2. ACE inhibitors, acetylsalicylic acid, MAO inhibitors ↑ the hypoglycemic effect of metformin. 3. Potentiation of insulin action. 4. Sulfonylurea derivatives - mutual enhancement of action 5. Antifungal agents of systemic action (azole derivatives), fluoroquinolones, tetracyclines, clarithromycin, chloramphenicol, para-aminosalicylic acid, beta-adrenoblockers, ACE inhibitors, NSAIDs, antidepressants (eg, fluoxetine, MAO inhibitors), clofibrate, besafibrate, probenecid, paracetamol, etionamide, anabolic steroids and male sex hormones, pentoxifylline, disopyramide, phenflouramine, cyclophosphamide, sulfonamides, insulin ↑ hypoglycemic/ Barbiturates, isoniazid, cyclosporine, phenothiazines, diazoxide, glucocorticoid and thyroid hormones, estrogens, gestagens, phenytoin, glucagon, adrenomimetic drugs, lithium salts, nicotinic acid derivatives, calcium channel blockers, saluretics, rifampicin ↓ hypoglycemic effect 6. In concomitant use with digoxin, valproic acid ↓ of the latter in blood plasma concentrations 7. Drugs that cause hyperglycemia, such as thiazide diuretics, glucocorticosteroids, phenothiazine, estrogens, oral contraceptives, isoniazid, nicotinic acid, phenytoin, adrenomimetics, thyroid hormones, "slow" calcium channels, significantly ↓ acarbose activity. 8. When using thiazolidinedione derivatives simultaneously with oral contraceptives containing ethinylestradiol and norethindrone, plasma concentrations of both hormones decrease by 30%, which leads to a decrease in the contraceptive effect 9. ↑ diuretic effect of thiazide and loop diuretics

SDGTT-2 inhibitors - inhibitors of sodium-dependent glucose transporter type 2 or

SGCTT-2 inhibitors - inhibitors of the type 2 sodium-glucose co-transporter.

GLP-1-glucagon-like peptide