Pharmacology Cito

Read: it is important!

Dear future physicians and pharmaceutists!

The scientific and pedagogical staff of the Pharmacology department of the National University of Pharmacy (Kharkiv) presents a new textbook "Pharmacology – Cito!" to you. We want to change the myth that it is impossible to learn pharmacology quickly and qualitatively. The textbook "Pharmacology – Cito!" is published for those, who have decided to connect his or her profession with medicines, but think that a great amount of the information in pharmacology is hard to learn. Taking this fact into account we have decided to help those, who wish to master pharmacology in logical, fast - "Cito!"-version.

Not be afraid of pharmacology!

The 40-year experience of teaching pharmacology testifies that for the last 10-15 years a tendency of reducing the amount of classroom hours in pharmacology because of increasing the amount of the individual work is being observed. However, because of the lack of time and the constant increasing volume of information in pharmacology, everyone has not enough time to master it soundly and qualitatively. This textbook trains future pharmaceutists and physicians in the pharmacological logic, i.e. knowing the mechanisms of drug action one can understand their pharmacodynamics, naturally, on the basis of pharmacodynamics one can find logically the indications to their application and from their side effects the contraindications can be seen. The information about the peculiarities of medicines has been generalized and given as a pharmacological "face" in tables. The volume of this textbook in pharmacology is sufficient for acquiring the confidence in the opportunity of the further improving of knowledge in this discipline, which is important for a physician and a pharmaceutist. Here we have concentrated such amount of information that is necessary enough for getting a pharmacological "portrait" of new and traditional medicines; we have provided physicians, pharmaceutists and students with **the algorithm of the pharmacological logic, thinking and intuition.**

Today the assortment of medicines, which a physician and a pharmaceutist are "armed" with, is more than 400 thousand trademarks. The textbook gives the information on those blockbusters, brands and generics of the world pharmacy, without knowing them either a physician or a pharmaceutist cannot "step over the threshold" of a ward and a chemist's shop; every physician and pharmaceutist should know them. Frequently the insufficient survivability of knowledge in the basic subjects (pathology, physiology, biochemistry) has obliged us to help those, who had lost this knowledge. That's why in the section "Glossary" we have reminded you the terms and concepts, which you had known, but forgot. The unique feature of this textbook is the presentation of the information, which corresponds to the credit-module organization of the academic process according to the European educational standards.

This textbook is the first step for those, who want to succeed in pharmacotherapy, to master the pharmacological logic. Despite of the conciseness description of a "pharmacological face" of each pharmacological group all the elements of the drug characteristics in the textbook (INN and trade names, the mechanism of action, pharmacodynamics, indications, side effects and contraindications) are presented at the advanced up-to-date level. The authors hope that **''Pharmacology – Cito!''** (the **pharmacological logic**) will be the start for further improving your pharmacological knowledge.

This edition is intended for students, physicians and pharmaceutists, who want to catch everything in this life!

With sincere hope for mutual understanding, professor S. Drogovoz

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GENERAL PHARMACOLOGY ("PHARMACOLOGICAL ALPHABET")

PHARMACOLOGY AND ITS BASIC TERMS

Pharmacology in its literal translation means "the science about medicines" (*Pharmakon* in Greek is "medicine, poison"; *logos* in Latin means "science"). Nowadays pharmacology is a complex science studying the action of medicines on healthy and diseased organisms, the science about the purposeful search of new medicines and their rational use. A future physician and a pharmaceutist must understand clearly the actual meaning of common terms (approved by the WHO), which characterize drugs and changes in the organism occurred after their introduction.

A medicine (drug, medication, remedy, medicinal agent) is a pharmacological agent in a definite medicinal form approved for application with the purpose of treatment, prophylaxis and diagnostics of diseases.

A medicinal substance is an individual pharmacological substance approved for application.

A pharmacological substance is an individual substance with the pharmacological activity under research.

A pharmacological agent (remedy) is a pharmacological substance or their combination in a definite medicinal form under research.

Other names of medicines are pharmaceutical agent, physiologically, biochemically and pharmacologically active substance. These names are lame or unpractical synonyms for the word "medicine".

A medicinal form is the form of a medicine, which is convenient for use, appropriate for the aims of therapy and provides the required effect.

Medicines introduced into the organism interact with the cell receptors, as a result functions of cells intensify (stimulate) or suppress (inhibit). The intensification or suppression of biophysical, biochemical and physiological processes in a cell under the action of medicines is called a **pharmacological reaction**. A **pharmacological effect** is the result of the successive changes in the functions of the organism's organs and systems under the action of medicines. The complex of changes (pharmacological effects), which takes place in the organism under the influence of medicines, is called **pharmacodynamics** or **pharmacological properties** of a medicine.

The method, by which a medicine's pharmacological effect is achieved, is called the **mechanism of its action.**

THE MECHANISM OF DRUGS' ACTION

To reveal its pharmacological effect that is realized via the mechanism of action, a medicine must contact with molecules of the organism's cells. A contact of a medicine with a biological substrate – ligand (*ligo* means "to connect") can occur with the help of chemical, physical, physicochemical interaction. Receptors, enzymes, ion channels, transport systems and others are the primary "targets" for medicines. Receptors are specific cell structures, which provide the interaction between a medicine and the organism. They interact only with medicines that have a certain chemical structure, i.e. they possess the property of selectivity.

The typical mechanisms of drug and receptor interaction:

1. A medicine that has structural similarity to a metabolite (for example, mediator) interacting with the receptor promotes its excitation (imitating the mediator's action). Such medicine is called **agonist** (in Greek *agonistes* is "a rival", *agon* is "a struggle") or **mimetic** (in English "to mimic"). Durability of a medicine binding to certain receptors is stipulated by their structure and it is termed as **"affinity"** (in Latin *affinis* is "relative").

2. A medicine is similar to a metabolite; it binds to a receptor, but does not give a chance to a true metabolite to bind to a receptor causing effects opposite to the metabolite. Such medicines are called **antagonists** or **blockers** (*antagonista* is "rivalry").

3. Acting on the receptors medicines can combine the properties of agonists and antagonists. In this case they are called **agonists-antagonists**.

4. When interacting with the receptor's allosteric centre medicines promotes the conformational changes in the structure of the receptor modifying its sensitivity to the organism's metabolites. They are medicines - **modulators**.

Many medicines modify the functioning of the **ion channels**. One of the "targets" for medicines are potential-depending ion channels that conduct Na^+ , K^+ , Ca^{2+} selectively through the cell membrane. Medicines can **block** potential-depending ion channels (break the penetration of ions by channels through the cell membrane) or **activate** these channels (assist their opening and passing of ion flows).

The variants of the drug action mechanisms listed above do not exhaust all possibilities of their interaction with the body cells. Nowadays the mechanism of action has not been found for all medicines.

TYPES OF THE DRUG ACTION

To analyze complex and various phenomena of **pharmacodynamics** there are several types of the drug action.

Local (preresorptive) action is all changes occurring in the site of the drug application. The local action is revealed if a medicine is applied on the skin, mucous membranes and is directly introduced into organs. It should be remembered that the local action cannot be considered separately from the reaction of the whole organism. The local action is characterized, for example, by astringent, irritant, cauterant, local anesthetic effect of medicines. To reveal the local action ointments, gels, solutions for external use, powders, pastes, liniments and plasters are often used.

The resorptive action (in Latin *resorbeo* means "I absorb") appears when a medicine absorbs in the blood and can develop effects in the different organs and tissues that it interacts with. There is a **direct** and **indirect** resorptive action. The **direct action is** the effect caused by a direct influence of a medicine on the target organ. The **indirect effect** appears indirectly in other organs and tissues and it is a result of the drug's direct action. For example, the improvement of the cardiac activity under the influence of cardiac glycosides (direct action) leads to the normalization of the blood circulation and increase of diuresis (indirect action).

The direct action is always **primary**, the indirect one is **secondary**. The subtype of the drug's direct action is the **selective action**, i.e. the influence of the medicine only on the limited group of cells, organs.

Reflex action is the indirect action of a medicine, in which mechanism of reflexes development take part. The reflex action is carried out distantly and it is the consequence of the afferent nerves endings stimulation. For example, the ammonium hydroxide while inhaling irritates the mucous membrane receptors of the respiratory tract and stimulates the respiratory and vasomotor centres by reflex.

The **main** action and **side effect** of medicines are distinguished. The main (positive) action is a desirable action, it is for it the medicine is used. The side effect (negative) action, as a rule, is undesirable action of the medicine and it can impede the main action.

There are also **reversible** and **irreversible** actions. If the changes in the organism occurring as a result of the drug's action disappear without any consequences over a period of time, then a medicine possesses a reversible action. In opposite case the irreversible action takes place.

The drug action also subdivides into **pharmacotherapeutic** and **negative**. The one determines, where a medicine acts treating a disease (the cause, pathogenesis, symptoms); the other is used for characterizing the safety of the drug's use. Nowadays pharmacotherapy uses medicines with etiotropic, pathogenetic, symptomatic, stimulative and substitutive actions.

The etiotropic (causal) pharmacotherapy is directed to elimination of the disease's cause. As etiotropic therapy chemotherapeutic, antihelminthic, vitamin-containing medicines and some antidotes are used. Medicines with the **pathogenetic** type of action are those, which eliminate or decrease functional and structural abnormalities arised in the process of the disease's development (pathogenesis). As pathogenetic therapy anti-inflammatory, antihistaminic medicines and cardiac glycosides are used.

The "oldest" type of pharmacotherapy is **symptomatic**, which is directed to elimination of the disease's symptoms. This type of treatment is palliative (in Latin *pallio* is "to mask, to smooth"). In this case medicines with the symptomatic action such as analgesics, spasmolytics, antihypertensives, antipyretics, etc. are applied.

The stimulation pharmacotherapy is directed to increase of host defences (the process of sanogenesis) and stimulate the organism's compensatory mechanisms. This is the least developed type of the drug therapy. Vaccines, actoprotectors, adaptogens, some immunostimulants possess a stimulating action.

In a number of cases the **substitution** (replacement) pharmacotherapy is used. It is directed to restore deficiency of substances not produced in the sufficient amount in the organism (vitaminous, enzymatic, hormonal therapy).

THE NEGATIVE EFFECTS OF DRUGS

Cumulation (in Latin *cumulatio* means "accumulation") develops due to the accumulation of a medicine in the organism (**material cumulation**) or summation of its effects when after excretion of the medicine the changes caused by it remain for a long time (**functional cumulation**). The material cumulation is typical for cardiac glycosides, salts of heavy metals, bromides; the functional one is for ethyl alcohol. Sometimes the cumulation phenomenon is used to achieve the required therapeutic effect of the medicine (for example, cardiac glycosides).

Habituation (syn. steadiness, tolerance; *tolerantia* means "endurance, resistance") is the state when the effectiveness of medicines decreases with their repeated administration. A

rapid drug habituation is called **tachyphylaxis** (*tachys* means "rapid", *phylaxis* is "protection"). It is typical for naphthizin, ephedrine hydrochloride.

Addiction (drug dependence) is characterized by an overmastering desire to use a medicine regularly. As a rule, addiction appears to the drugs that cause euphoria (e.g. narcotic analgesics).

Abstinence is a feeling of discomfort, uncertainty, mental stress, functional disorders, sense of fear, and conflictness as a response to the absence of a medicine that caused addiction.

Drug allergy is an acquired unnatural reaction of the organism to medicines that appears after their repeated intake (on the $7^{th}-12^{th}$ day from the beginning of administration).

Sensibilization is the process of the organism's sensitivity increase to a medicine. Some medicines interacting with proteins form complexes (haptens) and become true antigens.

Drug idiosyncrasy is an inherited qualitatively unnatural reaction to a medicine appearing after the first contact with it.

Dysbiosis (dysbacteriosis) is a disorder of the normal microflora content and development of non-typical microorganisms in the organism.

The embryotoxic action appears on the early terms of pregnancy (the first two weeks) and it is the result of the drug toxic action on the fertilized ovule at first, and then on the embryo. Often the embryotoxic action of medicines ends by the spontaneous abortion. If the embryotoxic effect does not end with abortion, then it is the beginning of the teratogenic action. Anomalies of the fetus development – the **teratogenic** (in Greek *teratos* is "freak, deformity") **action** - develop from the 3rd up to the 10th week of pregnancy when differentiation of the fetus tissues occurs most intensively; and because of this the most severe defects of fetus development occur. Functional and structural disorders of the fetus organs under the influence of drugs, which are capable to penetrate through the placenta in the IIIrd trimester of pregnancy, are called the **fetotoxic** action.

The mutagenic action is the drug's teratogenic effect fixed firmly in the genes, it arises more often when a woman and sometimes a man takes a medicine during a period of gonadogenesis. The **blastomagenic** (cancerogenic) action is the ability of a medicine to stimulate the development of tumors. Withdrawal syndrome (the exacerbation of the disease) develops with a long-term application of a medicine and then its sudden withdrawal.

PRINCIPLES OF THE DRUG DOSING

Dose (in Greek *dosis* is "a portion") is the amount of a medicine that has come into the organism. It is usually expressed in gram or gram parts. Drugs doses, which are used for treating and do not cause pathological deviations in the organism's vital activity, are called curative or **therapeutic** doses. A therapeutic dose is subdivided into **single**, **daily** and a **course** dose. A single dose is prescribed for one intake, a daily one is for the whole day and a course dose is taken the whole course of treatment. These doses are subdivided into minimal, average, maximal doses respectively. **The minimal therapeutic dose** (threshold) causes the minimal therapeutic effect; it is in 2-3 times smaller than the average therapeutic dose. **The average therapeutic dose** causes the optimal therapeutic effect in most patients without any toxic manifestations. The pharmaceutical industry produces an average therapeutic dose of a medicine in one unit of a medicinal form (in one ampoule, tablet), as a rule. **The maximal therapeutic dose** causes the most powerful therapeutic effect. A minimal dose, which causes side effects, is called **minimal toxic**. **The minimal lethal dose** (fatal) is called a minimal dose that causes death.

The principle of dosing for chemotherapeutic medicines and cardiac glycosides differs from those for the other drugs. At first a **loading dose** is prescribed with the aim of creating a high concentration of a medicine in blood and tissues to obtain a fast therapeutic effect. And then a **maintaining dose**, which equals the amount of the excreted medicine during the time between intakes, is introduced.

In medical practice only those doses of medicines that are in the **range from the minimal therapeutic to the minimal toxic dose** can be used. This **interval** is called the **range of the drug therapeutic action.**

The more width the therapeutic action has, the safer a medicine is. To characterize the drugs' safety the **therapeutic value** (TV) is also used. The therapeutic value is a ratio of an average lethal dose to an average therapeutic one: $TV=LD_{50}/ED_{50}$, where LD_{50} is a dose causing death of 50% of the experimental animals; ED_{50} is a dose that results in the pharmacological effect of 50% of the animals. The more therapeutic value is, the safer a medicine is.

THE ROUTES OF DRUG ADMINISTRATION

All routes of drug administration can be conditionally divided into ones used as the local action and others used as the resorptive action. The **local administration** of medicines has the aim of the long-term action in the site of application. Medicines are used locally in pathological processes on skin, the mucous membrane of eyes, nose, gastrointestinal tract, urinary bladder and pleura. Hydrophilic substances (sugar, ions) are not absorbed by the skin and act surfactantly, and lipophilic substances (steroid hormones, etc.) penetrate through the skin proportionally to their solubility in fats.

The routes of drug administration with the aim of the resorptive action are divided into enteral and parenteral.

The enteral route of drug administration through the gastrointestinal tract (*ento* means "deep into", *enteron* is "intestine") includes their intake *sub linguam* – under the tongue, sublingually; *per rectum* - through the rectum, rectally; *per os* – through the mouth, orally, perorally. These routes are given according to the onset of the drug action in the organism. The fastest onset of the drug action is when introducing them sublingually.

The parenteral route is the introduction of medicines without getting into the gastrointestinal tract. By the increase of the drug action onset routes can be arranged as follows: subcutaneous, intramuscular, inhalant, intravenous and intra-arterial one.

A positive aspect in the drug's peroral administration is that it is the most suitable route, which does not require special equipment, sterility, participation of the medical staff and appliances. Liquid and solid medicinal forms can be taken by this way. The presence of the "biological filtration" provides a rare appearance of drug negative effects. The most favourable time for internal intake of medicines is 30-40 minutes before meals or in 3-4 hours after meals.

The main disadvantage of this route of drug administration is the fact that many medicines inactivate in the gastrointestinal tract interacting with food, enzymes and the

hydrochloric acid. Protein medications (insulin, heparin, etc.) are not prescribed perorally as they are disintegrated in the gastrointestinal tract. This route is unsuitable for rendering a rapid aid (the onset of action occurs slowly). In the pathological states of the gastrointestinal tract the onset and the complete absorption of medicines change. All medicines absorbed in the gastrointestinal tract get into the liver, where they undergo chemical transformations and inactivation. The peroral route is unsuitable for reaching the accurate drug concentration in blood. The doses of medicines when taken them internally should be much more greater than when introducing them parenterally.

Medicines are introduced via the rectum in the case when it is impossible to take them per os: in the unconscious state of a patient, while vomiting, in gastric diseases, to patients with mental disorders, as well as if a substance is destroyed quickly while passing through the liver. The rectal route of drug administration remains one of the rational routes in the pediatric practice. By onset of the effect this route is similar to the intramuscular one; in this case effect appears in 5-15 minutes. And medicines are destroyed in the liver not so rapidly, because from the rectum they come into blood, not through the portal vein, but via the postcava system, where up to 50% of the introduced dose does not get to the liver. With this route of introduction medicines have the biological filtration and their negative effect on the liver is decreased. The dose of medicines introducing through the rectum is more accurate, and it can be reduced in one third comparing to the peroral route of administration. Disadvantages of this route are discomfort of taking a medicinal form (suppositories, enema 40-45 ml), as well as the fact that not all substances are absorbed.

Some medicinal substances are absorbed especially well from the sublingual area. When introducing medicines sublingually and behind the cheek (**subbucally**) they act rapidly (the effect develops in 1-3 minutes), avoid the liver barrier, do not interact with the hydrochloric acid and enzymes of the gastrointestinal tract. This route of administration can be used mainly for strong effective medicines, as well as for medicines that are destroyed by gastrointestinal enzymes.

The parenteral route of drug administration has the advantage over the enteral one: a medicine gets into blood (accurate dosing) more rapidly and completely; a possible introduction of medicines to the unconscious patient, medicines are not destroyed in the liver and the gastrointestinal tract. The **negative** features of the parenteral route of drug introduction are the necessity of keeping the strict aseptics, participation of the medical staff, the presence of instruments, the risk of the organism's contamination, injuries while introducing a medicine.

Aqueous and oil (camphor) solutions of medicines, suspensions (the prolonged forms of insulin) are introduced **subcutaneously**.

The intramuscular route of drug administration provides their coming into the general blood circulation in 10-15 minutes. Due to a good blood supply the muscular tissue absorption of medicines into the blood occurs rather fast.

Medicines that are absorbed well through the mucous membrane of alveoli and possess the systemic action are used in the **form of inhalations** (remedies for inhalation narcosis).

The intravenous route of drug introduction is used in the emergency cases when very rapid onset of action is necessary to reach the required effect. It is forbidden to introduce oil solutions, suspensions, medicines causing hemolysis, thrombosis, conversion

of hemoglobin into methemoglobin, containing air into the vein. The introduction of the medicines with the irritative properties in the vein can result in the development of phlebitis.

Medicines that penetrate through the blood-brain (haematoencephal) barrier poorly are introduced under the membranes of the brain - **subarachnoidly** and **subdurally** (antibiotics in the cases of infectious diseases of the brain tissues).

In order to avoid or reduce the negative effect of medicines physicians and pharmaceutists should always remember that the right choice of a dose, the route of drug administration, simultaneous administration of etiotropic, pathogenetic and symptomatic therapy are the important conditions for successful pharmacotherapy of any disease.

PHARMACOKINETICS OF MEDICINES

The pharmacokinetics (*pharmakon* means "medicine", *kinetikos* is "motion") studies transport (absorption), distribution (deposition), transformation (biotransformation, metabolism) of medicines and their excretion (elimination) from the organism.



Fig. 1. Steps of pharmacokinetics

Absorption of medicines

The process of drug absorption from the gastrointestinal tract, via skin, the respiratory system organs and the vessels' wall is mainly provided by 4 types of the biological membranes as processes of the passive diffusion, the facilitated diffusion, the active diffusion and pinocytosis.

The passive diffusion is characterized by such features as: a) molecules of a medicine move from the area with a high concentration to the area with a low concentration; b) the rate of transport is proportional to the concentration gradient on the both sides of the membrane.

Membranes of the second type (**facilitated diffusion**) contain substances – specific carriers that provide the transport for particular medicines only. This transport occurs by the concentration gradient and is not connected with the energy loss, and the rate of this diffusion is high.

In the membranes of the third type the drug absorption takes place by the **active diffusion** with the consumption of energy. Here transport can occur against

the concentration gradient. It is provided by the presence of a carrier, which changes its structure during the transport of a drug molecule, and this process requires the consumption of energy. This mechanism is called the biological pump.

The essence of pinocytosis process, absorption of medicines by the fourth type membranes, is in that substance, which is being carried, contacts with a definite part of the cells' membrane surface and this section sags inwards, the edges of the hollow closes forming a bubble with the substance transported. It separates from the outer surface of the membrane and is transferred into the cell. The fourth type membranes are located in the renal glomeruli. The first type membranes with some areas of the membranes of the second and the third type are functioning in the renal tubules. The first type membranes are mainly in the gastrointestinal tract. Capillaries possess the properties of the first type membranes containing some areas with the fourth type membranes.

During absorption medicines get over the histohematic, blood-brain and placental barriers.

The blood-brain barrier (BBB) is the membranes that separate the cerebral tissue and the cerebrospinal liquid from blood. The ability of medicines to pass the blood-brain barrier depends on their solubility in fats. If a substance is soluble in fats, it penetrates quickly into the brain and the cerebrospinal liquid. Because of children of the younger age have an incomplete BBB comparing to the adult's BBB, medicines pass it much faster.

The placental barrier separates the blood circulation of the mother and the fetus. It has a high permeability (erythrocytes penetrate through it) at the early stages of pregnancy, then it strengthens and acquires all the features of the lipoid membrane with the active transport of metabolites. The placental permeability increases in the period of toxicosis, at early stages of pregnancy, in hypoxia, hemorrhage, endocrine dysfunctions. Those substances, which in the normal conditions do not cross the placental barrier, can penetrate through it in these cases. The penetration of medicines through the placental barrier is the cause of their negative (teratogenic) effect on the fetus.

The distribution of medicines in the organism

The drug distribution in the organism depends on its ability to bind with the ingredients of blood or other tissues. It leads to the drug deposition. Binding of a medicine to proteins limits its distribution in the organism because only the free form of a medicine can diffuse through the biological membranes. There are three fractions of medicines: free, bound with proteins, fixed in tissues. **Only free fraction possesses the pharmacological effect and undergoes biotransformation and excretion.**

The process of drug binding influences considerably on revealing their specific activity. A high level of binding substances to proteins stipulates their prolonged effect (sulphadimethoxin). The peculiarity of the drug distribution is determined by their ability to dissolve in water or lipids. Medicines distribute faster in organs with the intensive blood flow (heart, liver, kidneys) and this process is much slower in tissues with a relatively low blood flow (subcutaneous cellular tissue, adipose and

bone tissue). When the blood supply of the internal organs becomes worse, the distribution and effectiveness of medicines decrease too. Fats, proteins and mucopolysaccharides play the main role in depositing of medicines. Binding of medicines to proteins can decrease in the diseases of liver, kidneys, as well as in sepsis, burns, gastritis, enteritis, gastric ulcer, protein starvation or during the simultaneous administration of some medicines.

The biotransformation of medicines (The main ways of the drug metabolism)

Biotransformation is the process of utilization, transformation of a medicine into metabolites that are dissolved well in water and excreted by kidneys. The importance of the biotransformation is in transformation of a foreign medicine potentially dangerous for the organism (xenobiotics) into a water soluble compound that eliminates fast from the organism. That is why the main aim of the biotransformation is the transformation of lipophilic substances (easily reabsorbed in the renal tubules) into the hydrophilic polar compounds that are easily excreted by kidneys (not reabsorbed in the renal tubules). Metabolites can be excreted from the organism or undergo further transformations. The biotransformation of medicines proceeds in 90-95% in the liver cells (in their microsomes that contain the sets of enzymes required for the drug metabolism), as well as in the intestine, lungs, kidneys, blood and placenta.

The processes of the drug metabolism are conditionally divided into two phases. A drug molecule transforms forming the functional groups with the active hydrogen atoms: oxy-, amino-, carboxy-groups, etc. in the first phase owing to oxidation, reduction or hydrolysis. The conjugation to highly polar acid residues of the glucuronic, sulphuric and some aminoacids occurs in the second phase with the participation of these functional groups. As a rule, the biotransformation leads to the decrease of the pharmacological activity (inactivation) of medicines. However, in a number of cases the formation of the active metabolites can take place. First of all, it concerns the precursors of medicines – prodrugs, which become active in the process of metabolism. In some cases in the process of the drug metabolism toxic metabolites are formed. This phenomenon is called the "lethal synthesis".

The drug metabolism determines the time of the drug circulation in the organism and, as a consequence, the duration of the therapeutic effect and the scheme frequency of usage of a drug dosing as well.

The rate of the drug biotransformation depends on the activity of enzymes metabolizing them, age and the state of the organism, simultaneous administration of other medicines. The rate of the drug metabolism is determined by the genetic factors. **Pharmacogenetics** is the part of pharmacology, which studies the congenital peculiarities of enzymes that metabolize medicines in humans. The damage of the structure and the function of the metabolizing enzymes is called **enzymopathy** (the enzyme defect).

The phenomenon of **induction** and **inhibition** of metabolizing (microsomal) enzymes affects the rate of a drug metabolic transformation. There are about 250

substances known, which are capable to cause induction of metabolizing enzymes (e.g., barbiturates). While using these medicines the effectiveness of those medicines, biotransformation of which occurs with the help of cytochrome P-450, is especially decreased. The induction of metabolic enzymes is a reversible process. The enzymatic activity decreases reaching the initial level in the period of time after the inducers stop their coming into the organism.

The inhibitors of cytochrome P-450 include salts of heavy metals, chloramphenicol, metronidazole, oleandomycine, indometacin, tetracycline, erythromycine, spironolactone, etc. It is necessary to correct the doses of medicines in case of their simultaneous administration with inductors or inhibitors of the microsomal liver enzymes.

The elimination of medicines from the organism

Elimination is the process of removing a medicine from the organism by biotransformation and/or excretion. The main way of the drug excretion in the unchanged state or as metabolites is their elimination with urine and faeces. Besides, medicines can be eliminated from the organism with the exhaled air, with the secret of the mammary, perspiratory and salivary glands.

To estimate the elimination rate with urine a special parameter is used. It is the renal clearance (Cl_{ren}), which determines the amount of plasma (serum) being cleaned by kidneys from a medicine for a unit of time.

Medicines not absorbed in the intestine (Phthalazole, magnesium sulphate) are eliminated with **faeces**.

The information about the pharmacokinetic parameters of medicines stipulates the scheme of their administration and supporting of their concentration in blood in the therapeutic level, which is especially important for medicines with a low range of the therapeutic action.

THE COMBINED ADMINISTRATION OF MEDICINES

Medicines are combined for decreasing or removing undesirable effects of pharmacotherapy, increasing the therapeutic effect or reducing the period of treatment. Such types of the drug interaction as pharmaceutical, pharmacokinetic and pharmacodynamic interactions can be observed in case of combined administration of medicines.

The pharmaceutical interaction is based on physical, physical-chemical and chemical reactions of medicinal substances, which are in the composition of one medicinal form, or which appear with their simultaneous administration. The pharmacokinetic interaction of medicines is revealed at the stages of their absorption, transport, distribution, biotransformation and excretion. The pharmacodynamic interaction is observed when with drugs simultaneous administration the changes of their pharmacological effects appear as a result of their effect upon the specific receptors, cells, organs and systems. The result of this interaction is decrease or disappearance of the effect, distortion of the drug action or increase of the effect up to the development of toxic phenomena. If two medicines act in the same direction, such an interaction is called **synergism** (in Greek *synergos* is "acting together"). It is displayed in 3 forms: additive, summarized (direct) and potentiated (indirect). In the additive synergism the pharmacologic effect of the combination is higher than that of one of the components, but less than their sum is (1+1=1.75); in the summarized synergism the effect of the combination is equal to the arithmetic sum of the monodrugs effects (1+1=2); in the potentiated synergism (from English "to potentiate") the total effect exceeds the sum of drug effects (1+1=3). The summarized action is observed in the **direct** synergism: medicinal substances affect the same receptors (e.g., noradrenaline and adrenaline). Potentiation is typical for the **indirect** synergism when substances have different mechanisms of action and affect different receptors. The synergism phenomenon is used for obtaining the desired therapeutic effect while taking smaller doses of medicines; it decreases the possibility of their side effect.

If the effects of a medicine decrease or disappear while interacting with another one, this phenomenon is called **antagonism** (in Greek *anti* means "against" and *agon* is "struggle"). Antagonism is widely used to remove the negative effects of medicines, as well as in poisonings.

There is physical, chemical and functional antagonism. The **physical** antagonism is observed in the absorption of different toxic substances by adsorbents (the activated carbon absorbs different toxins on its surface). In the **chemical** antagonism inactive substances appear as a result of chemical reactions (the interaction of alkalies and acids). **The functional antagonism** is a phenomenon when medicinal substances affect the same receptors, but in the opposite directions (cholinomimetics and cholinoblockers). Medicines used to remove the effects of other substances when poisoning are called **antidotes**.

FACTORS AFFECTING THE DRUG PHARMACOKINETICS AND PHARMACODYNAMICS

All the factors that can affect the drug pharmacokinetics and pharmacodynamics can be divided into exo- and endogenous factors.

The chemical structure and physical properties of a medicine, medicinal form, the route of its administration and a dose, the scheme of nutrition, the composition of food, the state of the environment (the circadian rhythms, the atmospheric pressure, temperature of the air), etc. belong to the **exogenous factors**, which are not related to the patient's organism.

The **endogenous factors** connected with the patient's organism are the body weight, sex, age, the physiological (pregnancy, lactation, climacterium, hypodynamia, the body temperature) and the pathological (diseases of the thyroid gland and the gastrointestinal tract, alcoholism) state of the organism. One of the leading endogenous factors determining the success of the therapy is age. It is connected with the fact that the level of the biochemical processes functioning differs in different age periods. **The geriatric pharmacology** studies the peculiarities of the drug action in elderly people and the **pediatric pharmacology** deals with the same problems in children.

PARTICULAR PHARMACOLOGY (A guarantee to become a physician or pharmaceutist)

I. MEDICINES AFFECTING AFFERENT INNERVATION

ASTRINGENT, COATING, ADSORBENT, ANTACID AGENTS and MEDICINES CONTAINING VOLATILE OILS are medications that increase or decrease excitability and conductivity of the afferent nerves.

Clussification of medicines							
Local anesthetics, expectorants, laxatives, bitters - see other chapters							
Astringent ^o , co	oating*, antacid**	Adsorbents	Containing volatile oils				
a	gents						
Of plant origin:	Salts of metals:	Activated	Menthol				
Oak bark ^o	Aluminium	carbon	Espol				
Sage leaves ^o	Sage leaves ^o phosphate [*]		Mustard seeds				
Chamomile Colloidal bismuth		Diosmectit	Menthol in				
flowers ^o	subcitrate ^{o**}		bromisovalerianate				
Tannin ^o	Almagel ^{***}						
	Vicalin ^{o**}						
	Anacid ^{***}						

Classification of medicines

The mechanism of action

These medicines coat the afferent nerve endings forming colloid solutions (aluminium phosphate, almagel, anacid, enterosgel) in water; neutralize the free HCl of the gastric juice (aluminium phosphate, almagel, anacid); cause precipitation of proteins forming albuminates that make a film-like cover and protect receptors of the skin or the mucous membrane of the gastrointestinal tract (colloidal bismuth subcitrate, vicalin, plant astringents); adsorb chemical substances on their surface (anacid, adsorbents). Volatile oils irritate the afferent nerve endings and dilate arterioles and capillaries by reflex.

Pharmacodynamics (effects)	\rightarrow Indications						
Coating and gastro-protective (salts	Inflammatory diseases of the						
of metals); antacid (antacids);	gastrointestinal tract: enterites, gastrites,						
antimicrobial, astringent, anti-	peptic ulcer, etc.						
inflammatory and antiseptic (plant							
origin ones)							
Astringent, anti-inflammatory,	Catarrhal-inflammatory diseases: tonsillitis						
antiseptic, sudorific, wound healing	(fauces), laryngitis (vocal cords),						
(plant origin agents)	pharyngitis (throat). Inflammatory diseases						
	of the gum (stomatitis), vagina, uterine						
cervix and the skin. Decubituses, ulcers,							
	intertrigoes, dermatites, erosions, diatheses						
Adsorptive (adsorbents)	Poisonings by alkaloids, food.						
	Enterosorption. Diarrhea						

Local irritants (espol, mustard seeds)	Arthrites, myosites, rheumatism, radiculitis, myalgia		
Astringent, gastro-protective,	Food poisonings		
antiseptic (plant origin agents)			
Sedative, spasmolytic (menthol,	Migraine, angina pectoris		
validol)			
Side effects —	Contraindications		
Constipation or diarrhea, skin irritation	Skin irritation (for the local-acting ones)		

The list of medicines					
INN, (Trade name)	Medicinal form, dosage				
Activated carbon (Carbolen)	Pwd, tabl. 0.5				
Almagel	Susp. per os				
Aluminium phosphate	Gel 16.0				
Anacid	Susp. per os				
Chamomile flowers	Pack 100.0				
Colloidal bismuth subcitrate (De-nol)	Tabl. 0.12				
Diosmectit (Smecta)	Pwd., package 3.0				
Enterosgel	Gel, pack				
Espol	Ointment, tube				
Menthol	Oil sol. 1%				
Menthol in bromisovalerianate	Tabl. 0.06				
Mustard seeds (Mustard paper)	Package				
Oak bark	Pack 100.0				
Sage leaf	Pack 100.0				
Tannin	Pwd, package				
Vicalin	Tabl.				

Glossary

Enterosorption is the introduction of a sorbent in the gastrointestinal tract. **Diarrhea** is a loose stool. **Migraine:** its main symptom is a strong headache.

LOCAL ANESTHETICS

Local anesthetics are medicines causing the local reversible loss of pain and other kinds of sensibility in the site of introduction.

Classification of medicines

Para- aminobenzoic acid esters	Benzofurocarboxylic acid derivatives	Substituted amides of acetanilide
Procaine	Benzofurocaine	Articaine
Benzocaine		Lidocaine
		Trimecaine hydrochloride

The mechanism of action

Due to the membrane stabilizing effect local anesthetics reduce the membrane permeability for different ions (Na⁺, K⁺), inhibit the release of neurotransmitters. It leads to the change of the bioelectric potential on the cell membrane and disturbs the transfer of the nervous impulses through synapses.

Pharmacodynamics (effects) \rightarrow	Indications			
Local anesthetic	Different types of the local			
	anesthesia			
Side effects \rightarrow	Contraindications			
Hypotension, convulsions, disorders in the cardiac	Hypotension, epilepsy,			
conduction system	arrhythmia			

There is the latent period, which exists from the moment of introducing a local anesthetic till the development of the local anesthetic effect. That is why it is necessary to wait for the beginning of the drug action and do not administrate the medicine repeatedly, as it can lead to intoxication. Vasoconstrictive medicines potentiate and prolong the effect of local anesthetics.

	Amor	Dommo	Tori	Effect			
Medicines	thesia	ability	city	antiar- rhythmic	hypoten- sive	central analgesic	
Procaine	+	++	<u>±</u>	+	+		
Benzocaine	+		±				
Benzofuro- caine	++	+++	±			+	
Articaine				+	+		
Lidocaine	++	+++	++	+	+		
Trimecaine	++	+++	+				

The pharmacological "face" of local anesthetics

The list of medicines

INN, (Trade name)	Medicinal form, dosage
Articaine (Ultracaine)	Sol. for inj. 1%
Benzofurocaine	Aer. 50.0
Benzocaine (Anesthesine)	Sol. for inj.1%
Lidocaine	Sol. for inj. 1%; gel 2.5%
Procaine (Novocaine)	Sol. for inj.1%; oint. 10%
Trimecaine hydrochloride	Sol. for inj.1%

Glossary

Local anesthesia is a temporary, reversible loss of all kinds of sensibility (pain, temperature, tactile) only in the site of the drug introduction without impairment of consciousness. Main types of the local anesthesia are surface (terminal) (in the site of application), conduction (by the nerve fibre) and infiltration (soaking of a tissue by anesthetics layer-by-layer) anesthesia.

II. MEDICINES AFFECTING EFFERENT INNERVATION

functions of the efferent nerves are provided Normal by such (mediators) acetylcholine, noradrenaline, adrenaline, neurotransmitters as which action is similar dophamine. Medicines, or opposite these to neurotransmitters, are widely used for the pharmacological correction of functional disorders of different organs and they are called medicines of the mediator action or mainly affecting the efferent division of the nervous system (efferent innervation). As these medicines change the rate of the nervous impulse conductivity in synapse, they are also called synaptic-acting medicines.

Synapse is the place of action for the drugs primary influencing on the peripheral processes of neurotransmission (the efferent section of the nervous system).

In order to conceive clearly the localization, the mechanism of action and pharmacodynamics of medicines influencing selectively on the efferent section, it is necessary to know physiological and biochemical peculiarities of the efferent section, its role in the functions of the whole nervous system.

The efferent section of the nervous system is presented by nerves-"executors" (centrifugal), unlike the afferent section that includes sensible nerves (centripetal). The efferent nerves are divided into motor (somatic) and vegetative (autonomic). The latter are divided into the parasympathetic and sympathetic nerves. The motor nerves do not break, and the vegetative nerves break in ganglia. Ganglion (the cluster of neurons) is the multiplying apparatus of the nervous system due to it the CNS provides regulation of functions for the whole organism. Synaptic contacts of one neuron and another occur in ganglia.

The structural unit of the nervous tissue – neuron - joins another neuron or a cell of the internal (working) organ in synapse (from Latin "close down"). There are the following structural elements in synapse:

1. A presynaptic membrane (the axon's ending) contains a neurotransmitter (neuromediator), which is formed in the neuron's mitochondrion and accumulates in the axon's vesicles (bubbles) in the inactive state. Acetylcholine and noradrenaline are the main neurotransmitters in the excitation transfer in the peripheral nerve endings.

2. A postsynaptic membrane (the dendrite ending or the cell membrane of the working organ) contains M- and N-cholinoreceptors (ChR), α - and β -adrenoreceptors (AR). They are sensitive to the corresponding mediators, as well as cations (Na⁺ and K⁺) and anions (Cl⁻, organic acids), which create the potential difference on the postsynaptic membrane.

3. The synaptic cleft is area, where such enzymes as cholinesterase inactivating acetylcholine (ACh), MAO and COMT (monoamine oxidase and catechol-o-methyltransferase) enzymes, inactivating noradrenaline and adrenaline, are secreted. Besides, for example, choline, which is formed after acetylcholine breakdown, undergoes the recapture (re-uptake) by the presynaptic membrane.

To transmit the nervous impulse from one neuron to another (or on the working organ), synapse must pass through three states: polarization \rightarrow depolarization \rightarrow repolarization.

Polarization (the state of rest) is characterized by the presence of neurotransmitters (mediators) in the inactive state in vesicles, receptors of the postsynaptic membrane are not excited and it is impermeable for Na^+ and K^+ .

Depolarization is the state when under the nervous impulse stimulation a mediator releases into the synaptic cleft by portions and reaches receptors in milliseconds. The configuration of receptors changes because of their interaction with mediators and the ion canals open; along them Na^+ ions go into the cell, and K^+ ions come out of the cell. The action potential and the membrane polarization phase appear.

Repolarization is the state when an enzyme inactivates the part of a mediator, and the unbroken part of the latter is captured by the presynaptic membrane. Sodium is displaced out of the cell and potassium returns into the cell with the help of the membrane's sodium-potassium pump. The membrane repolarization, i.e. the reconstruction of the initial state (polarization), takes place.

The mediator ACh stimulates M- and N-cholinoreceptors. Depending on their sensitivity to definite compounds ChR are divided into M-ChR (they are also stimulated by muscarine – alkaloid, poison of fly-agaric mushrooms) and N-ChR (they are also stimulated by nicotine – alkaloid of tobacco leaves). Noradrenaline (NA) (mediator) and adrenaline (hormone) stimulate AR. M-ChR and AR are located mainly in organs, N-ChR are in the skeletal muscles, ganglia, the carotid sinus and the adrenal medulla; all ChR and AR are also found in the CNS. Synapses and nerves, where the nervous impulse transfer occurs with the help of ACh, are called cholinergic. Motor, parasympathetic, preganglionic sympathetic nerves, postganglionic sympathetic innervating sweat glands, skeletal muscles vessels, the adrenal medulla and the carotid sinus belong to **cholinergic** nerves. Postganglionic sympathetic nerves, excluding innervating sweat glands, vessels of the skeletal muscles, the adrenal medulla and the carotid sinus belong to **adrenergic** nerves.

Classification of medicines affecting efferent innervation

I. Cholinergic (the action is similar to acetylcholine functions) medicines.

II. Anticholinergic (the action is opposite to acetylcholine functions) agents. Medicines block ChR and make them insensitive to a neurotransmitter.

III. Adrenergic (their action is similar to noradrenaline and adrenaline functions) medicines.

IV. Anti-adrenergic (opposite to adrenergic agents) medicines.

Comparing the classification and the effects of these medicines it can be conditionally considered that when using of cholinergic medicines the effects connected with the stimulation of parasympathetic nerves dominate in the organism, while with adrenergic medicines sympathetic nerves are stimulated.

Therefore, to understand pharmacodynamics of the medicines affecting efferent innervation, particularly, autonomic nervous system it is necessary to know the basic effects occurring in organs when parasympathetic or sympathetic nerves are stimulated.

The influence of the parasympathetic and sympathetic nervou	s system
on the organs' functions	

on the organs junctions					
Organ	Effects under the nerves stimulation				
	Parasympathetic	Sympathetic			
Eye	Constriction of pupil	Dilation of pupil (mydriasis),			
	(myosis), IOP decrease	IOP increase (\uparrow) ,			
	$(\downarrow),$ accommodation	accommodation paralysis			
	spasm (myopia)	(hyperopia)			
Exocrine glands (sali-	The secretion increase	The secretion decrease			
vary, lacrimal, etc.)					
Bronchi	Spasm	Dilation			
Heart	Rhythm \downarrow (bradycardia),	Rhythm \uparrow (tachycardia),			
	contractility ↓	contractility ↑			
GIT	Acceleration of peristalsis	Deceleration of peristalsis			
Sphincters	Relaxation	Spasm			
Urinary bladder	Increase of the urine	Decrease of the urine			
	secretion (tone \uparrow)	secretion (tone \downarrow)			
Uterus	Contractility and tone ↑	Contractility and tone \downarrow			
Vessels	Vessels dilation, BP \downarrow	Vessels spasm, BP ↑			

CHOLINERGIC MEDICINES (CHOLINOMIMETICS, CHOLINERGIC AGONISTS)

By the mechanism of action this group of medicines is divided into **direct-acting cholinomimetics** (from English "to mimic") and **indirect-acting cholinomimetics (anticholinesterase agents)**.

DIRECT-ACTING CHOLINOMIMETICS

M-, N-cholinomimetics	M-cholinomimetics	N-cholinomimetics	
Acetylcholine	Pilocarpine	Cytisine	
Carbacholine	Aceclidine	Lobeline	

Classification of medicines

The mechanism of action

M-cholinomimetics stimulate M-ChR, N-cholinomimetics stimulate N-ChR, M- and N-cholinomimetics stimulate both M- and N-ChR. Binding to the corresponding receptors these medicines provide effects, which are similar to the effects of the endogenous ligand, i.e. they act as agonists of ACh.

Pharmacodynamics (effects) \rightarrow			→ Indications					
Local	action:	IOP	decrease,	myosis,	the	Glaucoma	(except	t N-
accommodation spasm					cholinomimetics)			
Resorptive action : increase of the smooth muscles			Atony of the GIT, uterus,					
tone of the GIT, uterus, gall and urinary bladder,			urinary bla	dder; radi	ography			
increase of the exocrine glands secretion; reflex			of the C	GIT (exce	ept N-			
stimulation of the respiratory centre (stimulation of			cholinomimetics). Asphyxia					
the carotid sinus N-ChR)			(N-cholinomimetics only)					

Side effects	\rightarrow	Contraindi	Contraindications		
BP decrease, bradycardia, bronch	nospasm	Hypotension,	bradycardia,		
		bronchial asthr	na (BA)		

The pharmacological juce of allect-acting cholinomimeties						
Medicines		Act	Peculiarities			
	Strength	Duration	Resorptive	Local		
Acetylcholine	+	+	+	-	not introduced iv	
Carbacholine	++	++	+	+		
Pilocarpine	+	+	-	+	toxic	
Aceclydine	++	++	+	+		
Cytisine	++	+	+	-	↑ respiration	
Lobeline	++	+	+	_	↑ BP	

The pharmacological "face" of direct-acting cholinomimetics

The list of medicines

INN, (Trade name)	Medicinal form, dosage
Aceclydine	Sol. for inj. 0.02%
Acetylcholine	Pwd. for inj. 0.2
Carbacholine (Carbachol)	Sol. 3%
Cytisine (Cytiton, Tabex)	Sol. for inj. 0.15%; tabl. 0.0015
Lobeline	Sol. for inj. 1%
Pilocarpine	Sol. 1%

Glossary

Agonist is a medicine that while binding to receptors causes effects similar to the effects of the corresponding mediator. Atony (atonia) is the absence of the muscle tone. Intraocular pressure (IOP) is the pressure of the intraocular liquid in the eye cavity. Hypotension is the BP decrease. Glaucoma is the eye disease, its main feature is the IOP increase. The carotid sinus is the sinus of the carotid artery. Myosis is the pupil's constriction. Accommodation spasm (myopia) is the vision of objects located near-by. Endogenous ligands are endogenous substances that bind to the receptors or other formations of the organism.

INDIRECT-ACTING CHOLINOMIMETICS (Anticholinesterase medicines)

Anticholinesterase medicines are medicines that inhibit acetylcholinesterase enzyme and, thus, increase the acetylcholine concentration in the synaptic cleft.

Classification of medicines				
Reversible- and irreversible*-acting anticholinesterase medicines				
Physostigmine	Galanthamine	Neostigmine methylsulphate	Armine*	

The mechanism of action

Anticholinesterase medicines block (reversibly or irreversibly) the acetylcholinesterase enzyme that leads to increase of the ACh content in the synaptic cleft and stimulation of the postsynaptic M- and N-ChR (ACh is a common mediator for them). While taking these medicines the effects of the parasympathetic nerve

system prevail and that is why the effects of these medicines are similar to the effects of ACh and direct-acting cholinomimetics.

Pharmacodynamics (effects) –	→ Indications		
M-cholinomimetic:	Glaucoma. Paresis and paralysis of the		
-decrease of the IOP, myosis, the	intestine (more often after operations on		
accommodation spasm;	the abdominal cavity organs), atony of		
-increase of the smooth muscle, tone of	the urinary bladder, the uterine inertia		
organs			
N-cholinomimetic:	Myasthenia. Postsymptoms after polio-		
-relief of the neurotransmission through	myelitis and dysfunction of the cerebral		
the neuromuscular synapses;	circulation, neuritis		
-improvement of the neuromuscular			
conductivity			
M- and N- cholinomimetics:	As antidotes in poisoning by non-		
	depolarizing myorelaxants, M-cholino-		
	blockers		
Side effects	\rightarrow Contraindications		
Bronchospasm, bradycardia, BP	Bronchitis, BA, severe heart diseases,		
decrease, convulsive reactions	bradycardia, hypotension, epilepsy		

	The pharmacolo	gical "fac	e" of indir	ect-acting ch	olinomimetics
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Medicines		Action				
	Strength	Duration	Resorptive	Local	effects	
Galanthamine	+	++	+	-	+	
Physostigmine	+	+	+	+	++	
Neostigmine	++	+	+	+	++	
Armine*	+++*	+++*	-	+	+++	

*- in glaucoma only.

The	list	of	medicines
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INN, (Trade name)	Medicinal form, dosage
Armine	Sol. 0.01%
Galanthamine (Nivalin)	Sol. for inj. 1%
Neostigmine methylsulphate (Proserin)	Sol. for inj. 0.05%
Physostigmine (Eserin)	Sol for inj. 0.1%

Glossary

Myasthenia is the disease when the skeletal muscle tone is absent partially or completely. **Neuritis** is the inflammation of nerves. **Paralysis** is the absence of the voluntary movements because of the muscle innervation disorder. **Paresis** is decrease of muscular sensitivity and force due to disorders of neurotransmission. **Poliomyelitis** is the acute infectious viral disease accompanied by paresis and paralysis of the extremities.

ANTICHOLINERGIC MEDICINES (CHOLINOBLOCKERS, CHOLINERGIC ANTAGONISTS)

Anticholinergic medicines block ChR selectively being competitive antagonists of the ACh mediator and cholinomimetics. According to their action on the receptors they are divided into **M-cholinoblockers** and **N-cholinoblockers**.

Cussification of medicines			
Ones of plant origin	Synthetic ones		
Atropine sulphate	Ipratropium bromide		
Homatropine hydrobromide	Methacine iodide		
Platyphyllin hydrotartrate	Pirenzepine		
Scopolamine hydrochloride	Tropicamide		

M-cholinoblockers

The mechanism of action

Medicines of this group block M-ChR of organs reversibly and selectively, thus, they stop the impulse transmission from the postganglionic parasympathetic nerve endings to the internal organs cells stipulating the prevalence of the sympathetic innervation effects. At present because of the M-ChR (M_1 - M_5) subtypes identification medicines, which act selectively on different M-ChR subtypes have appeared. Pirenzepine blocking selectively M_1 -ChR of the stomach mucous membrane belongs to selective M_1 -cholinoblockers.

Pharmacodynamics (effects)	\rightarrow Indications
The dilation of pupil (mydriasis),	Diagnosis of the eye diseases, inflammatory
IOP [↑] , accommodation paralysis	eye diseases
Inhibition of the exocrine glands	BA, peptic ulcer, gastritis, anesthesiology
secretion, the smooth muscles	(the prophylaxis of bronchospasm), colics
relaxation (in case of the spasm) of	
organs	
Tachycardia	Bradycardia, prophylaxis of heart stoppage
Side effects	\rightarrow Contraindications
Accommodation paralysis, IOP [↑] ,	Bradycardia, glaucoma, atony of the GIT,
intestinal peristalsis \downarrow , dry mouth,	tachycardia
tachycardia	

Atropine sulphate (alkaloid from the Solanaceae family plants) is the reference drug of this group. The effects of atropine sulphate and similar medicines are opposite to the effects of cholinomimetics.

Medicines	Action					Peculiarities
	Strength	Duration	Re-	Lo-	Spas-	
			sorp-	cal	mo-	
			tive		lytic	
Atropine	A (refe-	8 days	+	+	+++	\downarrow M ₁ -ChR (of the
sulphate	rence)					stomach), M ₂ -ChR
						(of the heart), M ₃ -
						ChR (of the eyes)

The pharmacological "face" of M-cholinoblockers

Homatropine	<a< th=""><th>1,5 days</th><th>-</th><th>+</th><th>-</th><th>\downarrowM₃-ChR (of the</th></a<>	1,5 days	-	+	-	\downarrow M ₃ -ChR (of the
hydrobromide						eyes)
Scopolamine	<a< td=""><td>4 days</td><td>+</td><td>+</td><td>++</td><td>Sedative, hypno-tic,</td></a<>	4 days	+	+	++	Sedative, hypno-tic,
hydrochloride						inhibition of motion
						sickness
Platyphyllin	<a< td=""><td>5 hours</td><td>+</td><td>+</td><td>+++</td><td>Sedative, ↓BP</td></a<>	5 hours	+	+	+++	Sedative, ↓BP
hydrotartrate						
Methacine	≥A		+	-	++++	Tocolytic
iodide						
Ipratropium	<a< td=""><td>8 hours*</td><td><u>±</u></td><td>+</td><td>+++</td><td>\downarrow M₃-ChR (of the</td></a<>	8 hours*	<u>±</u>	+	+++	\downarrow M ₃ -ChR (of the
bromide						bronchi, nose)
Pirenzepine	<a< td=""><td>8</td><td>+</td><td>-</td><td>±</td><td>\downarrow M₁-ChR (of the</td></a<>	8	+	-	±	\downarrow M ₁ -ChR (of the
		hours**				stomach)
Tropicamide	<a< td=""><td>3-4</td><td>-</td><td>+</td><td>-</td><td>\downarrow M₃-ChR (of the</td></a<>	3-4	-	+	-	\downarrow M ₃ -ChR (of the
		hours				eyes)

- action on the eyes, * - on the bronchi, ** - on the stomach.

The list of medicines

INN, (Trade name)	Medicinal form, dosage
Atropine sulphate	Sol. for inj. 0.1%; sol. 1%
Homatropine hydrobromide	Sol. 0.25%
Ipratropium bromide (Atrovent, Rinatec)	Sol. for inhalation 0.025%; aer.
	0.05%
Methacine iodide	Sol. for inj. 0.1%; tabl. 0.002
Pirenzepine (Gastrocepine)	Sol. for inj. 0.5%; tabl. 0.005
Platyphyllin hydrotartrate	Sol. for inj. 0.2%; tabl. 0.005
Scopolamine hydrochloride	Sol. for inj. 5%
Tropicamide (Midriacyl)	Sol. for inj. 0.5%

Glossary

Accommodation paralysis is the vision of objects located at distance (hyperopia).

N-Cholinoblockers

N-ChR are located in the ganglia of the autonomic nervous system, synapses of skeletal muscles, adrenal enterochromaffin tissue and the carotid sinus. N-cholinoblockers are different: some of them block N-ChR in ganglia, others act in the skeletal muscles. The former are called **ganglionic blockers**, which are used for stopping the impulse transmission through the autonomic ganglia, the latter are **muscle relaxants** applied for relaxation of the skeletal muscles.

Ganglionic blockers - N-ChBl is

Classification of medicines

Tertiary* and quaternary nitrogen-containing compounds			
Azamethonium bromide	Dimecoline iodide		
Pachicarpine hydroiodide*	Hexamethonium benzosulphonate		

The mechanism of action

Ganglionic blockers are similar to ACh by their chemical structure. As a result of their competitive antagonism with ACh for N-ChR of the sympathetic and parasympathetic ganglia they block these receptors and interrupt the nervous impulse transmission through ganglia. While introducing ganglionic blockers the "pharmacological denervation" of the internal organs occurs. Ganglionic blockers stopping the neurotransmission in ganglia act by the principle of breaking the interaction of the nervous centres and the effectory organs, and it results in the state of a relative rest of the latter.

Pharmacodynamics (effects)	\rightarrow	Indications
Dilation of arterial vessels and the	BP	Hypertension, the HC reduction,
decrease (the postload on the myocar	dium	artificial (controlled) hypotension in
decreases), improvement of the b	blood	the surgery of the vessels that is the
circulation and microcirculation in the ve	essels	most dangerous by vast bleedings,
of the extremities		surgery of heart and in neurosurgery
Dilation of the venous vessels, decreas	se of	Endarteritis, Raynaud's disease, the
preload to the myocardium and the pre-	ssure	pulmonary and brain edema
in the pulmonary circulation		
Blockade of the cardiovascular reflexes	In surgery for decreasing the risk of	
pathological (for example, in sl	hock,	the shock development risk
infarction) and compensatory ones		
Decrease of the gastric juice secre	etion,	Ulcer of the stomach and
motility and peristalsis of GIT organs		duodenum, spastic colitis
Stimulation of the uterine contractions	and	Labour induction (Pachicarpine
tone		hydroiodide)
Side effects \rightarrow		Contraindications
Tachycardia, orthostatic collapse, atony Myo		cardial infarction at the acute stage,
of intestine and urinary bladder, IOP mark		ed hypotension, atony of the stomach
increase, dry mouth, dizziness	and t	he intestine, glaucoma, pregnancy,
(vertigo), general weakness	athere	osclerosis, thrombosis

The pharmacological "face" of Ganglionic blocke

Medicines	Effect		Peculiarities of
	Strenth	Duration	administration
Azamethonium bromide	+	+	For cystoscopi in men
Pachicarpine hydroiodide	+	++	Increase of uterine tone,
Dimecoline iodide	+++	++	BP↓
Hexamethonium benzosulphonate	++	+	For HC

The list of medicines

INN, (Trade name)	Medicinal form, dosage
Azamethonium bromide (Pentamine)	Sol. for inj. 5%
Dimecoline iodide (Dimecoline)	Tabl. 0.025
Hexamethonium benzosulphonate (Benzohexonium)	Tabl. 0.25; sol. for inj. 2.5%
Pachicarpine hydroiodide	Tabl. 0.1; sol. for inj. 3%

Glossary

Raynaud's disease is spasms of fingers, hands and feet arteries, which turn pale, with pain and paresthesia. **Hypertension** is the chronic disease of the cardiovascular system characterized mainly by the stable increase of the BP. **Hypertensive crisis (HC)** is an acute exacerbation of hypertension. **Orthostatic collapse** is an acute decrease of the BP when the body position changes from horizontal to vertical one. **Postload** is the power that the heart needs to overcome the total peripheral vascular resistance of arteries to the blood stream. **Preload** is the pressure on the heart valves in the venous return of blood to the heart. **Endarteritis** is the spasm of the lower extremity arteries.

MUSCLE RELAXANTS

Muscle relaxants (myorelaxants) or curare-like medicines stop the impulses' transmission from the motor (somatic) nerves to the skeletal muscles causing the relaxation of the skeletal muscles.

The forefather of this group is considered to be curare, the arrow poison of the South-American Indians, it is the mixture of extracts from several species of tropical plants.

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	. J		- J			

Depolarizing agents	Non-depolarizing agents		
Suxamethonium iodide	Diplacine dichloride	Pipecuronium bromide	
	Tubocurarine chloride		

The mechanism of action

By the mechanism of action muscle relaxants are divided into:

1. Antidepolarizing (non-depolarizing) agents (pachicurare). Medicines, which are competitive antagonists to ACh, block N-ChR in the postsynaptic membrane of the neuromuscular synapse and stop the appearance of the membrane depolarization and excitation (stimulatory impulse) of the muscle fibre.

2. Depolarizing agents (leptocurare). They are chemically similar to ACh and that is why they interact with N-ChR causing a prolonged depolarization of the postsynaptic membrane and, thus, they disturb the transmission of excitation from the nerve to the muscle.

Pharmacodynamics

Myorelaxants cause relaxation of the skeletal muscles in a certain sequence. At first, the paralysis of small muscles of face, neck, fingers and toes and speaking disorders develop. Then the muscles of extremities, trunk, intercostal muscles, muscles of abdomen and, at last, diaphragm stop functioning consistently. But consciousness and sensitivity are not disturbed. Death can be caused by hypoxia (diaphragm and breathing muscles stop working). The recovery of the muscle tone occurs in the reverse order.

Indications

Multicomponent narcosis (for stopping the physiological respiration and relaxation and performing the controlled ones).

Setting of dislocations and reposition of bone fragments in fractures. Relief of convulsions. **NB!** It is necessary to introduce muscle relaxants only after the intubation of a patient and his transferring to the artificial controlled respiration.

Side effects

All **non-depolarizing muscle relaxants** are histamine liberators (stimulation of histamine release), so they can cause false allergic reactions (pseudoallergy), especially bronchospasm, the BP decrease. **Suxamethonium iodide** causes arrhythmia, apnoea, potassemia and the heart stoppage.

Contraindications

Myasthenia, diseases of liver and kidneys, shock, early terms of pregnancy and elderly age. **Suxamethonium iodide** is contraindicated to children, in glaucoma, vertebral fractures, anemia, cachexia.

Medicines	Act	tion	It caus	es	BP
	Strength	Duration	Bronchospasm	Pseudo- allergy	
Suxamethonium	+	+	-	-	-
iodide					
Diplacine	++	++	-	+	↑
dichloride					
Tubocurarine	+++	+++	+	+	\downarrow
chloride					
Pipecuronium	++++	+++	+	+	\downarrow
bromide					

The pharmacological "face" of muscle relaxants

The list of medicines

	J
INN, (Trade name)	Medicinal form, dosage
Diplacine dichloride	Sol. for inj. 2%
Pipecuronium bromide	Pwd. for inj. 0.004
Suxamethonium iodide	Sol. for inj. 2%
Tubocurarine chloride	Sol. for inj. 1%

Glossary

Approved is the absence of respiratory movements. Cachexia is the emaciation of the organism. Polarization (the state of rest) \rightarrow depolarization (transmission of a nervous impulse) \rightarrow repolarization (return to the state of rest) are the obligatory sequential states of the postsynaptic membrane. Reposition is matching of the bone fragments. Controlled respiration is the artificial respiration with the help of the specific equipment.

ADRENERGIC MEDICINES (ADRENOMIMETICS, ADRENERGIC AGONISTS)

In the adrenergic synapses the noradrenaline (NA) neurotransmitter and the hormone adrenaline are functioning. The main one is NA.

NA, adrenaline and dophamine are catecholamines, as they have oxygroups at the 3^{rd} and 4^{th} position of the aromatic ring. The inactivation of NA and

adrenaline is performed by two enzymes: catechol-o-methyltransferase (COMT) and monoamine oxidase (MAO). These two catecholamines interact with different receptors: α_1 , α_2 , β_1 , β_2 , β_3 –AR.

Table 2

Location	Function	IS	
	α-adrenoreceptors	β_1 and β_2 -adrenoreceptors	
Vessels (the number	Skin and mucous	Skeletal muscles > heart >	
of receptors)	membranes > kidneys >	lungs > brain > abdominal	
	abdominal cavity organs	cavity organs	
	> skeletal muscles > lungs		
	> brain	Dilation (β_2)	
	Constriction	-	
Heart: rate and		Increase (β_1)	
contractility			
Bronchial tone		Decrease (β_2)	
Uterus	Contraction	Relaxation (β ₂)	

Distribution in organs and effects of the adrenoreceptors in case of stimulation

There are two subtypes of α_1 -AR located on the postsynaptic membrane: α_{1A} and α_{1B} -AR. α_{1A} -AR are located in the smooth muscles of the prostate gland, the urinary bladder's cervix and the prostatic part of the urethra. When stimulating them the tone of the smooth muscles of the organs mentioned increases. α_{1B} -AR are located in the smooth muscles of the vascular wall. When stimulating them the tone of vessels increases. α_2 -AR are located on the presynaptic membrane and outside synapses: in the vasomotor centre and on thrombocytes. The stimulation of α_2 -AR causes aggregation of thrombocytes (and β_2 -AR, visa versa, decrease it). The physiological role of the presynaptic α_2 -AR is also in their participation in the system of the negative feedback that regulates the release of noradrenaline and the vascular tone. Thus, when stimulating α_2 -AR the release of noradrenaline into a synapse and the excitability of the vasomotor centre decrease. It leads to the BP decrease. The stimulatory effects of catecholamines are mainly connected with the activation of α_1 -AR (table 2), whereas the inhibitory effects (excluding the heart) occur with activation of β -AR. Noradrenaline activates mainly α_1 -AR and adrenaline activates all types of AR (but stronger β -AR). At present β_3 -AR are also discovered, they together with β_2 -AR when stimulated increase the processes of glycogenolysis and lipolysis.

α_1 - adrenomimetics, α_2 - adrenomimetics*	β_1 - adrenomimetics *, β_2 - adrenomimetics, $\beta_1+\beta_2$ - adrenomimetics **	$\alpha_1, \alpha_2, \beta_1, \beta_2$ - adrenomimetics
Norepinephrine	Dobutamine	Epinephrine

Classification of medicines

Phenylephrine	Fenoterol	Ephedrine hydrochloride
hydrochloride	Salbutamol	
Xylomethazoline	Isoprenaline **	
Oxymethazoline	Orciprenaline sulphate **	
Tetrizoline Clonidine*		

The mechanism of action

Medicines of this group stimulate AR:

- α_1 - adrenomimetics stimulate α_1 -AR of vessels;

- α_2 - adrenomimetics stimulate α_2 -AR of the vasomotor centre and sympathetic nerve fibres;

- β_1 -adrenomimetics stimulate β_1 -AR of the myocardium;

- β_2 -adrenomimetics stimulate β_2 -AR of the bronchi, uterus and vessels;

- $\beta_1+\beta_2$ -adrenomimetics stimulate β_1 - and β_2 -AR of the myocardium, bronchi, uterus, vessels;

- α_1 , α_2 , β_1 , β_2 - adrenomimetics stimulate α_1 -, α_2 -, β_1 -, β_2 -AR.

Ephedrine hydrochloride is an indirect-acting adrenomimetic (sympathomimetic) that suppresses the activity of MAO and COMT and the recapture (re-uptake) of catecholamines and it leads to the increase of the neurotransmitter's concentration in the synaptic cleft.

Pharmacodynamics (effects)		\rightarrow Indications	
Stimulation of α_1 -AR: the vasoconstri	ctive	Shock, collapse, hypotension,	
effect, the BP increase. "Centralization o	of the	conjunctivitis, prolongation of the	
blood circulation" - the vasoconstriction	on of	local anesthetics effect	
the skin, subcutaneous tissue, mu	icous		
membranes, organs of the abdominal c	avity		
$(\alpha_1 AR)$, but (because of the stimulation of	of β_2 -		
AR) dilation of vessels (improvement o	f the		
blood circulation) of heart, brain, lu	ungs,		
skeletal muscles			
Stimulation of a_2 - AR : the hypotensive ef	fect	Essential hypertension (EH),	
		hypertensive crisis	
Stimulation of β_1 -AR: the cardio-stimul	ating	Heart stoppage, cardiogenic shock,	
effect (the positive inotropic and chronot	ropic	bradyarrhythmia	
effects), the increase of the ox	ygen		
consumption by myocardium			
Stimulation of β_2 - AR : the broncholytic effective of β_2 - AR : th	ffect	BA, chronic asthmatic bronchitis	
Stimulation of β_2 -AR: the tocolytic e	effect	Threatened preterm labour	
(decrease of the uterine tone and contract	ions		
Stimulation of β_2 - and β_3 -AR: the		Hypoglycemic coma	
enhancement of glycogenolysis and lipolysis			
Side effects		Contraindications	
Tachycardia, hyperglycemia,	Coror	narosclerosis, diabetes mellitus, EH	
hypertension (excluding Clonidine) (excl		uding Clonidine)	

Adrenomimetics reproduce in organs the same effects, which are observed when irritating the postganglionic sympathetic nerves. The effects of adrenomimetics on the cardiovascular system and the bronchial tone are the most practically useful.

Medicines	Adrenoreceptors				Duration
	α_1 α_2 β_1 β_2				of action
Epinephrine	+++	-	++++	+++	+
Ephedrine	+	-	+++	++	+++
Norepinephrine	++++	-	+	+	+
Tetrizoline	+++	-	-	-	++
Clonidine	-	+++	-	-	++

The pharmacological "face" of adrenergic agonists

Dobutamine	-	-	+++	-	+
Salbutamol	-	-	-	+++	+++
Salmeterol	-	-	-	++++	+++++
Terbutaline	-	-	+	+++	++++
Orciprenaline	-	-	+	+++	++++
Isoprenaline	-	-	++	+++	++

The list of medicines

INN, (Trade name)	Medicinal form, dosage
Clonidine (Clofelin)	Sol. for inj. 0.1%; tabl. 0.00075
Dobutamine (Dobutrex)	Sol. for inj. 0.5%
Ephedrine hydrochloride	Sol. for inj. 5%; tabl. 0.01
Epinephrine (Adrenaline hydrochloride, Adrena-	Sol. for inj.0.1%
line hydrotartrate)	
Fenoterol (Berotek)	Sol. 0.1%
Isoprenaline (Isadrine, Novodrine)	Sol. for inj. 1%; tabl. 0.005
Norepinephrine (Noradrenaline)	Sol. for inj. 0.2%
Oxymethazoline	Sol. 0.05%
Orciprenaline sulphate (Alupent, Asthmopent)	Sol. for inj. 0.1%; tabl. 0.02
Phenylephrine hydrochloride (Mesaton)	Sol. for inj.1%
Salbutamol	Sol. for inj. 0.1%; tabl. 0.002
Tetrizoline (Visin, Tizin)	Sol. 0.01; 0.05%
Xylomethazoline (Galazoline)	Sol. 0.1%

Glossary

Hypoglycemic coma is an acute decrease of the glucose level in blood. **The increase of glycogenolysis and lipolysis** is the increase of disintegration of carbohydrates and lipids that leads to the increase of the glucose and lipid level in blood.

ANTI-ADRENERGIC MEDICINES (ADRENOBLOCKERS AND SYMPATHOLYTICS)

According to the presence of two types of AR anti-adrenergic medicines (adrenergic antagonists) of this group are divided into α - and β -adrenoblockers

(adrenolytics) with different pharmacodynamics and the spectrum of application. Sympatholytics are non-selective anti-adrenergic medicines.



Fig. 2. The classification of anti-adrenergic medicines.

a-Adrenoblockers

Classification of medicines

α_1 -, α_2^* -adrenoblockers		$\alpha_1 + \alpha_2$ - adrenoblockers		
Tamsulosine	Yohimbine*	Proroxan	Phentolamine	
Doxazosine	Prazosine	Dihydroergotamine	Nicergoline	

The mechanism of action

a-Adrenoblockers possess a competitive mechanism of blocking effect, though their structural similarity to catecholamines is slightly marked. Medicines of this group block both the postsynaptic α_1 -AR and the presynaptic α_2 -AR.

Pharmacodynamics	$(effects) \rightarrow$	Indications	
Blockade of the a _{1B} -AR in ve	essels decreases the	e EH, endarteritis,	
sympathetic influence on vessel	s. As a result the	e bedsores,	
vasodilating and hypotensive effects	s occur	pheochromocytoma	
Blockade of α_{1A} -AR decreases the tone of the smooth Benign hyperplasia of			
muscles of the urethra prostatic	part and the urinary	the prostate (BHP)	
bladder cervix		(adenoma)	
Blockade of α_2 - AR improves the b	blood supply of smal	l Psychogenic impotency,	
pelvis organs and increases potency		male climacterium	
Side effects	\rightarrow Con	<i>traindications</i>	
Orthostatic collapse, hypotension	Hypotension, scler	osis of the coronary and	
	brain vessels		

Medicines	\downarrow	Duration of	Peculiarities of using/		
	BP	action, h	pharmacodynamics		
Phentolamine	++	6	Pheochromocytoma, but not EH;		
			insulin level ↑		
Proroxan	++	6	Sedative, hypnotic, antipruritic		
			effects; for motion sickness		

The pharmacological "face" of α-adrenoblockers

Dihydroergotamine	<u>±</u>	6	Migraine
Nicergoline	+	6	Spasmolytic effect; migraine, dis-
			orders of the cerebral blood
			circulation
Prazosine	++	8	Adenoma, \uparrow the sensitivity to insulin
Doxazosine	++	24	Causes the "phenomenon of the first
			dose" (collapse), the hypolipidemic
			effect
Tamsulosine	±	20	Adenoma (block of α_{1A} -AR)
Yohimbine			Impotency

β-Adrenoblockers

Classification of medicines

β_1 -adrenoblockers			$\beta_1 + \beta$	2-adrenoblocke	rs
Metoprolol	Betaxolol	Talinolol	Propranolol	Oxprenolol	Sotalol
Bisoprolol	Atenolol				

By the duration of the effect the medicines can be divided into short acting (Propranolol, Metoprolol, Oxprenolol), middle-acting (Pindolol) and long-acting (Sotalol, Atenolol) ones.

The mechanism of action

Medicines block β -AR of the heart, bronchi, vessels and other organs. They are similar to Isoprenaline in their chemical structure. β_1 -Adrenoblockers are called cardioselective, $\beta_1+\beta_2$ - adrenoblockers are called non-cardioselective ones.

Pharmacodynamics (effects)	\rightarrow	Indications
The β_1 -AR blockade in the myocardium: the anti	anginal effect-	Ischemic
decrease of the heart rate and contractility resulting ir	the decrease of	heart
oxygen consumption by myocardium		disease
		(angina
		pectoris)
The β_1 -AR blockade of the heart's conductive	system – the	Tachyar-
antiarrhythmic effect		rhythmia
The β_1 -AR blockade of the heart (decrease of the heat	art function) and	Hypertensio
kidneys (the renin-angiotensin system activity d	ecrease) – the	n
hypotensive (antihypertensive) effect		
Side effects \rightarrow Contr	raindications	
Bradycardia, bronchospasm, angiospasm, Bradycar	dia, BA, perij	oheral blood
hypotension circulation	on disorders, hypo	otension

The β_2 -AR blockade causes the blood vessel constriction (including the coronary vessels), increase of the bronchial tone and uterine contractions, suppression of glycogenolysis and decrease of the glucose level in blood.

The pharmacological	l "face" of β-adrenoblockers
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Medicines	↓ BP, h	MS	ISM	Peculiarities
Metoprolol	6-8	-	-	Prophylaxis of migraine
Betaxolol	12-24	+	-	Glaucoma

Talinolol	24	-	-	Does not cause the orthostatic
				collapse
Atenolol	24	-	-	Does not penetrate through
				the BBB
Propranolol	6-8	+	-	Does not cause the orthostatic
_				collapse
Oxprenolol	6-8	+	+	Side effects are less than in
				propranolol
Sotalol	24	-	-	The marked anti-arrhythmic
				effect

MS is the membrane stabilizing effect, **ISM** is the inner sympathomimetic (less side effects) activity.

 β_1 - adrenoblockers are safer than β_1 + β_2 -adrenoblockers, as they practically do not cause bronchospasm connected to the β_2 -AR blockade. However, when taking β_1 -adrenoblockers for a long period of time, the tolerance to these medicines develops and it often leads to the dose increase and the loss of selectivity.

Sympatholytics (indirect-acting anti-adrenergic medicines)

Reserpine and Octadine belong to this group.

The mechanism of action

These medicines turn off the sympathetic innervation selectively: decrease the synthesis and release of a neurotransmitter, exhaust the noradrenaline reserve in the presynaptic membrane.

Pharmacodynamics	\rightarrow	Indications
Hypotensive effect		EH
Side effects	\rightarrow	Contraindications
Enhancement of the parasympathetic	innervation	Peptic ulcer, BA
(hypersecretion in the GIT, bronchospasm))	-

The pharmacological face of sympatholytics				
Medicines	$Max \downarrow BP at$	Peculiarities		
Reserpine	8-10 day	A weak neuroleptic and sedative effects; it is used in		
		the initial stage of EH		
Octadine	7-8 day	Does not penetrate through the BBB, cause the		
		orthostatic collapse; it is used in the severe form of EH		

The pharmacological "face" of sympatholytics

The list of medicines

INN, (Trade name)	Medicinal form, dosage
Atenolol	Tabl. 0.01
Betaxolol (Locren)	Tabl. 0.001; sol. 0.5%
Bisoprolol (Concor)	Tabl. 0.005
Dihydroergotamine	Tabl. 0.025; sol. for inj. 1%
Doxazosine (Cardura)	Tabl. 0.002
Metoprolol (Vasocardine)	Tabl. 0.05; sol. for inj. 0.1%

Nicergoline	Tabl. 0.005
Oxprenolol	Tabl. 0.02
Octadine	Tabl. 0.025
Phentolamine	Tabl. 0.025
Proroxan (Pyrroxan)	Tabl. 0.15; sol. for inj. 1%
Prazosine (Adversuten)	Tabl. 0.005
Propranolol (Anaprilin)	Tabl. 0.01; sol. for inj. 2.5%
Reserpine	Tabl. 0.0001
Sotalol	Tabl. 0.08; sol. for inj. 0.1%
Talinolol (Cordanum)	Tabl. 0.05; sol. for inj. 0.2%
Tamsulozine (Omnic)	Caps. 0.0004
Yohimbine hydrochloride	Tabl. 0.005

Glossary

BHP is a benign hyperplasia (tumour) of the prostate (adenoma). **IHD** is the ischemic or coronary heart disease (stenocardia or angina pectoris and myocardial infarction). **Pheochromocytoma** is a benign tumour of the adrenal medulla that causes a marked increase of adrenaline secretion and, therefore, the BP increase.

III. PAIN PHARMACOCORRECTORS

Local anesthetics (see above), general anesthetics and analgesics belong to this group of medicines.

GENERAL ANESTHETICS

Narcosis (in Greek *narkosis* means "numbness") is a state when consciousness and all types of sensitivity are absent, skeletal muscles are relaxed, reflexes are suppressed. The state of narcosis (or general anesthesia) (*indication* of anesthetics) consists of 4 successive stages (*pharmacodynamics of medicines*): **analgesia** (short-term period) - the loss of pain sensitivity; **stimulation** (operations are not performed) – decrease of inhibitory processes, fluctuation of blood pressure, heart rate, breathing frequency; **surgical narcosis** - all types of sensitivity and consciousness are absent, the complete myorelaxation; **awakening** - returning of all organism's functions in a reverse order.

Classification o	f medicines
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Medicine	s for inhalation narcosis	Medicines for non-	-inhalation narcosis
Ftorotan	Nitric oxide	Propanidide	Ketamine
Enfluran	Ether for narcosis	Sodium oxybutyrate	Sodium thiopental

The mechanism of action

Lipoid, protein, synaptic and other theories of action for anesthetics have been suggested. The following changes caused by these medicines are distinguished while their acting: disorders of the ions transport through the membranes of neurons, activation of the endogenous antinociceptive and GABA-ergic systems, inhibition of cholin-, dophamin- and serotoninergic processes in the CNS.

Medicines	Acti- vity	Going out from	Myo- rela-	Stimula- tion stage	Narcosis ma-	Other effects
		narcosis*	xation		naging	
Ftorotan	+++	++	++	±	+++	\downarrow of BP, breathing;
	+					bradycardia
Enfluran	+++	+++	+++	+	++	\downarrow of BP, breathing
Nitric	+	++++	-	+++	+++	A component of the
oxide						combined narcosis
Ether for	++	+	++	+++	++	\downarrow of BP, irritates mucous
narcosis						membranes
Propani-	+++	++	++	-	-	Laryngospasm, thrombo-
dide	+					sis, irritation. A short-
						term narcosis
Thiopental	+++	+++	+++	-	-	Convulsions,
	+					laryngospasm
Sodium	+		++	<u>+</u>	-	Sedative, hypnotic, anti-
oxy-						hypoxic effects
butyrate						
Ketamine	+	+++	-	-	-	BP↑, hallucinations,
						convulsions

The pharmacological "face" of general anesthetics

* - the speed of going out from narcosis (awakening).

The list of medicines				
INN, (Trade name)	Medicinal form, dosage			
Enfluran	Vial 250 ml			
Ether for narcosis	Vial 140 ml			
Ftorotan	Vial 250 ml			
Ketamine	Sol. for inj. 5%			
Nitric oxide	Balloon metal.			
Propanidide (Sombrevin)	Sol. for inj. 5%			
Sodium oxybutyrate	Sol. for inj. 20%			
Sodium thiopental	Vial 1.0			

Glossary

Antinociceptive system is the endogenous system of analgesia.

ANALGESICS

Analgesics (in Greek *an* means "negation" and *algos* is "ache") are medicines that suppress selectively the pain sensitivity. Depending on their chemical structure, the mechanism of action and pharmacodynamics peculiarities they are divided into **narcotic** (big) and **non-narcotic** (small) analgesics.

Narcotic analgesics

Pain and analgesia are provided by two functional systems – the **nociceptive** system (in Latin *noceo* is "I damage") that perceives pain and take part in its

transmission, and **antinociceptive** one that suppresses pain. The initial nociceptive structures are nociceptors – receptors, which perceive the pain stimulation. They are located in the skin, muscles, mucous membranes, arteries, capsules of joints and internal organs. A pain impulse is transmitted to the central neurons along afferent nerves with the help of the pain mediators. Opiate receptors (OR) and their endogenous ligands (ligo is "I connect") also participate in the pain perception and analgesia. OR are located in the presynaptic membranes of neurons, which take part in the transmission of nociceptive impulses both in the CNS and tissues. They are the sites of membranes with a high sensitivity towards their ligands (endo- and exogenous) and perform the inhibitory (antinociceptive) function. Endogenous ligands of OR are analgesic neuropeptides: encephalins and endorphins. They bind to OR and as a result, the output of algogens – the pain mediators (acetylcholine, substance P, prostaglandins, catecholamines, serotonin, histamine), which take part in transmission of nociceptive impulses into the synaptic cleft, is delayed. There are 5 types of OR: μ (myu), χ (cappa), σ (sigma), δ (delta), ϵ (epsilon). The role of μ -receptors is particularly important as they provide analgesia, the sedative effect, inhibition of the respiratory centre, bradycardia, myosis, decrease of the GIT motility, euphoria and drug addiction.

Narcotic analgesics, or opioids (OA), inhibit or decrease pain, in high doses they cause sleep and if they are used recurrently, physical and psychological dependence – drug addiction – develop.

Natural and semi- synthetic*	Synthetic					
Agonists of	opioid receptors		Agonists-antagonists and antagonists* of opioid receptors			
Morphine	Trimeperidine		Pentazocine			
Codeine	Suphentanyl		Butorphanol			
Omnopone	Phentanyl		Naloxone *			
Ethylmorphine	Pyritramide					
hydrochloride*	Buprenorphine	Tramadol				

Classification of medicines

The mechanism of action

The mechanism of the analgesic effect of opioids is stipulated by their action on OR and the activation of the endogenous antinociceptive system. As the result of presynaptic OR stimulation the release of algogens decreases, and it leads to disorder of the pain impulses transmission.

Pharmacodynamics (effects)		\rightarrow	Indications	
	Strong and very strong pain caused by traumas (excludi			
Analgesic	the craniocerebral	trauma,	hemorrhagic	stroke),
	myocardial infarction,	massive	burns, shock,	malignant
	tumours, acute infla	ammatory	processes (peritonitis,
	cholecystitis), colics;	insomnia	caused by the	excessive
	pain; prevention of the	traumatic	shock; premed	ication

Antitussive (anti-	Cough in pneumothorax, lung bleeding; operations on the		
cough)	thoracal organs; persistent dry cough		
Anti-emetic	Strong uncontrolled vomiting of the central genesis, which		
	cannot be stopped by other medicines (in radiation		
	sickness, etc.)		
Inhibition of the respi-	Acute pulmonary edema (small doses of morphine cause		
ratory centre	the rate decrease and the depth increase of breath		
	movements and it leads to the breath relief)		
Stimulation of the	Radiography of the GIT		
vagus nerve (parasym-			
pathetic innervation			
prevails: the increase			
of the smooth muscles			
tone, etc.)			
Stimulation of the	Diagnostic importance when intoxicated by morphine and		
oculomotor nerve	other opioids		
(myosis)			
Side eff	$ects \rightarrow Contraindications$		
Drug dependence	Chronic pain (excluding cancer diseases)		
(physical,			
psychological),			
addiction, abstinence			
Inhibition of the	Pregnancy, labour, lactation, craniocerebral trauma,		
respiratory centre	hemorrhagic stroke, children under 2 years old, patients		
	over 60 years old		

The pharmacological face of harcolic analgesics					
Medicines	Analgesia	Duration of	Inhibition of	Addiction	
		action	breathing		
Morphine (M)	A reference-drug	6	++	++	
Phentanyl	200 times > M	0.5	++	++	
Buprenorphine	20-30 times > M	9	<u>+</u>	±	
Butorphanol	3-5 times > M	9	+	±	
Pyritramide	2 times > M	9	±	+	
Trimeperidine	< M	4	+	+	
Codeine	< M	6	+	±	
Pentazocine	< M	5	±	±	
Tramadol	< M	9	-	±	

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The list of medicines

INN, (Trade name)	Medicinal form, dosage
Buprenorphine (Bupremen)	Sol. for inj. 0.03%; tabl. 0.0002
Butorphanol (Moradol)	Sol. for inj. 0.2%
Codeine (Codeine phosphate)	Tabl. 0.015
Ethylmorphine hydrochloride (Dionine)	Tabl. 0.015
Morphine	Sol. for inj. 1%; tabl. 0.01
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Naloxone	Sol. for inj. 0.04%
Omnopone	Sol. for inj. 1; 2%
Pentazocine	Sol. for inj. 1; 2%
Phentanyl	Sol. for inj. 0.005%
Pyritramide (Dipidolor)	Sol. for inj. 0.75%
Suphentanyl (Suphentane)	Sol. for inj. 0.0005%
Tramadol (Tramal)	Sol. for inj. 5%; caps. 0.05
Trimeperidine (Promedol)	Sol. for inj. 1; 2%; tabl. 0.025

Analgesia is the pain relief. Drug dependence, drug addiction, is a strong desire for regular taking a medicine with a stable psychological and physical dependence on it and with the development of abstinence after stopping taking it. Myosis is constriction of pupil. Premedication is the medicinal preparation for narcosis for increase of its effectiveness and decrease of the dose of anesthetics. Habituation (tolerance) is the decrease of the therapeutic effect after repeated administration of a medicine. Euphoria is the state of the imaginary psychological well-being, causeless mood improvement, withdrawal from reality; it is the basis of the psychological dependence to psychotropic medicines.

Non-narcotic analgesics (Analgesics-antipyretics)

Non-narcotic analgesics (NNA) are medicines with a moderate analgesic effect. They are different from OA by the absence of the development of addiction or habituation, as well as the presence of antipyretic and anti-inflammatory (weak) effect. Non-steroidal anti-inflammatory drugs (NSAIDs) are close to NNA by their mechanism of action, their difference is in the intensity of anti-inflammatory effect.

With the central	Peripheral-acting	Spasmoanalgesics
component of	(monomedicines* and	
action	combined ones)	
Nephopam	Sodium methamizole*	Baralgetas
Paracetamol	Pentalgin	Spasmalgon
Ketorolac	Citramone	
	Sedalgin	
	Tempalgin	

Classification of medicines

The mechanism of action

NNA block cyclooxygenase (COG) enzyme, which leads to the inhibition of the prostaglandins (PGs) synthesis in the site of inflammation and the CNS, the decrease of nociceptors' sensibilization to the action of algogens and the disorder of the pain impulses transmission along the afferent nerves. NNA decrease the mechanical compression of nociceptors due to the anti-edemic effect of medicines. The pyrogenic effect of PGs towards the thermoregulation centre also decreases, the heat emission increases due to the dilation of the skin vessels and increase of sudation and the heat production decreases in the same time.

Pharmacodynamics	s (effects) \rightarrow Indications	
Analgesic	Acute and chronic pains, which are not dangerous	
	to life (toothache, headache, pain in joints,	
	muscular pain, etc.), neuralgia	
Antipyretic	Fever, ARVI, flu	
Side effects	\rightarrow Contraindications	
Dyspepsia, ulcerogenic effect	GIT diseases (gastritis, peptic ulcer)	
Inhibition of hemopoiesis,	Diseases of the blood (agranulocytosis,	
formation of methemoglobin	methemoglobinemia)	
Nephro- and hepatotoxic effects	Marked renal and liver dysfunctions	

The pharmacological "face" of non-narcotic analgesics

Medicines	Analgesic effect	Antipyre- tic effect	Anti-inflam- matory effect	Other peculiarities/effects
Sodium	++	+	±	
methamizole	(reference)			
Paracetamol	+	++		A narrow interval of
				the therapeutic action
Ketorolac	+++	+		
Tempalgin	+++			Tranquilizing
Baralgetas	+++			Spasmolytic
Spasmalgon	++		+	Spasmolytic
Sedalgin	+++			It contains ASA,
Pentalgin				Caffeine, Codeine,
				Phenobarbital
Citramone	+++		±	It contains ASA,
				Caffeine, Paracetamol

The list of medicines

INN, (Trade name)	Medicinal form, dosage	
Baralgetas	Tabl.; supp.; sol. for inj. 5 ml	
Ketorolac (Ketanov)	Tabl. 0.075	
Nephopam	Tabl. 0.03; sol. for inj. 2%	
Paracetamol (Panadol)	Tabl. 0.5	
Pentalgin, Sedalgin, Spasmalgon,	Tabl.	
Tempalgin, Citramone		
Sodium methamizole (Analgin)	Tabl. 0.5; sol. for inj. 50%	

Glossary

Afferent nerves (sensitive) are peripheral nerves that transmit an impulse from afferent receptors to the CNS. Dyspepsia is nausea, vomiting, diarrhea. Antipyretic effect is the decrease of the body temperature in fever. Pyrogenic effect is the ability of pyrogens to increase the body temperature. Prostaglandins are biologically active

substances that play a role of mediators and modulators of inflammation, pain, fever. **Ulcerogenic effect** is the ability to cause ulceration of the GIT.

NON-STEROIDAL ANTI-INFLAMMATORY DRUGS

Non-steroidal anti-inflammatory drugs (NSAIDs) are medicines that possess anti-inflammatory, analgesic and antipyretic effects.

The synthesis of prostaglandins activates in the site of inflammation under the action of different damaging factors. It is carried out involving the following cyclooxygenase enzymes: cyclooxygenase-1 (COG₁) and cyclooxygenase-2 (COG₂). **COG**₁ is constitutional, it performs such physiologic functions as: participation in the synthesis of PGs, stabilizing the cellular membrane with the cytoprotective effect in the GIT and kidneys and regulation of the thrombocytes function. **COG**₂ is "inflammatory", which controls the synthesis of PGs during inflammatory processes. PGs are mediators and modulators of inflammation, they activate the production of other mediators of inflammation (histamine, kinins, serotonin, complement, lysomal enzymes, etc.) and participate in developing the pain syndrome and fever. Under the action of PGs and other mediators of inflammation vessels dilate, the permeability of the vascular wall increases, the blood plasma goes into the interstitial area, edema develops, hyperemia appears, nociceptors are sensitized (their sensitivity to algogens increases).

Derivatives of			
salicylic acid	phenylpropionic and	pyrazolone and	
	phenylacetic* acids	indolacetic acid*	
Acetylsalicylic acid (ASA)	Ketoprofen	Phenylbutazone	
Lysin acetylsalicylate	Ibuprophen	Indomethacin*	
	Sodium diclofenac *		
Oxycams	Coxibs	Combined and other*	
		medicines	
Meloxycam	Celecoxib	Reopyrine Sigan	
Pyroxycam	Rofecoxib	Nimesulide*	

Classification of medicines

The mechanism of action

According to the mechanism of action NSAIDs are divided into selective COG_1 inhibitors (ASA in small doses); non-selective COG_1 and COG_2 inhibitors (ASA, Sodium diclofenac, Indomethacin, Phenylbutazone, etc.); selective COG_2 inhibitors (Meloxycam, Nimesulide); highly selective COG_2 inhibitors (Celecoxib, Rofecoxib). The most important chain in the mechanism of action of NSAIDs is the ability to inhibit COG (COG_1 , COG_2 or COG_1+COG_2). The decrease of the COG activity decreases the synthesis of PGs and other inflammatory mediators. NSAIDs also decrease the energy supply in the site of inflammation, inhibit subcortical pain centres, decrease the pyrogenic effect of PGs on the thermoregulation centre, increase the heat emission and decrease the aggregation of thrombocytes.

Pharmacodynamics (effects) \rightarrow Indications			
Anti-inflammatory	Inflammatory	diseases of the connective tissue	
	(collagenoses):	rheumatism, systemic lupus erythematosus,	
	etc.; arthrites, ar	rthroses, osteochondrosis, radiculitis	
Analgesic	Acute and chron	nic pain: headache, pain in joints, muscular	
	pain (myalgia),	toothache, algomenorrhea, neuralgia, injuries	
	of ligaments, bruises, etc.		
Antipyretic	ARVI, hyperthermia (fever)		
Anti-aggregant	Hypercoagulation syndrome, prophylaxis of postoperative		
	thrombosis, trombophlebitis, disorder of the cerebral blood		
	circulation, IHD, atherosclerosis		
Side	effects	\rightarrow Contraindications	
Ulcerogenic effect, dyspepsia Peptic ulcer, gastritis		Peptic ulcer, gastritis	
Allergic reactions	BA, allergic bronchitis, etc.		
Bleedings	Bleedings, thrombocytopenia, hemophilia		

The pharmacological "face" of NSAIDs

Anti-inflammatory effect

Diclofenac > Pyroxycam ≥ Indomethacin > Meloxycam > Ketoprofen > Phenylbutazone = Ibuprophen > Acetylsalicylic acid.

Analgesic effect

Diclofenac > Indomethacin > Pyroxycam > Ibuprophen > Ketoprofen \geq Acetylsalicylic acid \geq Phenylbutazone.

Antipyretic effect

Diclofenac > Pyroxycam > Indomethacin > Ibuprophen > Acetylsalicylic acid = Phenylbutazone.

Ulcerogenic effect

Indomethacin = Acetylsalicylic acid > Pyroxycam > Phenylbutazone > Diclofenac = Ibuprophen.

The list of medicines		
INN, (Trade name)	Medicinal form, dosage	
Acetylsalicylic acid (Aspirin)	Tabl. 0.5	
Celecoxib	Caps. 0.2	
Ibuprophen (Brufen)	Tabl. 0.2	
Indomethacin (Methindol)	Tabl. 0.05	
Ketoprofen (Ketonal)	Tabl. 0.2	
Lysin acetylsalicylate (Acelysin, Laspal)	Pwd. for inj. 2.0	
Meloxycam (Movalis)	Tabl. 0.015	
Nimesulide (Mesulide, Nimulide, Nimesil)	Tabl. 0.2	
Phenylbutazone (Butadione)	Tabl. 0.05	
Pyroxycam (Oxycam)	Caps. 0.2	
Reopyrine	Sol. for inj. 5ml	
Rofecoxib	Tabl. 0.025	

Sigan	Tabl. № 4
Sodium diclofenac (Voltaren, Orthophen)	Tabl. 0.025

Antiaggregant effect is decrease of aggregation (adhesion) of thrombocytes. Arthritis is the inflammatory disease of a joint. Arthrosis is the disease of joints with degeneration of articular cartilage and deformation of articular surfaces. Algomenorrhea is painful menstruation. Hemophilia is inherited decrease of the blood coagulability. Collagenoses are systemic autoimmune diseases with a diffuse damage of the connective tissue. **Osteochondrosis** is the disease that characterizes by a dystrophic process in the bone and cartilaginous tissue. Radiculitis is the inflammation of some radicles of the spinal nerves. **Rheumatism** is the inflammatory infectious allergic disease that damages the cardiovascular system, joints and the system. Systemic lupus erythematosus is the chronic systemic nervous disease of the connective tissue and vessels. inflammatory autoimmune Thrombophlebitis is inflammation of veins with their simultaneous thrombosis.

IV. MEDICINES SUPPRESSING THE CENTRAL NERVOUS SYSTEM (CNS DEPRESSANTS)

Neuroleptics, tranquilizers, sedative, hypnotic, anticonvulsant, antiparkinsonic medicines belong to this group.

NEUROLEPTICS (ANTIPSYCHOTIC MEDICINES, MAJOR TRANQUILIZERS)

Neuroleptics are psychotropic medicines that are able to reveal the inhibitory action on the CNS (without consciousness disturbing): eliminate hallucinations, delirium and stop the psychomotor excitation (motor and speech).

Derivatives of			
phenothiazine butyro-		thioxanthene,	
	phenone	dibenzodiazepine*,	
		benzamide**	
Chlorpromazine	Droperidol	Chlorprothixene	
Levomepromazine	Haloperidol	Sulpyrid**	
Perphenazine hydrochloride		Closapine*	

Classification of medicines

Derivatives of phenothiazine, butyrophenone and thioxanthene are called "typical" neuroleptics as they lead to development of drug-induced parkinsonism. The rest of neuroleptics cause such complications rather seldom, and that is why they are called "atypical" (closapine, sulpyrid).

The mechanism of action

The mechanism of action of neuroleptics is complex as they disturb the functions of many neurotransmitters in the CNS blocking different receptors (dophamine, α -AR, M-ChR-, H₁-histamine receptors and serotonin-5HT₂-receptors).

The **antipsychotic** effect is bound to blocking of the central dophamine D_2 -receptors located mainly in the reticular formation (the activating influence on the brain cortex is eliminated), in the nuclei of midbrain, the limbic system and the hypothalamus. Not only the antipsychotic effects of neuroleptics bound to inhibition of the mediator activity of dophamine, but also their main side effect – **extrapyramidal disorders**, which are similar with the Parkinson's disease symptoms. A highly selective binding to D_4 -receptors is characteristic for "atypical" neuroleptics.

The **neuroleptic** effect is stipulated by blockade of the central α -adrenoreceptors in the ascending part of the reticular formation, the limbic system and the hypothalamus.

The **potentiating** effect of neuroleptics is caused by blockade of α -adrenoreceptors of the brain's reticular formation.

The **anti-emetic** effect is caused by blockade of dophamine (D_2) and serotonin receptors of the medullar "trigger-zone" and halt of signals transmission into the emetic centre.

The **hypothermic** effect is the result of adreno- and serotonin receptors blockade and, therefore, decrease of the activity of the hypothalamic thermoregulation centres (decrease of the heat production and increase of the heat emission).

The **antihistaminic** effect is caused by H₁-histamine receptors blockade.

The **hypotensive** effect is the result of α -adrenoreceptors blockade in the hypothalamus and peripheral vessels.

Pharmacodynamics (effect	s) \rightarrow Indications
Antipsychotic, neuroleptic	Psychosis
Potentiating (for medicines that suppress the CNS)	Neuroleptanalgesia, potentiation of narcosis
Anti-emetic	Uncontrolled vomiting of the central genesis
Hypothermic	Controlled hypothermia during narcosis
Antihistaminic	Severe itching neurodermatitis
Hypotensive	Severe forms of hypertension
Side effects	\rightarrow Contraindications
Neuroleptic syndrome, drug-induced	parkinsonism, Depression,
dyspepsia	parkinsonism

The pharmacological "face" of neuroleptics

Antipsychotic effect:

Haloperidol > Droperidol > Closapine > Chlorprothixene = Chlorpromazine = Perphenazine hydrochloride = Sulpyrid > Levomepromazine.

Neuroleptic effect:

Derivatives of phenothiazine = butyrophenone > thioxanthene > Closapine > Sulpyrid.

Potentiating effect:

Haloperidol > Droperidol > Levomepromazine > Chlorpromazine.

Anti-emetic effect:

Haloperidol > Perphenazine hydrochloride > Droperidol > Sulpyrid > Chlorpromazine.

Sedative effect:

Chlorpromazine = Levomepromazine = Closapine > Chlorprothixene > Perphenazine hydrochloride = Haloperidol = Droperidol > Sulpyrid.

INN, (Trade name)	Medicinal form, dosage
Chlorpromazine (Aminazine)	Sol. for inj. 2.5%; dr. 0.025
Chlorprothixene (Cloxane)	Tabl. 0.05
Closapine (Azaleptine)	Tabl. 0.025
Droperidol	Sol. for inj. 0.25%
Haloperidol	Tabl. 0.5; sol. for inj. 0.5%
Levomepromazine (Tisercine)	Tabl. 0.025
Perphenazine hydrochloride (Etaperazine)	Tabl. 0.01
Sulpyrid (Eglonyl)	Tabl. 0.2

The list of medicines

Glossary

The antipsychotic effect is elimination of delirium and hallucinations. The hypothermic effect is decrease of the body temperature bellow the norm. Neuroleptanalgesia is a peculiar form of narcosis (with the partial presence of consciousness) that is reached by the combination of neuroleptics and narcotic analgesics that leads to potentiation of their action. The neuroleptic syndrome is hyperthermia with the extrapyramidal and autonomic nervous system disorders that can lead to death. The neuroleptic effect is the "will paralysis" appearing as the result of the inhibition of the psychomotor excitation (motor and speech) and patient's initiative. Psychoses are severe diseases of CNS, their main symptoms are delirium and hallucinations.

TRANQUILIZERS (MINOR TRANQUILIZERS, ANXIOLYTICS, ATARACTICS, ANTIPHOBIC MEDICINES)

Tranquilizers (in Latin *tranquillare* is "to make calm") are medicines that remove selectively fair, anxiety, emotional tension increased restlessness and are used mainly in neuroses and the related states.

	clussification	of meanemes
Derivatives of benzodiazepine		Derivatives of other chemical groups
Diazepam	Alprazolam	Hydroxysine
Medazepam	Lorazepam	
Chlordiazepoxide	Gidazepam	Trimetosine

Classification of medicines

The mechanism of action

They decrease the excitability of subcortical regions of the brain (the limbic system, the thalamus, the reticular formation, the hypothalamus) that are responsible

for emotional reactions, inhibit the interaction between these structures and the brain cortex.

Benzodiazepines stimulate mainly benzodiazepine receptors and that leads to activation of GABA-receptors and intensification of the inhibitory functions of GABA.

Pharmacodynamics	(effects) \rightarrow Indications		
Anxiolytic	Neuroses, mild psychoses		
Hypnotic	Insomnia (especially caused by negative emotions)		
Sedative	Neurogenic diseases		
Anticonvulsant	Convulsions (epilepsy)		
Potentiating	Premedication		
Side effects	\rightarrow Contraindications		
Drowsiness, weakness, disorders	s of Activities that require rapid psychomotor		
attention and locomotion, tolerar	nce, reactions, long-term courses of treatment,		
addiction	increase of doses		

Medazepam, Gidazepam, Trimetosine are "day time" tranquilizers as they cause less inhibition of CNS than other medicines, therefore, they can be used in day time.

Medicines	Tranquili- zing effect	Addiction / tolerance	SE	Other effects
Diazepam	+++	+/+	++	Anticonvulsant, hypnotic,
Chlordiaze-	++	+/+	+	sedative, spasmolytic
poxide				(diazepam), vegetostabilizing,
				myorelaxant, potentiating
				(diazepam, chlordiazepoxide)
Lorazepam	+++	+/+*	+	Accumulation, anticonvulsant,
				hypnotic
Alprazolam	+++		+	Anticonvulsant, antidepressant
Gidazepam	++		±	Anticonvulsant, potentiating,
				stimulating
Hydroxysine	+		+	Analgesic, myorelaxant, anti-
				emetic

The pharmacological "face" of tranquilizers

SE – side effect; * – in the long-term administration

The	list	of	medicines
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INN, (Trade name)	Medicinal form, dosage
Alprazolam (Xanax)	Tabl. 0.001
Chlordiazepoxide (Chlozepide, Elenium)	Tabl. 0.01
Diazepam (Relanium, Sibazone)	Tabl. 0.005; sol. for inj. 0.5%
Gidazepam	Tabl. 0.05
Hydroxysine (Atarax)	Tabl. 0.01
Lorazepam (Merlit)	Tabl. 0.001
Medazepam (Mezapam, Rudotel)	Tabl. 0.01
Trimetosine (Trioxasine)	Tabl. 0.3

Anxiolytic (psychosedative, tranquilizing) effect is inhibition of the feeling of anxiety, fear, restlessness, uncertainty; decrease of psychic tension and emotional excitation. **GABA** is γ -aminobutyric acid, one of the main inhibitory mediators of the CNS. **Neurosis** is the disease of the CNS (curable) that is characterized by fear, anxiety, increased excitability and irritability. **Neurogenic diseases** are diseases provoked by the psychoemotional stress (peptic ulcer, hypertension, IHD). **Premedication** is the medicinal preparation of a patient to narcosis with the aim to increase its effectiveness and decrease the dose of general anesthetics.

SEDATIVE MEDICINES

Sedative medicines (in Latin *sedatio* is "calming") are medicines that cause a moderate sedative effect as a result of decrease of the CNS excitability and its reactivity to different stimuli.

Classification of medicines				
Medicines of the p	lant origin	Bromides* and combi	ned medicines	
Persen	Valerian extract	Sodium bromide *	Corvalol	
Motherwort herb tincture	Novo-passit	Valocormide		

The mechanism of action

They increase of the inhibitory processes in the CNS and decrease of the excitability of the reticular formation and the brain cortex.

	Pharmacodynamics (effect	ets) \rightarrow Indications		
Sedative	Mild form of neuroses, inc	creased irritability, neurogenic diseases		
	(hypertention, peptic ulcer, angina pectoris)			
Potentiating	Intensification of effects of CNS depressants			
	$\underbrace{Side \ effects} \rightarrow Contraindications$			
Decrease of t	he mental and physical	Activities that require rapid psychomotor		
activity, feeling of fatigue, drowsiness		reactions		

The peculiarity of sedative medicines is the low toxicity (lack of serious side effects); it allows using them widely in the ambulatory practice, especially while treating aged patients.

However, if they are used for a long time, bromine-containing medicines cause bromism that is characterized by such symptoms as drowsiness, general inhibition, memory impairment, apathy, decrease of potency, lacrimation, cough, rhinitis, appearance of rash on the skin. The treatment of bromism is the following: stoppage of drug administration immediately; using of a great amount of sodium chloride (up to 20 g a day) and abundant drinking.

Madiainas	E	ffects	Composition/other effects	
wieurchies	Sedative	Spasmolytic		
Sodium	+++		Anticonvulsant	
bromide				
Motherwort	+	<u>±</u>		
herb tincture				

The pharmacological "face" of sedative medicines

	Medicines containing valerian:			
Valerian	+	+	Spasmolytic	
extract				
Persen	+	+	Mint, Melissa	
Corvalol	++	+	Phenobarbital, mint oil	
Valocormide	+	+	Sodium bromide, Convallaria,	
			Belladonna, Menthol	
Novo-passit	+++	+	Guaphenesine, extracts of Crataegus,	
			Humulus, Hypericum, Melissa,	
			Passiflora, Sambucus	

The list of medicines

INN, (Trade name)	Medicinal form, dosage
Corvalol (Valocordin)	Sol. 25 ml
Motherwort herb tincture	Tinct. 30 ml
Novo-passit	Sol.100ml
Persen	Tabl.
Sodium bromide	Sol. 3%
Valerian extract (Valeran)	Tabl. 0.02
Valocormide	Sol. 30 ml

Glossary

Sedative effect is the soothing effect, decrease of excitability and irritability, conflictability, nervous tension.

HYPNOTIC MEDICINES

Disorders of sleep (insomnia, somnipathies, hyposomnia) are one of the frequently met states appeared both independently (the primary insomnia) and in different somatic and psychic diseases (the secondary insomnia).

There are three forms of insomnias that are stipulated by:

1) Disorder of the process of falling asleep (more than 40 min) (it is observed more frequently in young people with neurasthenia and overwork).

2) Frequent night awakening (more than 3 times a night).

3) Insufficient duration of a night sleep (less than 6 hours). Though the process of falling asleep is not disturbed a person wakes up in 2-5 hours and cannot fall sleep any more ("the sleep of an old man").

If disorders of sleep are repeated more than 3 times a week, it should be corrected pharmacologically as insomnia (disorder of the physiological rhythm in work of the CNS) leads to overexcitation, fatigue, exhaustion of the brain, and therefore, to different forms of neurogenic disorders.

Hypnotic medicines (hypnotics) are medicines that are able to restore the process of falling asleep, duration and depth of sleep if these processes are disturbed.

Derivatives of benzodiazepine, barbituric acid*	Derivatives of cyclopyrrolone, imidazopyridine*, methylbutamide**	Combined medicines
Nitrozepam	Zopiclone	Reladorm

Classification of medicines

	Phenobarbital*	Zolpidem*	Bromisoval **	(cyclobarbital+diazepam)
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The mechanism of action

They inhibit polysynaptic regions in the brain; reduce the activating impulsation of the reticular formation on the brain cortex; intensify the function of a natural inhibitory mediator GABA. The drug interaction with benzodiazepine and barbituric receptors leading to increase of the GABA's functions plays the main role in the mechanism of action of benzodiazepine and barbituric acid derivatives.

Pharmacodyna	umics (effects) \rightarrow Indications
Hypnotic	Disorders of sleep
Potentiating	Intensification of the effects of CNS depressants
Sedative (low doses)	Mild neuroses, neurotic syndrome
Side effects	\rightarrow Contraindications
Apathy, drowsiness,	Activities that require the rapid psychomotor reactions
weakness	

	tion	Effect disor	tive in der of	f the ses	Synd	rome	tion	ice/
Medicines	Sleep dura	falling asleep	sleep duration	Disorder of sleep pha	After action	With- drawal	Accumula	Dependen toleranc
Phenobarbital	8-10	+	+	+++	+++	+++	++	++/+
Cyclobarbital	4	+		+++	++	+++	+	++/+
Nitrazepam	6-8	+	+	++	++	++	<u>±</u>	+/+
Zolpidem	6	+	+	+	±			+/-
Zopiclone	8	+	+	±	±			±
Bromisoval	5-7	+		±	++	+	+	+/+
Reladorm	8	+	+	+	++	+++	+	++/+

The pharmacological "face" of hypnotic medicines

Besides the hypnotic effect, benzodiazepine derivatives have also the anticonvulsant, anxiolytic and myorelaxant effects, and derivatives of barbituric acid reveal the anticonvulsant effect.

Most of hypnotic medicines cause disorders of the sleep structure, the syndromes of "after (post-) action", "return", "withdrawal", physical and psychic dependence, tolerance, accumulation (especially barbiturates). At present one of the best hypnotic medicines, close to ideal, are Zopiclone and Zolpidem.

The list of medicines				
INN, (Trade name)	Medicinal form, dosage			
Bromisoval (Bromural)	Tabl. 0.3			
Nitrazepam (Radedorm)	Tabl. 0.01			
Phenobarbital (Luminal)	Tabl. 0.3; sol. for inj. 5%			
Reladorm (cyclobarbital+diazepam)	Tabl.			

The list of medicines

Zolpidem (Ivadal)	Tabl. 0.01
Zopiclone (Imovan)	Tabl. 0.0075

Disorder of the sleep structure is the change of the ratio between phases of the fast sleep and slow-waved sleep. **The syndrome of return** is a torturing insomnia, nightmares, frequent waking up appearing after the administration of medicines, especially barbiturates, is stopped. **The withdrawal syndrome** is insomnia and discomfort developing as the result of the abrupt discontinuation of the drug administration, as a rule, on the background of the drug addiction formed. **The syndrome of after action** is the feeling of apathy, drowsiness after waking up.

ANTICONVULSANTS

Anticonvulsant medicines decrease or stop convulsions in pathological states of the organism.

		<i>itemes</i>
Benzodiazepines	Valproates	Barbiturates
Diazepam	Valproic acid	Benzobarbital
Clonazepam		Phenobarbital
Succinimides	Iminostilbens	Others
Ethosuccimide	Carbamazepine	Tolperizone

Classification of medicines

The mechanism of action

They inhibit and limit the pathological activity of neurons in the epileptogenic sites of motor zones in subcortical regions of the brain.

Pharm	acodynamics (effe	cts) —	>	Indication	ıs
Anticonvulsant	Convulsions	of	different	origin	(epilepsy,	craniocerebral
effect	traumas, tumours of the CNS, meningitis)					
Side effects			\rightarrow	Contrai	ndications	
CNS inhibition, mental confusion,		, A	ctivities th	at requir	re attention;	depression
drowsiness, depress	sion, tolerance			_		

The principles of correct usage of anticonvulsants:

-if possible, do not apply one medicine, choose the required combination of medicines individually;

-the dose of a medicine should be increased gradually;

-estimate the drug effectiveness in some weeks of treatment (a number of attacks should be decreased by 50%);

-if necessary, a gradual substitution of one medicine (decreasing its dose) by another one (increasing its dose) should be done;

-carry out the continuous therapy (stoppage of the medicine usage is possible only in 4-5 years in the absence of pathological changes on the encephalogram).

Medicines	Convulsive attacks: g/s	Epileptic status	SE	Other effects
Benzobarbital	+/-		++	Sedative, hypnotic
Phenobarbital	+/-	+	++	
Diazepam	-/-	+	+++	Tranquilizing, sedative,
Clonazepam	+/+	+	++	hypnotic
Carbamazepine	+/-		++	Antidepressant, normothymic,
				antipsychotic, analgesic
Valproic acid	+/+		+	Anxiolytic
Ethosuccimide	+/+		+	Analgesic

The pharmacological "face" of anticonvulsants

g is for great, s is for small attacks; SE is side effect.

The list of	fmedicines
INN, (Trade name)	Medicinal form, dosage
Benzobarbital (Benzonal)	Tabl. 0.1
Carbamazepine (Tegretol, Phinlepsine)	Tabl. 0.2
Clonazepam (Anthelepsine)	Tabl. 0.001
Diazepam (Relanium, Sibazone)	Tabl. 0.005; sol. for inj. 0.5%
Ethosuccimide (Suxilep)	Caps. 0.25
Phenobarbital (Luminal)	Tabl. 0.1; sol. for inj. 5%
Valproic acid (Convulex)	Tabl. 0.2

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Glossary

Motor zones are sites of the cortex and subcortex, which are responsible for the organism's motor activity. **Epilepsy** is a severe chronic disease manifested in the form of great and small epileptic attacks (seizures) that can be accompanied by mental, motor and autonomic nervous system disorders. **An epileptogenic site** is a group of neurons in the CNS that is abnormally active and generates impulses for skeletal muscles.

MEDICINES FOR PARKINSONISM TREATMENT

Antiparkinsonian medicines are medicines used for treatment the Parkinson's disease and the syndrome of parkinsonism including drug-induced parkinsonism.

Classification of medicines

Anticholinergic (cholinolytic) ones	Dophamine	ergic ones		Antiglutamatergic ones
Trihexiphenydil	Levodopa	Selegiline	Nacom	Amantadine

The mechanism of action

The mechanism of action of this group is based on modern data about pathogenesis of the Parkinson's disease. It is known that this disease disturbs the balance of two neurotransmitters in the CNS: the amount of dophamine decreases and the content of acetylcholine increases. Antiparkinsonian medicines restore the balance between dophaminergic and cholinergic systems of the brain.

By the mechanism of their action medicines are divided into:

I. Anticholinergic (they block central M-cholinoreceptors decreasing the effect of acetylcholine in the CNS and periphery).

II. **Dophaminergic** (substitute the deficiency of dophamine in the CNS).

III. Antiglutamatergic (decrease the stimulating effect of glutamate neurons in the CNS that develops on the background of dophaminergic system insufficiency).

Pharmacodynamics (e		→ Indications
Antiparkinsonian effect	Parkinson`s	disease, syndrome of parkinsonism
Side effects	\rightarrow	Contraindications
Anticholinergic: tachycardia, increa	ase of IOP,	Tachycardia, glaucoma
paralysis of accommodation, dry mo	outh	
Dophaminergic: hypotension,	arrhythmia,	Disorders of the cardiac activity,
development of psychoses		psychoses
Antiglutamatergic: convulsions, hyp	ootension	Epilepsy, hypotension

All medicines should be used with short-term intervals (1-2 days per week) to prevent the appearance of tolerance.

Medi- cines	Antiparkinsonian effect	SE	Other peculiarities
Levo-	+++	++	Dophamine predecessor, penetrates
dopa	("a golden standard" of		through the BBB. A "off and in"
	the antiparkinsonian		phenomenon is characteristic (changes of
	therapy)		the well-being and immobile states)
Nacom	++	+	Composition: levodopa, carbidopa
	(short-term)		(dopha-decarboxylase enzyme inhibitor).
			The effect is rapid with the less toxicity
Sele-	++	+	Antidepressant. It should be combined
giline			with nacom or levodopa
Trihe-	++	++	Cholinolytic
xiphe-			
nydil			
Aman-	+	+	Antiviral effect, tolerance
tadine			

The pharmacological "face" of antiparkinsonian medicines

The list of medicines

	si oj medicines
INN, (Trade name)	Medicinal form, dosage
Amantadine (Midantan)	Tabl. 0.1
Levodopa (Levopa)	Tabl. 0.5
Nacom (Levodopa+Carbidopa)	Tabl.
Selegiline (Umex)	Tabl. 0.005
Trihexiphenydil (Parkopan, Cyclodol)	Tabl. 0.005

Glossary

The Parkinson's disease is the chronic disease of the CNS manifested by rigidity of muscles, tremor of hands and head, as well as increased salivation, perspiration, sebaceous face, irritability and the feeling of weeping. Dopha-

decarboxylase is an enzyme that destroys dophamine. **The antiparkinsonian effect** is removal of the symptoms of the Parkinson's disease and the syndrome of parkinsonism. **Rigidity** is the increase of the muscular tone. **The syndrome of parkinsonism** is the secondary disorder of the CNS functions (with the similar symptoms of the Parkinson's disease) that can be the result of the CNS infections, use of antipsychotics, atherosclerosis of the brain vessels and the trauma of the head. **Tremor** is constant and involuntary shivering.

V. MEDICINES STIMULATING THE CENTRAL NERVOUS SYSTEM (CNS STIMULANTS)

These medicines increase excitability and restore the CNS functions when they are suppressed, increase mental and physical activity, improve mood and health. Life, capacity of work (productivity) and longevity, of a human depends on these medicines.

CNS stimulants are divided into analeptics, psychomotor stimulants, antidepressants, nootropic medicines, adaptogens.

ANALEPTICS

Analeptics (in Greek *analepticos* means "recovery, reviving") are medicines stimulating inhibited vitally important centres of the medulla oblongata (respiratory and vasomotor ones) due to decrease of the excitability threshold of these centres. These are medicines of the emergency.

	Medicines		
Caffeine sodium benzoate	Bemegride	Ethimizole	Camphor
Nicethamide		Cytisine	Carbonic acid
Sulphocamphocaine			

The mechanism of action

Direct-acting analeptics stimulate the respiratory and vasomotor centres directly (Caffeine, Bemegride, Ethimizole).

Reflex-acting analeptics provide the reflex stimulation of the respiratory centre via chemoreceptors of the carotid sinus (Cytizine).

Mixed-acting analeptics provide the reflex action through the chemoreceptors of vessels together with the direct action on the vitally important centres of the medulla oblongata (Nicethamide, Camphor, Carbonic acid).

Pharmacodynamics (ej	$(fects) \rightarrow Indications$
Analeptic: the stimulation of the	Asphyxia, shock, collapse, reflex stoppage of
respiratory and vasomotor centres	breathing in trauma, etc.
Cardiostimulating	Acute heart failure, acute and chronic disorders
	of the blood circulation
"Awakening"	Acute poisoning by CNS depressants:
	hypnotics and general anesthetics, alcohol,
	narcotic analgesics

Side effects→ContraindicationsStimulation of the CNS, insomnia,
hypertension, convulsionsPsychoses, insomnia, essential hypertension,
predisposition to convulsions

The pharmacological "face" of analeptics

				oj unucprics		
	Stimula	ntion	Effects			
Medicines	RC*/**	VMC	"Awaken- ing"	Convulsant	Other effects	
Caffeine	+/-	+	+	++	As analeptic it is weaker than	
					bemegride and nicethamide	
Bemegride	++++/-	++	++++	++++	It is effective in intoxications	
					with OA and barbiturates	
Nicethamide	++/++	+++	+	++	Antipellagric	
Sulphocam-	++/+	++	++	++	It is stronger than camphor, can	
phocaine					be introduced i/v	
Ethimizole	++++/-	±	±		Spasmolytic, anti-inflammato-	
					ry, anti-allergic, nootropic	
Camphor	+/+	+	+	+	Locally: irritative, anti-inflam-	
					matory, antiseptic.	
					Resorptively: cardiostimulating	
Cytisine	-/++	++			If there is no effect in 5-8 min,	
Carbonic acid	++++/++				it means that cytisine and	
					carbonic acid do not act	

RC is a respiratory centre (* - direct, ** - reflex action); **VMC** is a vasomotor centre, **OA** are narcotic analgesics.

INN, (Trade name)	Medicinal form, dosage
Bemegride	Sol. for inj. 0.5%
Caffeine sodium benzoate	Sol. for inj. 10%, 20%
Camphor	Sol. for inj. 20%
Carbonic acid	Balloon
Cytisine	Sol. for inj. 0.15%
Ethimizole	Sol. for inj. 1.5%
Nicethamide (Cordiamine)	Sol. for inj. 25%
Sulphocamphocaine	Sol. for inj. 10%

Glossary

Asphyxia is a severe disorder of breathing. Hypotension is the decrease of the blood pressure. Collapse is a rapid strong decrease of the blood pressure. Awakening effect is the return of consciousness, recovery of the inhibited functions of the heart and lungs when using high doses of analeptics. Shock is the acute severe pathological process with the acute disorders of the CNS functions, blood circulation and breathing.

PSYCHOMOTOR STIMULANTS (PSYCHOSTIMULANTS, PSYCHOTONIC MEDICINES)

Psychomotor stimulants (*psyche* means "soul") are medicines that increase mental and physical activity.

Classification of medicines			
Derivatives of			
xanthine	phenylalkylamines	sydnonimines	
Caffeine sodium	Amphetamine sulphate	Mesocarb	
benzoate		Feprosidnine hydrochloride	

reprosidi

The mechanism of action

They increase and regulate the excitation processes in the brain cortex, promote release of catecholamines (noradrenaline and dophamine) in the CNS.

Pharmacodynamics (effe	$ects) \rightarrow Indications$	
Psychostimulating: increase of mental	To increase mental and physical activity of	
(cognitive functions) and physical	healthy people in the extreme conditions	
activity		
"Awakening", analeptic	Poisoning by general anesthetics, narcotic	
	analgesics and hypnotic medicines	
Elimination of drowsiness	Pathologic drowsiness	
Thymoleptic (improvement of	Psychic depression (neuroses, depression,	
depressed mood in patients)	alcoholism)	
Side effects –	→ Contraindications	
Insomnia, increased excitability In	nsomnia, increased excitement, essential	
and irritability, hypertension, h	ypertension, atherosclerosis, diseases of the	
tachycardia	rdiovascular system	

NB! The usage of psychomotor stimulants is contraindicated in the second half of the day, before going to bed and for aged people.

	r		
Medicines	↑BP	Thymoleptic	Other peculiarities
Caffeine	++		It is not prescribed to children under 2
sodium			years old. It potentiates the effect of OA;
benzoate			stimulates the gastric juice secretion; has
			the cardiostimulating and anti-aggregant
			effect, causes "centralization" of the blood
			circulation
Amphetamine	+++	+++	It is a powerful stimulant of the CNS
sulphate			("awakening" amine). It causes anorexia,
			euphoria, motor excitation, addiction. It is
			an indirect-acting adrenomimetic (dilates
			bronchi, pupils, etc.)
Mesocarb	+	++	It is less dangerous than amphetamine;
			there is no euphoria and excitation;
			moderate tachycardia

The pharmacological "face" of psychomotor stimulants

Feprosidnine	+	+	Moderate antidepressant and cholinolytic
hydrochloride			effect, it is weaker than mesocarb

The list of medicines		
INN, (Trade name)	Medicinal form, dosage	
Amphetamine sulphate	Tabl. 0.01	
Caffeine sodium benzoate	Sol. for inj. 20%	
Feprosidnine hydrochloride	Tabl. 0.005	
Mesocarb	Tabl. 0.005	

Cognitive functions are higher cognitive functions including the stock of knowledge and words, ability to abstract thinking, calculation and reproduction of flat and volumetric objects.

ANTIDEPRESSANTS

Depression is characterized by the following basic symptoms: depressive, dreary, worried mood, psychic and motor inhibition. These features are often accompanied by insomnia, sexual disorders, low voice, decreased efficiency of work. Disorder of neurotransmitters functions in the brain, namely the functions of serotonin (it has the leading part), noradrenaline and dophamine in less extent, is the basis of pathogenesis of depressive states. Serotonin is known to be neurotransmitter of a good mood: it improves mood, stimulates the brain's intellectual function, takes part in regulation of appetite (decreases it), in the "sleep-awake" cycle, in the sexual behaviour. Noradrenaline provides psychostimulating effect; participates in supporting of awaken state, in forming of cognitive, adaptation reactions. Dophamine provides the regulation of the motor activity and spatial orientation and it participates in the formation of memory.

Antidepressants (thymoleptics) are psychotropic medicines, which remove mainly the depressive mood or depression, they can stimulate the interest to life, activity and optimism.

Antidepressants are classified by their ability to affect the neurotransmitters functions and metabolism.

Cuissification of meaternes					
The I st generation (non-selective ones)					
Irreversible-acting	Inhibitors of the		Inhibito	rs of the receptor	
MAO inhibitors	monoamines re-uptake		action, plant origin ones*		
Nialamide	Amitrip	Amitriptyline		Mianserine	
	Imipramine Doxepine		Hypericine*		
The II nd generation (selective ones)					
Reversible-acting	Inhibitors of the				
MAO inhibitors	serotonin re-uptake				
Pyrazidol	Paroxetine	Flu	oxetine	Sertraline	
The III rd generation (medicines with a "double" action)					
Venlafaxin]	Milnaciprane	

Classification of medicines

The mechanism of action

The common mechanism of action for all antidepressants is the increase of monoamines' activity (noradrenaline, serotonin, dophamine) that realizes due to the inhibition of monoamineoxydase (MAO) enzyme, inhibition of the monoamines re-uptake and intensification of neurotransmitters release from the presynaptic membranes.

Pharmacodynamics (effe	$cts) \rightarrow Indications$
Antidepressant (removal of	Depression and depressive states in
melancholy and depression,	schizophrenia, stroke, tumours, post-traumatic
worsening of memory, weakness,	states, alcoholism, senile psychosis, manic-
low speech, absence of emotions,	depressive and climacteric psychosis,
slowing down of movements)	atherosclerosis
Side effects	\rightarrow Contraindications
Headache, dry mouth, dizziness,	The states requiring quick psychic and physical
drowsiness, decrease of attention	reactions; disorders of the cerebral blood
and efficiency of work	circulation
Hepatotoxicity, nephrotoxicity,	Diseases of kidneys and liver, pregnancy,
nausea, vomiting	lactation

NB! The simultaneous use of **MAO inhibitors** with food products, which are rich in thyramine (cheese, cream, smoked food, coffee, beer, red wine, chocolate), leads to the appearance of the "cheese" syndrome.

	1	ne pnui	macorogi			
			Effects			
Medicines	thymoleptic	psychostimulating	sedative	cholinolytic	anxiolytic	Other effects/peculiarities
Amitriptyline	+++		+++	+++	++	Antihistaminic, analgesic,
Imipramine	+++	++		+++	+	decrease of libido
Mianserine	++		++	±	+	Antihistaminic, hypnotic, anti-ulcer
Doxepine	++		+++	++	++	Antihistaminic, analgesic, spasmolytic, anticonvulsant
Pyrazidol	++	+	±			Nootropic
Sertraline	++		++		++	Treatment of severe
						depressions. It causes
						sexual disorders
Nialamide	++	++		+		Marked side effects

The pharmacological "face" of antidepressants

Milnaciprane	++	+				
Paroxetine	++		±	±	++	It is a strong selective inhibitor of the serotonin reuptake

The	list	of	medicines
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INN, (Trade name)	Medicinal form, dosage
Amitriptyline	Tabl. 0.075
Doxepine (Spectra)	Caps. 0.025
Fluoxetine (Prozak)	Tabl. 0.02
Hypericine (Deprim)	Tabl. 0.06
Imipramine (Melipramine)	Tabl. 0.075
Mianserine (Lerivon)	Tabl. 0.01
Milnaciprane	Caps. 0.025
Nialamide (Nuredal)	Tabl. 0.025
Paroxetine (Paxyl)	Tabl. 0.02
Pyrazidol (Pyrlindol)	Tabl. 0.025
Sertraline (Zoloft)	Tabl. 0.05
Venlafaxine	Tabl. 0.075

The "cheese" syndrome is the increase of blood pressure up to the hypertensive crisis. **Schizophrenia** (syn. the Bleuler's disease) is the chronic progressive psychosis.

NOOTROPIC MEDICINES

Nootropic medicines (*noos* means "thinking, mind" and *thropos* is "affinity") are medicines that improve the mental activity increasing the brain's resistance to the damaging factors.

	Medicines		
GABA	Pyritynol	Fenibute	
Calcium gopantenate	Pyracetam		

The mechanism of action

Most nootropic agents are similar to GABA by their structure and the principle of action, and that is why they are called GABA-ergic medicines. GABA is not only the endogenous inhibitory mediator of the CNS, but it also takes part in metabolic processes in the brain: it increases energy and plastic processes in the CNS (increasing the biosynthesis of RNA, DNA, proteins, respiratory activity of brain's tissues, utilization of glucose by the brain). These medicines promote the increase of the brain's resistance to hypoxia, improvement of the blood supply in the brain and the easier elimination of toxic metabolic products from the brain. All the phenomena mentioned lead to the enhancement of the brain's functions.

Pharmacodynamic	es (eff	$ects) \rightarrow$ Indications		
Nootropic effect (improvemen	t of	Craniocerebral traumas, stroke, mental		
memory, speech, learning; increa	retardation in children, senile dementia,			
the brain's resistance to hypoxia	disorders of memory, attention, speech;			
intoxication, decrease of dizz	ziness,	atherosclerosis, encephalopathy		
headache, drowsiness, apathy)				
Side effects \rightarrow Contraindications				
Insomnia, irritability, nausea D	isorde	rs of sleep, neurosis, pregnancy		

The pharmacological "face" of nootropic medicines

	Effect	ts	
Medicines	psycho- stimu- lating	sedative	Other peculiarities
Pyracetam	+		The reference medicine. The stressprotective,
			adaptogenic effects. It increases the effect of anti-
			anginal medicines
Pyritynol	++	+	Antidepressant, anti-asthenic
Calcium	+	+	Anticonvulsant, analgesic; it has a low toxicity,
gopantenate			increases the action of barbiturates and anticonvulsants
GABA	+		Hypotensive, anticonvulsant effects
Fenibute		+	Tranquilizing and antipellagric effect, it potentiates the
			effect of CNS depressants

The list of medicines

INN, (Trade name)	Medicinal form, dosage
Calcium gopantenate (Pantogam)	Tabl. 0.02
Fenibute	Tabl. 0.25
GABA (Aminalon, Gammalon)	Tabl. 0.25
Pyracetam (Nootropil)	Tabl. 0.2
Pyritinol (Encephabol)	Tabl. 0.2

Glossary

Stroke is the acute disorder of the blood circulation in brain or in spinal cord resulting in the disorders of the CNS functions.

ADAPTOGENS

Adaptogens are medicines of plant and animal origin that have the general tonic action on the CNS functions, the endocrine system and metabolism. They increase organism's resistance to the unfavourable environmental factors. These medicines promote the changes in the organism, thanks to them it adapts better to changing conditions of the environment and that is why these medicines are called adaptogens. Unlike other CNS stimulants adaptogens do not have the stimulating effect with their first administration.

Classification of medicines					
Medicines of pl	Medicines of animal and				
		synthetic* origin			
Ginseng root tincture	Schizandra tincture	Pantocrine			
Aralia tincture	Leuzea extract	Citrullin*			
Eleutherococcus extract	Toniphyt				

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The mechanism of action

They stimulate non-specific resistance of the body, the synthesis of RNA and proteins in cells, improve the recovery processes and the activity of energy metabolism enzymes, reduce the catabolism of carbohydrates, proteins, fats leading to the "economization" of metabolism and the organism's adaptation to the unfavourable conditions.

Pharmacodynamics ($effects) \rightarrow Indications$
Adaptogenic effect: improvement of	Increase of the work efficiency of healthy
the mental, physical activity and the	people working in unusual climatic
organism's resistance to a great	conditions (the North, tropics, etc.); with
number of negative factors	static, functional (hearing, vision, etc.),
(exhausting physical work, hypoxia,	dynamic loadings; in sportsmen, elderly
infections, etc.); stimulation of the	people. Prophylaxis of infectiousl and non-
cardiovascular system. Unlike	infectious diseases, as well in the period of
psychomotor stimulants the effects	reconvalescence. The treatment of asthenic
of adaptogens reveal slowly	states, neuroses, hypotension, increased
	drowsiness
Side effects \rightarrow	Contraindications
Stimulation of the CNS, The	increased excitability of the CNS, neuroses,
insomnia, hypertension inso	omnia, hypertension

nnia, hypertensioninsomnia, hypertensionNB! To avoid the disturbance of sleep adaptogens should not be administered in the evening.

Medicines	Peculiarities
Ginseng root tincture	\downarrow the cholesterol level; a substitute – "Bioginseng"
Aralia root tincture	Antihypoxic effect
Eleuterococcus extract	A liquid and dry extract is manufactured
Leuzea extract liquid	↑ the protein synthesis
Schizandra tincture	It stimulates the cardiovascular and respiratory systems
Toniphyt	It contains 7 plants. The spasmolytic effect, increases
	appetite
Pantocrine	It is an extract of the stag's antlers. It has a tonic effect on
	the CNS, the GIT and skeletal muscles

The pharmacological "face" of adaptogens

The list of medicines

INN, (Trade name)	Medicinal form, dosage
Aralia root tincture	Tinct. 50 ml

Citrullin (Stimol)	Sol. 50%
Eleuterococcus extract	Extr. 50 ml
Ginseng root tincture	Tinct. 50 ml
Leuzea extract liquid	Extr. 40 ml
Pantocrine	Extr. 50 ml, tabl. 0.15
Schizandra tincture	Tinct. 50 ml
Toniphyt	Pack 100.0

Adaptation is the organism's accommodation to the changed conditions of its existence. Asthenia is the increased fatiguability with the change of mood, weakness, irritability, sleep disorders, etc. Hypotension is the decrease of the blood pressure. Catabolism is disintegration of tissue and cell elements, as well as splitting of carbohydrates, fats and proteins for energy or plastic providing of the life activity processes. Reconvalescence is the recovery of the organism's normal life activity after a disease.

VI. MEDICINES AFFECTING THE CARDIOVASCULAR SYSTEM CARDIOTONIC MEDICINES

Cardiotonic medicines are medicines that intensify the myocardial contractility and eliminate the symptoms of heart failure (cardiac insufficiency). **Cardiac glycosides** are the most widely used in treatment of heart failure (HF).

To understand the effects of cardiotonic medicines it is necessary to know that HF is developed when the heart loading does not correspond to the ability of the heart to perform its work and it is connected, first of all, with the myocardial contractility. There is the acute and chronic HF. The latter has compensated and decompensated forms. In the first case the heart incapability to provide normal blood circulation in the organism is compensated by its hypertrophy, especially one of the left ventricle. By further progressing of the disease the compensation stage characterized by tachycardia, increase of the circulating blood volume, increase of the venous pressure, hemostatic phenomena in the systemic circulation, the lower extremities edemas, as well as cyanosis and dyspnea. Tachycardia and dyspnea develop as compensation of hypoxia.

Cardiac glycosides (CGs) are basic medicines for the HF correction – they increase the myocardial productivity providing its economical but effective work. CGs are contained in different types of Digitalis, Strophanthus, Adonis, Convallaria and other medicinal plants.

Medicines of				
	Digitalis	Strophanthus	Convallaria,	Adonis*
Digoxin	Lantoside	Strophanthine G	Corglycon	Adoniside*
Digitoxin				

C1	C	7
	nt m	<i>odicinos</i>
Classification	$o_j m$	culculcs

The mechanism of action

The level of free calcium in the cardiomyocyte plays an important role in providing the heart muscle contractility. In the cell calcium binds to the protein troponin, which changes its spatial conformation and releases the contractile proteins (actin and myosin) interacting to each other with the formation of actomyosin, that it leads to the contraction of the muscular fibres.

The mechanism of the **positive inotropic** effect of the CGs is connected with their ability to increase the content of Ca^{2+} ions in the cardiomyocytes mainly due to the blockade of SH-groups of Na⁺,K⁺-ATP-ase enzyme. The increase of the Ca²⁺-ions concentration leads to the increase of the contractile proteins activity and as a consequence to the increase of the heart contraction force. More powerful contractions of the heart push the blood out of its cavities more completely, the residual blood volume and the myocardial tension decrease, and as a result the energy loss for its contraction also decreases. The decrease of the conductivity inside the heart, the **negative dromotropic** effect, and the increase of excitability of the myocardium, the **positive batmotropic** effect, is based on the same mechanisms of the CGs action.

The negative chronotropic effect (the diastole's prolonging) occurs due to the delay of the change of the cardiomyocyte cell membrane functional states (inhibition of the polarization and depolarization processes of the atrioventricular node cell membranes and difficulty of the potassium return into the cell). The increase of the diastole's time promotes the delivery of oxygen and essential nourishing substances to the heart muscle.

The biochemical mechanism of the CGs action in HF is stipulated by their **trophic** effect: the values of energy, carbohydrate, protein, lipid and electrolyte metabolism are normalized. The **diuretic** effect of CGs is considered as a result of the systemic and renal blood circulation normalization.

Pharmacodynamics

The main effect in pharmacodynamics of CGs is the **cardiotonic effect**, which consists of 4 components:

1. **The positive inotropic effect**: the systole becomes more powerful and shorter and it leads to the increase of the cardiac output (the beat and minute blood volume).

2. The negative chronotropic effect: the diastole's prolonging and the cardiac rhythm delay. The heart has an opportunity for more complete "rest". The heart rate delay promotes the improvement of the metabolic processes in myocardium and the more complete blood supply of the heart's cavities.

3. **The negative dromotropic effect**: the decrease of the impulse conducting through the heart's conductive system.

4. **The positive batmotropic effect**: the increase of the myocardial excitability.

Thus, due to the **cardiotonic effect** CGs normalize the main blood circulation values: the beat and minute blood volume increases, the venous pressure decreases (i.e. **preload**); the blood circulation speed increases, the volume of the circulating

blood decreases. The phenomena of hypoxia weaken and disappear, the symptoms of cardiac insufficiency – dyspnea, cyanosis – decrease. The positive action of CGs is their ability to increase the efficiency of the heart: under the influence of CGs the heart works more, but at the same time its oxygen consumption does not increase, i.e. it works more economically. The cardiotonic effect of CGs differs from the cardiostimulating effect of epinephrine, ephedrine, isoprenaline and analeptic medicines (caffeine, nicethamide, etc.) by the effect over the myocardial energy processes: CGs promote the accumulation of the energy in the heart muscle, and cardiac stimulants waste energy and their prolonged application leads to the myocardial exhaustion and dystrophy. Besides, unlike cardiotonics cardiac stimulants increase the heart rate, i.e. have a positive chronotropic effect, and it increases the energy consumption too. That is why cardiac stimulants are administered during a short period of time as symptomatic medicines for the myocardial function normalization when it is inhibited by toxic substances. CGs are used as medicines for pathogenetic and often prolonged therapy.

Indications

Chronic and acute HF, tachyarrhythmias. Sometimes CGs are indicated as prophylaxis for preventing HF in pathological states that cause it (pneumonias, toxicoses, severe hypertension and heart rheumatic dysfunctions).

Pharmacokinetics

CGs consist of a non-saccharine part (aglycone or genine) and a saccharine part. The cardiotonic effect of these medicines is connected with aglycone. The main chemical structure of aglycone is cyclopentan-perhydrophenantren nucleus bound to the unsaturated lactone ring. The saccharine part affects the glycosides solubility, their absorption, bioavailibility and other pharmacokinetic peculiarities. So, by the solubility CGs are divided into lipophylic (Digitoxin), hydrophylic (Strophanthine), mixed hydrophylic and lipophylic (Digoxin, etc.). Lipophylic CGs are well absorbed from the GIT and bound actively to blood plasma proteins, they are eliminated slowly and accumulate. They are introduced perorally and are used in chronic HF. Hydrophylic CGs are absorbed poorly from the GIT and are not almost bound to plasma proteins, they are eliminated quickly and do not accumulate. They are introduced parenterally and are used in acute HF. Lipophylic and hydrophylic CGs have an intermediate position by their physical and chemical properties and that is why they can be introduced both perorally and parenterally.

Principles of correct usage

Therapeutic tactics of the glycoside treatment includes two phases:

Digitalization (the saturation phase) can be fast, middle and long, it lasts from 1 till 5 or more days. The medicine is administered until the marked therapeutic effect without the symptoms of intoxication is achieved. The twenty-four hours dose of digitalis medicines is 2-2.5 mg, the dose of strophanthus medicines is 0.6-1 mg.

Maintaining (supporting) phase provides stabilization of the achieved level of the therapeutic effect by prescribing a medicine in the maintaining dose (supporting a stable concentration in blood).

Side effects

Disorders of the heart conductivity and rhythm: bradycardia, up to the heart stoppage, arrhythmia. Worsening of the myocardial contractility. Increase of HF symptoms, retrosternal pain, myocardial ischemia. Neuritis of the optic nerve (the change of normal vision).

Contraindications

Glycoside intoxication, shock, marked bradycardia, ventricular extrasystolia, ischemic heart disease.

Medicines		Route of a	u	Absorption	in		
	intravenously		perorally		1- ntio	the GIT	
	Start	Duration	Start	Duration	ccu		
	(min)	(days)	(hours)	(days)	Am		
Digoxin	15-40	5-6	1.5-3	5-6	+	+	
Digitoxin			2-4	14-21	++	+	
Lantoside	10-30	5-7	1-2	5-7	<u>±</u>	+	
Strophanthine G	5-10	2-3					
Corglycon	5-10	3-4					
Adoniside			15-40	3-4		+	

The pharmacological "face" of CGs

The list of medicines

INN, (Trade name)	Medicinal form, dosage
Adoniside	Sol. 15 ml
Corglycon	Sol. for inj. 0.06%
Digitoxin	Tabl. 0.0001; supp. 0.00015
Digoxin	Sol. for inj. 0.025%; tabl. 0.0001
Lantoside	Tabl. 0.00025
Strophanthine G	Sol. for inj. 0.05%

Glossary

Atrioventricular node is one of the drivers of the heart's rhymth, the part of its conductive system. Cardiomyocyte is a cell of the myocardium. Preload is the pressure to the heart's valves in the venous return of blood towards the heart.

ANTIHYPERTENSIVE MEDICINES (HYPOTENSIVE MEDICINES)

These are medicines that decrease the blood pressure and are used for treatment hypertension or symptomatic arterial hypertension. The BP value depends on the vascular wall elasticity, total peripheral vascular resistance (TPVR), the heart and kidneys work.

The object of the pharmacological affection of hypotensive medicines is different links of the vascular tone regulation mechanism, which include pressor (vasoconstrictive) and depressor (vasodilating) components that are worked with the help of the neurohormonal factors.

Neuronormonal jaciors of the vascular tone regulation				
Vasoo	constrictors	Vasodilators		
const	trict vessels	dilat	e vessels	
Adrenaline	Noradrenaline	Nitrogen monoxide ()	NO)	
Angiotensin II	Vasopressin (ADH)	Acetylcholine	Histamine	
Dophamine		Bradykinin		

Neurohormonal factors of the vascular tone regulation

The mechanism of action of antihypertensive medicines is connected with their influence on different **links of the blood pressure regulation** (fig. 6):

- upon the nervous system: brain cortex, hypothalamus, vasomotor centre, autonomic ganglia, sympathetic postganglionic nerves and adrenoreceptors;

- out the nervous system (peripheral vasodilating medicines): smooth muscles of the vascular wall, myocardium, endocrine system, renal diuresis, tissue metabolism.

Medicines for treatment hypertension are classified considering all these facts.

Medicines decreasing the activity of the nervous system sympathetic part	Direct- and indirect-* acting vasodilators without the influence on the sympathetic nervous	Me	edicines for complex treatment of hypertension
Central-* and	system tone (peripheral		
peripheral-acting	vasodilating medicines)		
1. Stimulants of central	8. Calcium antagonists	14.	Diuretics
α_2 -adrenoreceptors*	9. Inhibitors of ACE*	15.	CNS depressants
2. Selective agonists of	10. Blockers of angiotensin		
imidazoline receptors*	receptors*		
3. β -adrenoblockers	11. Activators of potassium		
4. α - adrenoblockers	canals*		
5. $\alpha + \beta$ adrenoblockers	12. Peripheral vasodilators		
6. Ganglionic blockers	13. Myotropic spasmolytics		
7. Sympatholytics			

Classification of medicines

Medicines decreasing the activity of the nervous system sympathetic part

Classification of medicines

Agonists of cent- ral α ₂ -adreno- and imidazoline* receptors	Sympatholytics* and ganglionic blockers	β-adrenoblockers (cardioselective* and non- cardioselective)	α_1 - and $\alpha + \beta$ *- adrenoblockers
Clonidine	Reserpine*	Atenolol*	Prazosine
hydrochloride	Hexamethonium	Bisoprolol*	Doxazosine
Methyldopha	benzosulphonate	Propranolol	Labethalol*
Moxonidine*	-	_	

The mechanism of action

The mechanism of action of **central** α_2 -adrenomimetics is connected with stimulation of presynaptic α_2 -AR of the vasomotor centre causing the inhibitory effect on the vasomotor centre of the medulla oblongata. It causes decrease of the central

sympathetic influence on arteries and heart. Agonists of imidazoline receptors stimulate the latter ones in the vasomotor centre inhibiting catecholamines release and their influence on the cardiovascular system. Sympatholytics alter the synthesis and accumulation of catecholamines in the vesicles and it promotes decrease of the mediators reserve (noradrenaline, adrenaline and dophamine) in the presynaptic endings of neurons and decrease of the vasoconstrictive effect of catecholamines. β adrenoblockers blocking β_1 -AR decrease the cardiac output and systolic pressure, as well as the heart rate and it leads to the BP decrease. The inhibition of renin release is also important in the mechanism of the antihypertensive action of β -adrenoblockers and it leads to the decrease of angiotensin II and aldosterone production, the decrease of the TPVR and retention of sodium and water in the organism. α_1 -adrenoblockers block α_1 -AR of the peripheral vessels, and it leads to their dilation and decrease of BP. The mechanism of the hypotensive action of ganglionic blockers is connected with disorder of vasoconstrictive impulses transmission through the sympathetic ganglia.

Pharmacodynamics (effe	$ects) \rightarrow$ Indications	
Hypotensive effect	Hypertension, hypertensive crisis	
Medicines have the hypotensive, as well	Prevention and treatment of angina	
as anti-anginal, anti-arrhythmic effect a	pectoris, tachyarrhythmia, hypertension	
the same time	(β-adrenoblockers)	
Side effects	\rightarrow Contraindications	
Headache, dizziness, depression	Atherosclerosis of the cerebral vessels,	
orthostatic hypotension, bradycardia	depression, severe heart failure, diseases	
dyspepsia	of the GIT	

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INN, (Trade name)	Medicinal form, dosage
Atenolol	Tabl. 0.1
Bisoprolol (Concor, Coronal)	Tabl. 0.01
Clonidine hydrochloride (Clofeline)	Tabl. 0.00075
Doxazosine (Cardura)	Tabl. 0.002
Hexamethonium benzosulphonate (Benzohexonium)	Tabl. 0.1
Labetalol	Tabl. 0.1
Methyldopha (Dopegit, Methyldopa)	Tabl. 0.25
Moxonidine (Cint)	Tabl. 0.0002
Prazosine (Adverzuten)	Tabl. 0.002
Propranolol (Anaprilin, Pranolol)	Tabl 0.01
Reserpine (Rausedil)	Tabl. 0.1

Glossary

Angiotensin II is a vasoconstrictive polypeptide that increases the BP. Hypertension is a chronic disease of the cardiovascular system that is characterized mainly by a stable high BP. Hypertensive crisis is exacerbation of hypertension. Hypotensive (antihypertensive) effect is the BP decrease. Catecholamines are a group of physiologically active substances of the similar chemical structure that are mediators (noradrenaline, dophamine) and hormone (adrenaline). **Total peripheral vascular resistance** is the resistance of peripheral vessels to the blood flow (tone of vessels). **Cardiac output** is the volume of blood that is thrown out by the heart per one constriction; the heart constrictive function value.

Peripheral	Inhibitors of ACE	Blockers of	
vasodilators and	and antagonists of	calcium canals	Spasmolytics
activators of	angiotensin	(calcium	
potassium canals*	receptors*	antagonists)	
Hydralasine h/chl.	Enalapril	Amlodipine	Bendazole
Diazoxide	Lisinopril	Isradipine	Papazole
Sodium	Captopril	Nifedipine	Magnesium
nitroprusside	Potasium losartane*	Verapamil h/chl.	sulphate
Minoxidil*	Valsartane*	Dilthiazem	Papaverine h/chl.

Peripheral vasodilating medicines

The mechanism of action

Peripheral vasodilators and myotropic spasmolytics relax the smooth muscles of the peripheral vessels, that it is connected to their direct myotropic action on the vascular wall. A principle of the hypotensive effect of **potassium canals activators** is as follows: the potassium canals open and the K^+ ions leave the cell \rightarrow the Ca²⁺ ions come into the cell in less amount \rightarrow the smooth muscles tone of vessels decreases \rightarrow vessels dilate \rightarrow the BP decreases. **Inhibitors of ACE** block the angiotensin-converting enzyme and, thus, block the transformation of angiotensin I into angiotensin II that is an endogenous vasopressor substance (it constricts vessels, increases the production of aldosterone and vasopressin, promotes development of vascular "rigidity" and stimulates the sympathetic innervation). Inhibitors of ACE decrease the sympathetic system activity, inhibit the hypertrophy process of vascular muscles and the myocardium. Antagonists of angiotensin II receptors block angiotensin II receptors of vessels and it also leads to elimination of angiotensin II effects (including its stimulating effect on the release of aldosterone and activation of the sympathetic nervous system) and decrease of the BP. Calcium canals blockers block free transport of calcium ions in the muscular fibres. Disorder of calcium ions penetration inside the muscular cells leads to decrease of the vascular tone and decrease of the BP.

Pharmacodynamics (effe				$ets) \rightarrow$ Indications
Hypotensive	effect	(all	medicines	Hypertension and hypertensive crisis
decrease BP an	d TPVR,	dilate	arteries)	
Decrease of po	ost-load a	and/or	pre-load to	Hypertension in combination with
the heart				angina pectoris (calcium antagonists).
				Chronic HF (inhibitors of ACE,
				antagonists of angiotensin II receptors)
Spasmolytic	effect	t	(myotropic	Spasms of the smooth muscles of the
spasmolytics)				internal organs
Moderate immune-stimulating effect			effect	Decrease of immunity (Bendazol)

Side effects –	Contraindications
Headache and hypotension up to collapse;	Hypotension, marked cardiac, hepatic
HF	and renal insufficiency

I ne pharmacological "face" of hypotensive medicines					
Medicines	Application in		Effect in hypertensive		Effect to
	hypertension		CI	crisis	
	medium	severe	start, min	duration, h	load
Clonidine	+		15-20	4-8	
Reserpine	+				
Hexamethonium			1-5	4-6	
Sodium nitroprusside		+	1-5	2-5 min	pre/post
Diazoxide		+	1-2	4-12	post
Hydralasine	+	+	20-40	3-6	post
Enalapril	+	+	30	2-4	pre/post
Lisinopril	+	+			pre/post
Potassium losartane	+	+	60	24	post
Calcium antagonists	+	+	20	3-6	post
β -adrenoblockers	+				post
Spasmolytics	+				

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The list of medicines

INN, (Trade name)	Medicinal form, dosage
Amlodipine (Norvask, Amlocor)	Tabl. 0.001
Bendazole (Dibazole)	Tabl. 0.002; sol. for inj. 1%
Captopril	Tabl. 0.025
Diazoxide	Sol. for inj. 1.5%
Dilthiazem (Diacordine)	Tabl. 0.06
Enalapril (Ednit, Enap)	Tabl. 0.01
Hydralasine h/chl. (Apressine)	Tabl. 0.01
Isradipine (Lomir)	Caps. 0.001; sol. for inj. 0.01%
Lisinopril (Dirotone)	Tabl. 0.002
Magnesium sulphate (Cormagnesine)	Sol. for inj. 25%
Minoxidil (Depressan)	Tabl. 0.005
Nifedipine (Corinfar)	Tabl. 0.01; sol. for inj. 0.01%
Papaverine h/chl. (Papavin)	Tabl. 0.01; sol. for inj. 2%
Papazole (papaverine h/chl. + bendazole)	Tabl.
Potassium losartane (Kozaar)	Tabl. 0.05
Sodium nitroprusside	Pwd. for inj. 0.025
Valsartane (Diovan)	Caps. 0.06
Verapamil h/chl. (Isoptine, Finoptine)	Tabl. 0.04

Glossary

Angiotensin-converting enzyme (ACE) is an enzyme that promotes convertion of angiotensin I into angiotensin II. Hypertrophy is the tissue's overgrouth. Myofibril is the muscle's fibre.

ANTI-ANGINAL MEDICINES

Ischemic heart disease (IHD) or coronary heart disease – stenocardia (angina pectoris) and myocardial infarction – is the imbalance between the oxygen consumption by myocardium and its supply in oxygen along the coronary vessels, and it is accompanied by the development of the myocardial hypoxia and accumulation of partially oxidized products of metabolism that irritate receptors and cause pain. The heart supply with oxygen depends, first of all, on the state of the coronary circulation. **That is why the object of the pharmacological affection on the IHD pathogenesis is the regulation mechanisms** of the tone of large and small (especially arterioles) cardiac vessels, which provide the coronary circulation; as well as the decrease of the myocardium need in oxygen; providing the normal metabolism in the myocardium, the level of fibrinogen and prothrombin in blood and intravascular thrombocyte aggregation.

In the therapy of IHD the decrease of oxygen consumption by the myocardium is achieved by different ways: firstly, by decreasing the load on the myocardium, secondly, by decreasing the heart's work. The heart load can be decreased by dilation of veins and arteries, which leads to the decrease of the venous blood return towards the heart (decrease of the heart **pre-load**) and the decrease of the total peripheral vascular resistance (TPVR) (decrease of the heart **post-load**). The decrease of preand post-load reduces the oxygen consumption by myocardium. The heart work (the cardiac output value and rhythm) decreases when the adrenergic innervation (by β adrenoblockers) decreases or the Ca²⁺ ions transport into the myocardial cells (calcium canals blockers) is inhibited. As a result of reducing of the myocardial contractility its need in oxygen decreases. The increase of oxygen delivery to the myocardium is reached due to the improvement of the coronary circulation and the myocardium oxygenation by the dilation (by direct or indirect way) of coronary vessels. It is important to improve the trophism and metabolism of the myocardium, as well as to improve the rheological blood properties in the IHD therapy.

Anti-anginal medicines are medicinal agents that decrease the oxygen consumption by myocardium increasing its delivery; they optimize the energy metabolism in the myocardial cells. Antianginal medicines stop or prevent attacks of angina and acute myocardial infarction, increase the patients' tolerance to physical loads.

Medicines decreasing oxygen consumption by myocardium and increasing oxygen delivery to the myocardium			Medicines oxygen cor myoc	s decreasing nsumption by cardium
Nitrovasodilators (organic nitrates)	Calcium canals blockers (phenylalkylamines*,benzothi- azepines**, dihydropyridines), different medicines•		β-adren (β ₁ , β	$(b) blockers \ \beta_1 + \beta_2 *)$
Glycerol trinitrate Isosorbide dinitrate	Nifedipine Amlodipine Verapamil*	Amiodaron• Dilthiazem**	Atenolol Metoprolol Bisoprolol	Propranolol*

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Medicines increasing the or	Medicines	improving	the	
myocardium (coronarolytic	es)	metabolism	in myocardiu	ım
Carbocromen Dipyridamol		Trimethasidi	ne	
Menthol in bromisovalerianate		Inosine		

The mechanism of action

The discovery of ERF (endothelium relaxing factor) or NO (nitrogen monoxide) was a great contribution to understanding the mechanisms of therapeutic effect of organic **nitrates** (fig. 3).



Fig. 3. The mechanism of the anti-anginal effect development by nitrates.

The coronary vessels spasm is supposed to be conditioned mainly by insufficient formation of the endogenous nitrogen monooxide (NO) by the vessels' endothelium or by the increase of its destruction. In these cases organic nitrates substitute NO deficiency in the vascular wall. As a result, it leads to the calcium level decrease in the cells, then coronary and peripheral vessels dilation and heart's work decrease increasing blood supply of the myocardium. **Calcium antagonists** (calcium canals blockers) block a slow transmembrane flow of calcium into cardiomyocytes. Blockade of calcium canals is accompanied by the decrease of the heart's work with slowing its rhythm down, coronary and peripheral arteries dilation (decrease of BP and TPVR), as a result the myocardium need in oxygen decreases and its supply increases. **β-adrenoblockers** remove the sympathoadrenal influence on the myocardium and decrease the heart's work. **Amiodaron** blocks α - and β -AR, calcium and sodium canals non-competitively and it leads to the decrease of the heart rate, cardiac output and coronary vessels dilation. **Validol** dilates coronary vessels by

reflex and increase the oxygen supply to the myocardium by irritating the mouth mucous membrane receptors. **Carbocromen and dipyridamol** inhibit phosphodiesterase and adenosindesaminase enzymes, respectively, and it leads to the coronary vessels dilation. **Trimethasidine** provides transmembrane transfer of the sodium, calcium, potassium ions, supports the homeostasis in cardiomyocytes. **Inosine** increases the energy metabolism in the myocardium.

Pharmacodynamics

All medicines have the **anti-anginal** effect: they cause a negative inotropic effect to the myocardium and some of them have the negative chronotropic effect as well; promote the decrease of the oxygen consumption by the myocardium and the increase of the oxygen delivery. **Coronarolytics** have the coronarodilating effect. **Dipyridamol** has also the anti-aggregant effect. **Trimethasidine and inosine** improve metabolism in the myocardium.

Indications

Removal and prevention of attacks of stable and unstable **angina pectoris**, **acute myocardial infarction** (**MI**), recovering therapy after MI. The complex therapy of acute and chronic HF. Prophylaxis of the hypercoagulation syndrome (dipyridamol).

Side effects

Side effects of **organic nitrates** are pulsatory, bursting headache; orthostatic hypotension and reflex tachycardia; the feeling of fever, facial skin reddening. Tolerance (the decrease of effect duration and strengh due to regular administration of nitrates). The syndrome of abrupt discontinuation (it reveals by worsening the symptoms of stenocardia in 1-2 days after stopping the medicines intake). When using **\beta-adrenoblockers** disorders of heart rhythm and conductivity such as bradycardia, arterial hypotension, HF and bronchospasm can appear.

Side effects of **calcium canals blockers** are dysfunctions of the heart rate, hypotension, decrease of the myocardial contractility; **amiodaron** causes the muscular weakness, bradycardia, hyperthyroidism; **dipyridamol** causes the "stealing" syndrome, hypotension; **inosine** causes the tachycardia, exacerbation of gout; **trimethasidine** causes the pain in the epigastrium; **carbocromen** causes bradycardia; the side effects of **validol** are lacrimation and dizziness.

Contraindications

Anti-anginal medicines are contraindicated in the marked hypotension. **Nitrates** are not used in the close-angle glaucoma, epilepsy, cerebral forms of hypertension and cerebral bleedings. The absolute contraindications for using **calcium canals blockers** are cardiogenic shock, severe congestive HF, the acute period of MI, heart blockade, hepatic and renal insufficiency. β -adrenoblockers are contraindicated in the congestive HF, bradycardia, bronchospasm; **amiodaron** is not used in hypokalemia, weakness of the sinus node; **dipyridamol** is not used in the severe sclerosis of coronary vessels; **inosine** is not administered in gout; **trimethasidine** is not used in pregnancy; **carbocromen** is not administered in peptic ulcer, diseases of liver and kidneys, and atherosclerosis.

Modicino	The route of	Ef	fect	D/D	Medicinal
wieurchie	administration	Start, min	Duration, h	N/	form
Glycerol	sublingually	1-2	0.5	+/-	Tabl., caps.,
trinitrate					sol.
(Nitroglycerine)					
Trinitrolong*	buccally	2-3	3-5	+/+	Films
Suctac forte*	perorally	20-30	4-6	-/+	Tabl.
Isosorbide	sublingually,	3-10	1-2	±/+	Tabl.
dinitrate	perorally	20-50	3-6		
Nitroointment*	transdermally	15-60	3-8	-/+	Ointment
Nitroderm*		60-120	24	-/+	Plaster

The pharmacological "face" of nitrovasodilators

R-removal, **P**-prevention of the anginal attack; * - medicinal forms of nitroglycerine.

The pharmacological "face" of calcium antagonists (A) and β -adrenoblockers (B)

dı				Effect	
Grou	Medicines	T _{1/2} , h	hypotensive	anti-anginal	anti-arrhythmic
	Nifedipine (I)	4	+++	+++	+
Α	Amlodipine (III)	35-50	++	+++	+
	Verapamil (I)	6	++	+++	++
	Atenolol	6-9	+++	+++	+++
B	Metoprolol	3-7	+++	+++	+++
	Propranolol	2-5	++	+++	+++

I, **III** –generations of calcium canals blockers.

The list of medicines

INN, (Trade name)	Medicinal form, dosage
Amlodipine (Norvask)	Tabl. 0.01
Amiodaron (Cordaron)	Tabl. 0.2; sol.for inj. 5%
Atenolol	Tabl. 0.1
Bisoprolol (Coronal)	Tabl. 0.005
Carbocromen (Intencordine)	Tabl. 0.075
Dilthiazem (Diacordin)	Tabl. 0.06
Dipyridamol (Curantil)	Tabl. 0.05; sol. for inj. 0.5%
Glycerol trinitrate (Sustac forte, Nitroglycerine,	Tabl. 0.00025
Trinitrolong, Nitroointment, Nitroderm)	
Isosorbide dinitrate (Isoket)	Tabl. 0.01
Inosine (Riboxine)	Tabl. 0.2; sol. for inj. 2%
Menthol in bromisovalerianate (Validol)	Caps. 0.1
Metoprolol (Corvitol)	Tabl. 0.1
Nifedipine (Corinfar)	Tabl. 0.01; sol. for inj. 0.01%
Propranolol (Anapriline, Pranolol)	Tabl. 0.01; sol. for inj. 1%

Trimethasidine (Preductal)	Tabl. 0.02
Verapamil (Finoptine, Lekoptine)	Dr. 0.04

Anti-anginal effect is the removal of the IHD symptoms. Myocardial infarction is necrosis of the myocardium part. Cardiomyocyte is the myocardial cell. The "stealing" syndrome is redistribution of blood from ischemiazed sites to the healthy myocardium parts caused by dipyridamol and it worsens the symptoms of IHD.

ANTI-ATHEROSCLEROTIC MEDICINES

Anti-atherosclerotic medicines are medicines that decrease the level of cholesterol and atherogenic lipoproteins in blood, prevent the lipids deposition in the vascular wall, inhibit the growth of atherosclerotic plaques and cause the angioprotective effect.

It is known that there is an increased level of lipids and lipoproteins in blood (hyperlipidemia) in atherosclerosis. The main classes of lipoproteins are:

-lipoproteins of a very low density (LPVLD) (**atherogenic**) that are synthesized in the liver and they serve for transport of the endogenous triglycerides (TG) into the liver, where LPLD are produced from them;

-lipoproteins of a low density (LPLD) take part in transport of cholesterol (ChS) into the cells (**atherogenic**);

-lipoproteins of a high density (LPHD) participate in transport of ChS from tissues to the liver, where its catabolism occurs (**anti-atherogenic**). LPHD have the ability to block aggregation of thrombocytes and it is also important for prevention of atherosclerosis development.

While interacting with lipoproteid receptors of vessels ChS and TG are released from atherogenic lipoproteins (LPVLD and LPLD), they deposit in the vascular intima and it promotes to development of atherosclerosis. The increase of the LPHD concentration prevents atherosclerotic destruction of vessels due to isolation of ChS from arterial walls.

The main aim of prevention and treatment of atherosclerosis and its complications is to decrease of atherogenic lipoproteins (LPVLD and LPLD) content in blood and to increase the level of anti-atherogenic lipoproteins (LPHD). For this aim medicines that inhibit the synthesis of ChS in the liver, decelerate its absorption in the intestine, promote its transformation into bile acids, steroid hormones and vitamin D_3 or accelerate ChS elimination from the organism are used. Anti-atherosclerotic medicines protect the vascular wall directly or indirectly from development of the atheromatous process in it, i.e. they are angioprotectors. Besides, in atherosclerosis antioxidants and medicines that correct the rheological blood properties (anticoagulants and others) are used.

Hypolipidemic medicines				
Statins	Sequestrants of	Fibrates and	Antioxidants	Anticoagulants
	bile acids	others*		
Lovastatin	Cholestiramine	Phenofibrate	Tocoferol	Heparin
Simvastatin		Cyprofibrate		
		Nicotinic acid*		

Classification of medicines

The mechanism of action

By the mechanism of action anti-atherosclerotic medicines are divided into:

I. Decreasing mainly the content of ChS in blood:

- Inhibitors of the ChS synthesis (statins). **Statins** inhibit the synthesis of ChS in the liver from the mevalonic acid.

- Medicines increasing the elimination of bile acids and ChS from the organism (sequestrants of bile acids). **Sequestrants of bile acids** bind to ChS, TG and bile acids in the small intestine forming complexes, which are non-absorbable in the GIT.

II. Decreasing mainly the content of TG in blood: derivatives of the fibroic acid (fibrates). **Fibrates** increase the lipoproteinlipase activity.

III. Decreasing the content of ChS and TG in blood: the **nicotinic acid**.

It decreases the release of free fatty acids and their coming into the liver and it leads to decrease of the biosynthesis of TG in the liver and formation of lipoprotein residues.

IV. Antioxidants. Medicines inhibit the processes of peroxide oxidation of lipids and it leads to decrease of atherogenic lipoproteins formation and destruction of the vascular wall.

V. Anticoagulants. They inhibit the process of blood coagulation at all the stages, improving the rheological blood properties.

Pharmacodynamics	\rightarrow Indications
Anti-atherosclerotic effect	Atherosclerosis, hyperlipidemia
Side effects \rightarrow (Contraindications
Headache, giddiness, muscular atrophy	Pregnancy, lactation, child age,
and pain, nephropathy, anaemia,	myopathies; liver, kidneys and blood
hepatitis, thrombocytopenia	diseases

Medicines	Alternative of choice		Primary	Severe	↓ChS	↓ChS
	Ι	II	ΠL	ΠL	ausorption	synthesis
Lovastatin	+		+	+		+
Simvastatin	+		+	+		+
Phenofibrate	+	+	+			+
Cyprofibrate	+	+	+			+
Cholestiramine	+		+		+	

The pharmacological "face" of hypolipidemic medicines

HL – hyperlipidemia; I, II – the therapy line.

I ne list of medicines				
INN, (Trade name)	Medicinal form, dosage			
Cholestiramine (Cholestipol)	Tabl. 1.5			
Cyprofibrate (Lipanor)	Caps. 0.1			
Heparin	Sol. 5000 IU/ml			
Lovastatin (Mevacor)	Tabl. 0.01			
Nicotinic acid (Vitamin PP)	Tabl. 0.1			
Phenofibrate (Lipantil)	Caps. 0.1			

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Simvastatin (Zocor)	Tabl. 0.01
Tocoferol (Vitamin E)	Caps. 0.1

Myopathy is any pathologic state of the muscular tissue, mainly the skeletal muscles. Triglycerides, cholesterol are products of the lipid metabolism.

ANTI-ARRHYTHMIC MEDICINES

Anti-arrhythmics are medicines that normalize the rate and contractions of the heart preventing or removing arrhythmias.

The properties of the myocardium that provide the cardiac rhythm (automatism, excitability and conductivity) depend on the electrolyte metabolism, mainly on the K⁺, Na⁺, Ca²⁺, Mg²⁺ exchange. K^{+} is an intracellular ion, its deficiency leads to the development of tachycardia and its excess causes bradycardia (decrease of excitability and conductivity). Ca^{2+} promotes the increase of the myocardial excitability, conductivity and contractility. K^+ and Mg^{2+} are antagonists of Ca^{2+} .

Classification of medicines			
tachyarrhythmias bradyarrhythmias			
Membrane- stabilizers	β-adreno- blockers	Prolongers of repolarization, calcium canals blockers*, K ⁺ -containing medicines**	M-cholinoblockers, β -adrenomimetics*
Quinidine	Atenolol	Amiodaron	Atropine sulphate
Procainamide	Propranolol	Verapamil*	Isoprenaline*
Lidocaine	Metoprolol	Potassium and magnesium asparaginate**	Dobutamine*

The mechanism of action

Membrane-stabilizing medicines prevent Na⁺, K⁺, Ca²⁺ transport through the membranes of cardiomyocytes, slow down depolarization and repolarization. β **adrenoblockers** block β_1 -AR of the myocardium, decrease the myocardial automatism and conductivity. Amiodaron is a medicine of the combined action: it slows down the repolarization blocking potassium, sodium and calcium canals; possesses the non-competitive β -adrenoblocking effect. Calcium canals blockers (or **calcium antagonists**) inhibit the Ca^{2+} transport through slow L-calcium canals retarding the spontaneous depolarization of the myocardial cells and decreasing automatism and conductivity in the heart. Potassium and magnesium asparaginate normalizes metabolic processes in cardiomyocytes, decreases automatism, inhibits the myocardial conductivity and excitability, decreases the heart rate and contractility.

M-cholinoblockers eliminate the suppressing influence of the vagus nerve (bradycardia) on the heart conductive system. β -adrenomimetics stimulate β_1 -AR of the heart, increase the concentration of Ca^{2+} -ions and cAMP in cardiomyocytes increasing the myocardial excitability and conductivity and eliminating different forms of bradyarrhythmias.

P	harmacody	namics	(effects))	\rightarrow Indications
Anti-arrhythmic	(all	medicine	es), l	ocal	Atrioventricular tachyarrhythmia,
anesthetic (Lidocaine)			ventricular extrasystolia; local		
					anesthesia (Lidocaine)
Anti-anginal,	antihypert	ensive	(β-adr	eno-	Angina pectoris, hypertension
blockers, calcium antagonists) (fig. 4)					
Sid	e effects		\rightarrow		Contraindications
Neurotoxicity,	increase	of th	ne car	diac	Chronic cardiac, renal and hepatic
insufficiency symptoms, the BP decrease			insufficiency		

The pharmacological "face" of anti-arrhythmic medicines

	1	0	<u> </u>	
	Blocker of		er of	
Medicines	Ion	canals	β_1 -adreno-	Other effects
	Na^+	Ca^{2+}/K^{+}	receptors	
Quinidine	+++	- /++		Antipyretic, analgesic, local
				anesthetic, uterotonic
Procainamide	+++	- /++		Hypotensive, anticholinergic
Lidocaine	+			Local anesthetic
Propranolol	+		+++	Sedative, anti-anginal, hypotensive
Metoprolol	+		+++	Anti-anginal, hypotensive
Verapamil	+	+++/-		
Potassium and				Effective in poisoning by cardiac
magnesium	Th	e source o	$f K^{+}, Mg^{2+}$	glycosides
asparaginate				



Fig. 4. Effects of calcium canals blockers on the cardiovascular system

INN, (Trade name)	Medicinal form, dosage
Amiodaron (Cordaron)	Tabl. 0.02; sol. for inj. 5%
Atenolol	Tabl. 0.05

Atropine sulphate	Sol. 0.1%
Dobutamine	Sol. for inj. 0.5%
Isoprenaline (Isadrine, Novodrine)	Tabl. 0.005
Lidocaine (Xycaine)	Sol. for inj. 1%
Metoprolol (Corvitol)	Tabl. 0.1
Potassium and magnesium asparaginate	Tabl. 0.35
(Asparkam, Panangin)	
Procainamide (Novocainamide)	Tabl. 0.25; sol. for inj. 10%
Propranolol (Anaprilin)	Tabl. 0.01; 0.04
Quinidine	Tabl. 0.2
Verapamil (Lekoptine, Finoptine)	Tabl. 0.04; sol. for inj. 0.25%

Anti-anginal effect is the removal of the imbalance between the oxygen consumption by myocardium and its supply with blood (removal of the IHD symptoms). Arrhythmia is a dysfunction of the heart rhythm. Cardiomyocyte is the cell of myocardium. Polarization is the state of rest of the cell membrane. Sinoatrial and atrioventricular nodes are drivers of the heart rhythm, a parts of the heart conductive system. Extrasystolia is the extra heart contraction or contraction of any of its parts on the background of general rate.

VII. MEDICINES AFFECTING THE GIT

MEDICINES THAT AFFECT APPETITE

Appetite or feeling of hunger is determined by the activity of centres of hunger and satiation located in the hypothalamus. Stimulation of noradrenaline neurotransmission in the CNS leads to inhibition of the centre of hunger, and stimulation of serotoninergic neurotransmission activates the centre of satiation. Two main disorders of appetite are distinguished such as **anorexia** and **bulimia**.

Correction of appetite dysfunctions is performed with the help of anorectic or anorexigenic (appetite decreasing) and anti-anorectic or anti-anorexigenic (appetite increasing) medicines.

Clussification of incatentes		
Anti-anorectic medicines (bitters)	Anorectic medicines	
Wormwood herb	Amphetamine sulphate	
Dandelion root	Phepranone	
Sweet flag rhizome	Phenylpropanolamine	
Collection for appetite	Fluoxetine Sibutramine	

Classification of medicines

The mechanism of action

While irritating the afferent nerves endings *bitters* increase in reflex the excitability of the centre of hunger that causes the gastric juice secretion, increasing of appetite and improving of digestion. *Amphetamine, phepranone, phenylpropanolamine* increase the release of NA and inhibit its re-uptake stimulating the brain cortex and inhibiting the centre of hunger. *Fluoxetine* inhibits the re-uptake

of serotonin that leads to activation of the centre of satiation. *Sibutramine* inhibits the re-uptake of NA and serotonin and, thus, suppresses the centre of hunger and stimulates the centre of satiation.

Pharmacodynamics (effe	$cts) \rightarrow$ Indications
Anti-anorectic (increase of appetite,	Anorexia (neurogenic, in hypoacidic,
improvement of digestion)	atrophic gastritis, etc.)
Anorectic (decrease of appetite, loss of	Obesity, bulimia of the different genesis
weight)	
Side effects -	→ Contraindications
Addiction (in long-term administration of	Hypertension, tachyarrhythmia, the CNS
amphetamine, phepranone,	excitation, pregnancy
phenylpropanolamine), anxiety,	
insomnia, tachycardia, hypertension (all	
anti-anorectic medicines)	
Increase of the gastric juice secretion	Hyperacidic states
(bitters)	

	of meanemes affecting appende
Medicines	Peculiarities
Bitters	They are medicines of the plant origin
	that contain glycosides of a bitter taste.
	They are taken 15-20 min before meals.
	Their action reveals only the background
	of meals
Amphetamine (see psychomotor	Indirect-acting adrenomimetic; very
stimulants)	strong psychostimulating, cardio-
	stimulating, hypertensive effects. It is not
	used for the course treatment
Phepranone	Indirect-acting adrenomimetic with more
	selective anorectic effect, less toxic than
	amphetamine
Phenylpropanolamine	Sedative effect
Sibutramine	It affects simultaneously on the centres of
	satiation and hunger, has the
	antidepressant effect

The pharmacological "face" of medicines affecting appetite

The list of medicines

INN, (Trade name)	Medicinal form, dosage
Amphetamine sulphate (Phenamine)	Tabl. 0.01
Collection for appetite	Pack 100.0
Dandelion root	Pack 100.0
Fluoxetine (Prozak)	Tabl. 0.02
Phenylpropanolamine	Tabl. 0.025
Phepranone (Amphepranone)	Dr. 0.025
Sibutramine	Caps. 0.01

Sweet flag rhizome	Pack 50.0
Wormwood herb	Pack 100.0

Anorexia is the complete loss of appetite. Bulimia is pathologically increased feeling of hunger.

EMETIC AND ANTI-EMETIC MEDICINES

These medicines inhibit (anti-emetic) or stimulate (emetic) different parts of the nervous system selectively, responsible for the vomiting: receptors of the gastric mucous membrane, vestibular apparatus, trigger zone of the medulla oblongata.

Classification of medicines			
Emetic medicines:	Anti-emetic medicines		
central- and reflex*-	(M-cholinoblockers*, H_1 -histaminoblockers**, 5- HT_3 -		
acting	serotoninoblockers***, D2-dophaminoblockers)		
Apomorphine h/chl.	Scopolamine h/chl.*		
Ipecacuanha root syrup *	Diphenhydramine**	Tropisetron***	
	Metoclopramide	Haloperidol	

Classification of medicines

The mechanism of action

Reflex-acting emetic medicines irritate nerve endings of the gastric mucous membrane, do not affect the CNS; **central-acting medicines** stimulate the dophamine receptors of the emetic centre trigger zone.

Anti-emetic medicines block D_2 -dophamine, serotonin-5-HT₃-receptors of the emetic centre trigger zone; M-ChR and H₁-histamine receptors in the CNS.

Pharmacodynamics	$s(effects) \rightarrow Indications$
Emetic	Acute poisonings; production of the negative
	conditioned reflex in alcoholism
Anti-emetic	Vomiting in motion sickness, radiation affection,
	antitumour therapy, toxicosis in pregnant women
Side effects	\rightarrow Contraindications
BP decrease, extrapyrami-	Extrapyramidal disorders (D ₂ -dophaminoblockers),
dal disorders	diseases of the heart and the CNS

The pharmacological "face" of anti-emetic medicines

		Used in			
Medicines	motion	Chemo-, radiation therapy of	toxicosis		
	sickness	tumours			
Scopolamine h/chl.	+				
Diphenhydramine	+	+	+		
Tropisetron		+			
Metoclopramide		+	+		
Haloperidol		+			

The list of medicines

INN, (Trade name)	Medicinal form, dosage
Apomorphine h/chl. (Yuprima)	Sol. for inj. 1%

Diphenhydramine (Dimedrol)	Sol. for inj. 1%; tabl. 0.05
Ipecacuanha root syrup	Vial
Haloperidol (Halopril, Halidor)	Tabl. 0.005; sol. for inj. 0.5%
Metoclopramide (Cerucal)	Tabl. 0.05; sol. for inj. 0.5%
Scopolamine h/chl.	Sol. for inj. 0.5%
Tropisetron (Navoban)	Sol. for inj. 0.1%

Extrapyramidal disorders see neuroleptics (antipsychotics).

ANTI-ULCER MEDICINES

Classification of medicines

Anti	secretory medicines		Antacid and covering
Inhibitors of	H_2 -histamine	M_1 -cholino-	medicines (monocomponent
H^+/K^+ -ATPase	receptors blockers	blockers	and combined*)
Omeprazole	Famotidine	Pirenzepine	Aluminium phosphate
			Almagel*
			Maalox*
Gastroprotectors	Antihelicobacter	medicines	Medicines of plant origin
Bismuth subcitrate	Metronidazole		Gastrophyt
Misoprostol	Bismuth-containin	ng medicines	Plantaglucide

The mechanism of action

Inhibitors of H⁺/K⁺-ATPase or blockers of "proton pump" inhibit the activity of the H^+/K^+ -ATPase enzyme and, thus, they block the function of the "proton pump" stopping the hydrogen ions secretion by oxyntic cells of the stomach and it is accompanied by the inhibition of the hydrochloric acid formation there. Blockers of H₂-histamine receptors inhibit the secretion of the hydrochloric acid in the stomach by competing inhibition of the histamine interaction with H₂-histamine receptors of stomach cells. M₁-cholinoblockers block M₁-ChR of the gastric mucous membrane selectively and it leads to the inhibition of the hydrochloric acid and pepsinogen secretion by the gastric glands. Antacid medicines chemically react with the hydrochloric acid of the gastric juice and neutralize it. Covering medicines form a film from colloid that protects the sensitive nervous endings of the gastric mucous membrane from the action of irritants and the hydrochloric acid. **Bismuth-containing** medicines (bismuth subcitrate) as astringent medicines bind the tissue proteins forming albuminates that protect the gastric mucous membrane from aggressive affects (HCl and other substances). Misoprostol (a synthetic prostaglandine analogue) substitutes the natural component of the gastric mucus, replenishes its deficiency and stabilizes the protective barrier of the gastric mucous membrane; improves the microcirculation. Antihelicobacter medicines have the bactericidal effect against Helicobacter pylori. Plantaglucide, Gastrophyt are medicines of the plant origin, which mechanism of action is stipulated by their composition: they stimulate the reparative processes and decrease inflammation in the gastric mucous membrane, normalize the GIT functions.

Phar	macodynamics (effects) \rightarrow	Indications
Anti-ulcer effect	Peptic (stomach and duodenal) ulcer, hyperacidic gastritis
	(all, except Plantaglucide). Hyp	oacidic gastritis, peptic ulcer
	with normal or decreased acidity	(Plantaglucide, Gastrophyt)
Side effect	$fs \longrightarrow$	Contraindications
Dyspepsia,	Hepatic, renal functional disorder	ers; pregnancy
headache, dizziness		

The pharmacological "face" of anti-ulcer medicines

Madiainas	↓ of	↑of	↓ H .	Other offects/peculiarities
Medicines	HCl/pepsin	secretion**	pylori	Other effects/peculiarities
Aluminium	1 *			It is effective in
phosphate	+ ·	+	-	intoxications
Almagel	*/1	I		Adsorbent, covering,
	-/+	Ť	-	choleretic, laxative effects
Maalox	*/+	+	-	Covering effect
Bismuth				Antiseptic, astringent effect
subcitrate	-	+	++	
Omeprazole	++++/+	-	+	Cytoprotective
Pirenzepine	++/+	-	-	Spasmolytic effect
Famotidine				The III rd generation
	+++/+	-	-	medicine, 10 times more
				effective than ranitidine
Metronidazole	_/_	-	+++	Antiprotozoal
Misoprostol				Synthetic prostaglandin
	++/+	++	-	analogue. Cytoprotective.
				↑intestinal and uterine tone
Gastrophyt				Consists of 15 plants. Anti-
	/	-	-	inflammatory, choleretic
				effects

* – medicines that do not inhibit secretion, but neutralize the free HCl; ** - mucus and bicarbonates in stomach.

The list of medicines

INN, (Trade name)	Medicinal form, dosage
Aluminium phosphate (Phosphalugel)	Gel 16.0
Almagel	Gel, vial 200 ml
Bismuth subcitrate colloidal (De-nol, Ventrisol)	Tabl. 0.12
Famotidine (Famosan)	Tabl. 0.02
Gastrophyt	Pack 100.0
Maalox	Susp., vial 250 ml
Metronidazole (Clion, Trichopol)	Tabl. 0.25; sol. for inj. 0.5%
Misoprostol (Saytotek)	Tabl. 0.0002
Omeprazole (Omez)	Caps. 0.02
Pirenzepine (Gastrocepine)	Tabl. 0.025; sol. for inj. 0.5%
Plantaglucide	Granules 2.0

Anti-ulcer effect is decrease of clinical symptoms of peptic ulcer exacerbation and the ulceration area in the GIT. Helicobacter pylori is a gram-negative microorganism that takes part in the peptic ulcer formation.

HEPATOPROTECTORS

These are medicines that increase liver resistance to pathologic affections; they promote the renewal of its functions in different disorders.

Medicines and anim	of the plant al* origin	Medicines containing aminoacids and essential phospholipids*	Synthetic medicines
Hepatophyt	Flamine	Glutargine	Antral
Liv-52	Silibinine	Essential*	Lioliv
Tyqueol	Hepabene		Thiotriazoline
Syrepar*	-		Ursodesoxycholic acid

Classification of medicines

The mechanism of action

The common elements in the mechanism of the action of hepatoprotectors are their ability to:

-intensify the detoxication processes due to the improvement of the hepatocyte monooxygenase systems functioning and the intensification of the conjugation processes;

-inhibit the processes of free radical oxidation of hepatocytes (the antioxidant effect);

- stabilize the hepatocytes' membranes, decrease the cytolysis phenomena (the membrane-stabilizing effect);

- decrease the hepatocyte inflammation due to the influence on immunological and biosynthetic processes in the hepatic tissue (the anti-inflammatory effect);

-normalize the tissue respiration processes (mainly due to the cytochrome system) and oxidative phosphorylation;

- improve the energy supply of hepatocytes.

Essential phospholipids, besides these effects, provide the restoration of the structure and functions of cellular and sub-cellular membranes and, thus, they eliminate defects in the cell membranes caused by hepatotoxins.

Pharma	acodynamics (e	effects)	\rightarrow	Indic	ations	
Hepatoprotective,	antitoxic,	antiox	idant,	Hepatitis,	hepatic	cirrhosis,
membrane-stabilizing,	anti-inflammat	tory		chronic	ch	olecystitis,
				dyskinesia	of the bi	liary tract
				and the gal	l bladder	
Side effects			\rightarrow	Contrair	ndications	
Dyspepsia, discomfort	in the epigastri	ic area		Acute hep	atitis, hep	atic coma,
				chronic ren	al insuffic	iency

Madiainaa	Effects			Other		
Medicines	a/i	a/o	m/s	ch/r	effects/peculiarities	
Antral	+	+	+	+	Analgesic,	
Lioliv	+	+	+	+	immunostimulating	
Thiotriazoline	+	+	+	+	Cardioprotective, anabolic	
Tyqueol	+	+	+	+	Prostate-protective, anti- ulcer	
Silibinine	+	+	+			
Hepatophyt	+	+	+	+	It contains 9 plants; hypoglycemic	
Liv-52	+	+	+	+	BAS from 8 plants; ↑appetite, ↓ risk of cholelithiasis development	
Essential*	+	+	+		Protein synthesis stimulant, hypolipidemic effect, it contains essential phospholipids	
Glutargine		+	+		Combination of the glutamic acid and arginine; detoxication	

The pharmacological "face" of hepatoprotectors

a/i – anti-inflammatory; **a/o** – antioxidant; **m/s** – membrane-stabilizing; **ch/r** – choleretic effects; BAS – biologically active substances.

The list of medicines

INN, (Trade name)	Medicinal form, dosage
Antral	Tabl. 0.1; 0.2
Essential	Caps. 0.3; sol. for inj. 5 ml
Flamine	Tabl. 0.05
Glutargine	Tabl. 0.25; sol. for inj. 4%; 40%
Hepabene	Caps.
Hepatophyt	Pack 100.0
Lioliv	Pwd. for inj. 0.644
Liv-52	Tabl.
Silibinine (Carsil, Legalone, Silibor)	Tabl. 0.035; caps. 0.07
Syrepar	Sol. for inj. 1%
Thiotriazoline	Tabl. 0.1; supp. 0.2; oint. 2%
Tyqueol	Sol. 50 ml; 100 ml
Ursodesoxycholic acid (Ursofalk)	Tabl. 0.1

Hepatocyte is a cell of the liver. **Dyskinesia** is the motility disorder of the smooth muscle organ (biliary tract, etc.). **Choleretic (bile-expelling) effect** is increase of bile production and release. **Cytochromes** are enzymes that contain iron and have the function of the electrons and hydrogen ions transport, i.e. they take part in the tissue respiration.

LAXATIVE MEDICINES

Laxatives are medicines that increase the motor function of the intestine or make the intestinal contents soft fastening the defecation.

Medicines stimulating intestinal		Medicines stimulating intestinal
chemoreceptor	S	mechanoreceptors
<u>Plant origin</u> :		Medicines swelling in the intestine:
Glaxena	Regulax	Laminaria saccharina
Ramnus cathartica bark	Castor oil	
Synthetic:		Salt laxatives:
Sodium picosulphate		Magnesium sulphate
Medicin	es making inte	estinal contents soft
Vaseline oil		

Classification of medicines

The mechanism of action

Intensification of the GIT peristalsis by the stimulation of chemo- or mechanic receptors of the intestine or softening of feces with relieve of their movement along the intestine.

Pharm	acodynamics (effects	\rightarrow	Indications	
Laxative effect	Constipation, pre	paration to	operations, instrumer	ntal
	examination of the	GIT; food poi	sonings; regulation of stool	l in
	hemorrhoid and proctitis			
Sid	e effects	\rightarrow Cont	traindications	
Increase of the	GIT motility and	d Intestinal	obstruction, spastic coli	tis.
peristalsis (colic-lik	te pain). Disorder o	f Simultaneo	ous intake with medicines t	hat
drug and food absorption from the GIT		are absorb	ed from the GIT	

When magnesium sulphate is administered parenterally, it inhibits the CNS and depending on the dose has sedative, hypnotic, general anesthetic effects. The medicine has also spasmolytic, hypotensive, and in high doses – anticonvulsant effect.

Laxatives are not recommended to prescribe for a long period of time to avoid disorders of the intestine's functions (development of diarrhea with metabolic disorders, decrease of the intestinal enzymes function, digestion disorders, the large intestine atony, water-electrolyte balance disorder, etc.).

Medicines	The onset of action, h	Peculiarities of pharmacodynamics/application		
Glaxena Ramnus cathartica bark	8-10	Chronic constipation		

The pharmacological "face" of laxative medicines

Castor oil	2-6	Uterotonic effect, acute constipation, radiography of the GIT organs, labour induction		
Sodium picosulphate	6-10	Chronic constipation, urographics, recto- and coproscopy		
Laminaria saccharina	8-10	Chronic constipation		
Magnesium sulphate	3-5	Acute constipation, poisonings; choleretic effect		
Vaseline oil	1	Chronic constipation, poisonings by liposoluble poisons, anal cracks, hemorrhoid		

The list of medicines

INN, (Trade name)	Medicinal form, dosage	
Castor oil	Vial 50.0; caps. 1.0	
Glaxena	Tabl. 0.0135	
Laminaria saccharina	Syrup, pwd.	
Magnesium sulphate (Cormag-	Pwd. 50.0	
nesine)		
Ramnus cathartica bark	Pack 100.0	
Regulax	Sol.; blocks	
Sodium picosulphate (Guttalax)	Dr. 0.005; sol. 0.75%	
Vaseline oil	Vial 50 ml	

Glossary

Hemorrhoid is the pathological change of the straight intestine vessels with rectal bleedings, pain and prolapse of hemorrhoids. **Constipation** is a delayed, difficult or incomplete emptying of the intestine. **Proctitis** is inflammation of the rectal mucous membrane.

MEDICINES OF DIGESTION ENZYMES. ANTI-ENZYMATIC MEDICINES

Pancreas is an important digestion organ. Pancreatic enzymes (lipase, amylase and proteases) split the food components.

In pancreatic diseases medicines stimulating or substituting the exocrine function of the pancreas (**enzymatic medicines**) and medicines inhibiting the activity of its proteolytic enzymes (**anti-enzymatic medicines**) are used.

	Anti-				
Pancreatic enzymes	Pancreatic enzymes+bile+ hemicellulase	Pancreatic enzymes+bile+ aminoacids+ HCl	enzymatic medicines		
Pancreatine	Festal	Panzynorm-forte	Aprotinine		
Mezym-forte	Enzystal				

Classification of medicines

The mechanism of action

Enzymatic medicines split proteins (protease), lipids (lipase) and carbohydrates (amylase). Bile acids that are contained in enzymatic medicines emulsify lipids, increase the activity of lipase and improve absorption of lipids and liposoluble vitamins. Aminoacids stimulate secretion of the gastric juice, and hemicellulase promotes splitting of plant cellulose in the small intestine lumen, microflora normalization, decrease of gas formation.

Anti-enzymatic medicines inhibit the activity of trypsin, chemotrypsin, callicreine, plasmin and other proteases forming inactive complexes with these enzymes; inhibit fibrinolysis and suppress kinins formation.

Pharmacodynamics (eff	$ects) \rightarrow$ Indications
Deficiency substitution of pancreatic	Substitution therapy in pancreatic
enzymes, normalization of digestion	insufficiency (chronic pancreatitis,
(enzymatic medicines)	enterocolitis)
Stoppage of self-digestion of the	Prevention of autolysis of the pancreas in
pancreas, removal of hemorrhages and	acute pancreatitis; after operations on
edema there (anti-enzymatic medicines)	organs that are close to the pancreas
Side effects	\rightarrow Contraindications
Allergy to pork or beef protein. Diarrhea	Individual intolerance of pork or beef
or constipation (when using high doses).	protein. Intestinal obstruction. Acute
The syndrome of "abrupt	pancreatitis (first 7-10 days) and
discontinuation" in the prolonged	exacerbation of chronic pancreatitis (first
application (enzymatic medicines)	3-5 days)
Decrease of the secretion of pancreatic	Insufficient pancreatic function
digestive enzymes (anti-enzymatic	
medicines)	

The pharmacological	<i>"face" of enzymatic medicines</i>	"face"	
	—		

		Effect			
Medicines	Composition	↑ bile secre- tion	intestinal motility regulation	↓ me- teorism	↓ pain in chronic pancreatitis
Pancreatine	Extract of the cattle pancreas containing protease, amylase, lipase	-	-	-	+
Mezym- forte	Extract of the pork pancreas containing pancreatine	-	-	-	+
Festal	Pancreatine, bile components, hemicellullase	+	+	+	-
Enzystal	Pancreatine, bile components, hemicellullase	+	+	+	-

Panzynorm-	Pancreatine, bile				
forte	components,	+	+	-	-
	aminoacids, HCl				

ine usi of medicines			
INN, (Trade name)	Medicinal form, dosage		
Aprotinine (Gordox)	Pwd. for inj. 12 U/vial		
Enzystal	Tabl.		
Festal	Dr.		
Mezym-forte	Dr.		
Panzynorm-forte	Dr.		
Pancreatine	Tabl. 0.25		

The list of medicines

Glossary

Autolysis is a self-digestion of the pancreas. Fibrinolysis is a process of dissolution of a fibrin blood clot.

VIII. MEDICINES AFFECTING THE RENAL FUNCTION DIURETIC MEDICINES (DIURETICS)

Diuretics are medicines that increase diuresis, excrete the excessive amount of liquid from an organism and remove edemas.

There is a retention of liquid in the organism with formation of edamas in renal diseases (nephritis, nephrosis, pyelonephritis), urinary tract diseases (pyelitis, cystitis), cardiovascular system diseases (cardiac insufficiency, decompensated heart diseases, myocardial infarction, cardiosclerosis), hepatic pathology (cirrhosis, etc.). The main role in the development of edemas of any origin belongs to the primary retention of sodium in the organism. The increase of its concentration in blood and in the interstitial liquid leads to the increase of the osmotic pressure and the secondary retention of water in tissues. That is why diuretics are prescribed simultaneously with treating the basic diseases (heart, kidneys, liver, etc.) to accelerate the sodium and water elimination. Their action is mainly directed to the renal function, in particular, to the processes of the primary urine filtration in glomeruli, reabsorption – inverse absorption of water and diluted substances - in tubules, secretion – excretion of substances by the tubular epithelium.

The process of the urine formation is under neurohormonal control. Thus, adrenal hormones, especially aldosterone, affect the elimination of sodium and chlorine. A sodium-uretic factor, which causes the marked sodium-uresis (elimination) and increases diuresis, was isolated from cardiomyocytes of the atria and liver. The renal function is also regulated by prostaglandins causing the increase of the blood flow in the kidneys and, correspondingly, the intensification of filtration process.

Classification of medicines

There are several classifications of diuretics.

Firstly, diuretics are divided by the impact of action: those intensifying mainly the water diuresis (osmotic); those intensifying the elimination from the

organism mainly Na^+ , K^+ , Cl^- : loop and thiazide diuretics (they are called **saluretics**); those intensifying Na⁺ elimination and blocking K⁺ elimination (**potassium-saving or** potassium-sparing diuretics). Secondly, they are divided by the strength of the diuretic effect (mainly by their ability to increase Na⁺ excretion with urine) into strong-acting diuretics: loop diuretics (inhibit Na⁺ reabsorption by 10-25%); mediumacting diuretics (inhibit sodium reabsorption by 5-10%): thiazide and thiazide-like, osmotic diuretics; weak-acting diuretics: potassium-saving, plant origin diuretics, carboanhydrase inhibitors, xanthine derivatives. Thirdly, by the onset and duration of action diuretics are divided into fast- (30-40 min) and short- (2-4 h) acting: furosemide, urea, triamteren, ethacrynic acid, mannitol; ones with medium onset (2-4 h) and duration (8-14 h) of action: theobromine, aminophylline, acetazolamide, amyloride, hydrochlorthiazide, clopamide; slow- (2-5 days) and long- (2-3 days) acting ones: spironolactone.

By the influence on the acid-base balance in blood diuretics are divided into those causing the marked metabolic acidosis: acetazolamide; those causing metabolic acidosis: amyloride, triamteren, spironolactone; and those causing moderate alkalosis: chlortalidone, furosemide, etc.

Diuretics are also classified by localization of their action in different parts of the nephron.

Table 4.

Proximal section of convoluted tubules including other nephron sections*	Ascending section of the Henle's loop	Distal section of convoluted tubules
Carboanhydrase inhibitors• and osmotic diuretics *	Loop diuretics	Thiazide and thiazide-like* diuretics
Acetazolamide● Mannitol* Urea*	Furosemide Ethacrynic acid	Hydrochlorthiazide Chlortalidone Clopamide* Indapamide*
Collecting ducts area and the distal tubular section*	Nephron's glomeruli	Glomeruli and tubules
Potassium-sparing	Xanthines	Plant origin: monomedicines and combined* ones
Spironolactone Triamteren Amyloride* Triampur compositum*(comb.)	Aminophylline Theobromine	Nephrophyt* Orthosiphone leaf Bearberry leaf Lespenephril Horse-tail herb

Divertics acting on

The mechanism of action

The mechanism of the acetazolamide's action is connected with the inhibition of the carboanhydrase enzyme activity that activates the carbonic acid

formation process in cells of the tubular epithelium and dissociation of the carbonic acid on H^+ and HCO_3^- ions. It inhibits H^+ ions coming into urine in exchange for Na⁺ ions. The metabolic reabsorption of sodium and hydrogen ions is slowing down, and NaHCO₃ (sodium hydrocarbonate) of the primary urine is intensively excreting by the kidneys. With the intensive excretion of sodium hydrocarbonate by urine the latter gets the alkaline properties, and blood (because of the H⁺ ions retention by the kidneys) gets the acidic properties (acidosis). The decrease of the IOP and ICP by carboanhydrase inhibitors is connected with block of the vascular plexus carboanhydrase in the brain's ventricles (the production of the cerebrospinal fluid is decreased) and in the ciliary body (the production of the intraocular fluid is decreased). Carboanhydrase inhibitors decrease the content of sodium and water in the brain's neurons and it leads to inhibition of their excitability. As a result, the anti-epileptic effect of diuretics from this group develops. Osmotic diuretics do not influence on the electrolyte reabsorption. When introducing intravenously they increase the osmotic pressure in the vascular bed. Consequently, the increased osmotic pressure, which decreases reabsorption of sodium and water, appears in the primary urine since water is retained by osmotically active substances. Medicines act along the whole tubules. Excretion of sodium using osmotic diuretics occurs slower than excretion of water, and excretion of potassium does not change. Owing to the blockade of sulphohydryl groups of enzymes loop diuretics inhibit the energy forming processes (for example, oxidative phosphorilation) and it leads to decrease of reabsorption of sodium, magnesium and partially potassium ions from urine to cells, the latter one reduces water reabsorption. They promote the excretion of Na⁺, K^+ , Cl⁻, Ca²⁺, Mg²⁺ salts from the organism and inhibit carboanhydrase in high doses. Thiazide and thiazide-like diuretics inhibit the activity of Na⁺, K⁺-ATP-ase, succinate dihydrogenase and bind carboanhydrase. Consequently, the supply of the sodium pump by the energy and Na⁺, Cl⁻ reabsorption reduces. It stipulates the increase of diuresis and sodium elimination. The mechanism of action of potassium-sparing diuretics is not the same. Spironolactone has a steroid structure, which is similar to the aldosterone's structure, being its competitive antagonist. Promoting the Na⁺ transfer through the cell membranes the medicine intensifies the sodium ions excretion from the organism and inhibits the elimination of K^+ and Mg^{2+} . Triamteren and amyloride are non-competitive antagonists of aldosterone, cause a direct blocking action on the Na⁺ transport through the sodium canals of distal tubules of the kidneys. That is why they decrease the Na⁺ reabsorption and the K^+ secretion, increase divisitions. Triampur compositum contains triamteren and hydrochlorthiazide. The main mechanism of xanthine diuretics action is intensification of the renal blood flow in the kidneys and filtration intensification in the glomeruli. These medicines also decrease the processes of the Na^+ , Cl⁻, H₂O tubular reabsorption. The mechanism of the diuretic action of **plant** diuretics has not been studied enough. Volatile oils, organic acids, glycosides, saponins, flavonoids containing in plants are considered to intensify the blood circulation in the kidneys, increase their filtration ability and partially affect the tubular reabsorption.

Pharmacodynamics (effect	$ets) \rightarrow$ Indications
The main effect of diuretics is diuretic	Pulmonary edema, edemas in diseases
	of heart, vessels, kidneys and liver
Loop, thiazide and thiazide-like	The complex therapy of hypertension,
diuretics have the hypotensive effect	hypertensive crisis
Spironolactone decreases the cardiac	Edema in heart failure
post-load, loop diuretics decrease the	
pre-load on the heart	
Osmotic and loop diuretics,	Brain edema, glaucoma
carboanhydrase inhibitors cause the	
dehydrative effect, decreasing the IOP	
and ICP	
Acetazolamide has the anti-epileptic	Epilepsy (petit-mal)
effect	
Medicines of the plant origin have also	Prevention of edemas in cardio
the hypoazotemic (Lespenephril,	vascular, renal and hepatic diseases
Nephrophyt), anti-inflammatory,	
antimicrobial, spasmolytic, choleretic	
effects; some of them excrete urinary	
Concrements (Cowberry lear,	
Nephrophyt)	
Side effects –	→ Contraindications
Hypokalemia (carboanhydrase inhibitors,	Acidosis, uremia, hepatic cirrhosis,
thiazide, loop diuretics); hyperkalemia	renal diseases, Addison's disease
(potassium-sparing); hyposodemia ,	(carboanhydrase inhibitors);
nypomagnemia (loop diuretics,	nypomagnemia, nypokalemia,
potassium-sparing, thiazide diuretics);	nyposodemia, denydration, severe
hypercalcemia (thiazide and thiazide-	forms of diabetes (loop, thiazide
this ride and this ride like divisions);	diureucs)
hyperchloremic metabolic acidesis	
(carboanhydrase inhibitors potassium-	
(carboannyerase minotors, potassium-	
(loon thiazide and thiazid-like	
notassium-sparing diuretics)	
Potussium spuring uniteries)	

The pharmacological" face" of diuretics					
	Effect Cause				
Medicines	strength start		duration (h)	acidosis	alkalosis
Furosemide	++++	5 min i/v; 30-40	4-8		+
		min per os			

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Urea	+++	15-20 min	8		
Triamteren	+	2-4 h	8		
Mannitol	++++	20 min	8		
Theobromine	+	2-4 h	8-14		
Acetazolamide	+	2-4 h	8-14	+	
Amyloride	+	2 h	24	+	
Spironolactone	+	2-4 h	24-48	+	
Hydrochlorthiazide	++	1-2 h	10-12		+
Indapamide	++	2 h	12-24		+
Clopamide	++	2-3 h	15-16		+
Nephrophyt	+	It contains 12 plants			
Chlortalidone	++	2-4 h	24-48		+

The list of medicines

INN, (Trade name)	Medicinal form, dosage
Amyloride	Tabl. 0.005
Aminophylline (Euphylline)	Tabl. 0.15; sol. for inj. 2%
Acetazolamide (Diacarb, Fonurit)	Tabl. 0.25
Bearberry leaf	Pack 100.0
Chlortalidone (Hygrotone)	Tabl. 0.05
Clopamide (Brinaldix)	Tabl. 0.2
Ethacrynic acid (Uregit)	Tabl. 0.05
Furosemide (Lazix)	Tabl. 0.04; sol. for inj. 1%
Horse-tail herb	Pack 100.0
Hydrochlorthiazide (Hypothiazide)	Tabl. 0.025
Indapamide (Ariphon)	Tabl. 0.0025
Lespenephril	Sol. 120 ml
Mannitol (Mannit)	Sol. for inj. 20%
Nephrophyt	Pack 100.0
Orthosiphone leaf	Pack 100.0
Spironolactone (Verospirone)	Tabl. 0.025
Theobromine	Tabl. 0.25
Triamteren (Pterofen)	Caps. 0,05
Triampur compositum	Tabl.
Urea	Pwd. for inj. 30.0; 60.0

Glossary

Acidosis is the shift of the blood pH to the acid side. Alkalosis is the shift of the blood pH to the alkaline side. IOP (intraocular pressure) is the pressure of the intraocular fluid in the eye's cavity. Dehydration is the decrease of the water content in tissues.

ANTIGOUTY MEDICINES

Gout is the disease of metabolism with localization of the inflammatory site and deposition of uric acid salts crystals (urates) in joints that is accompanied by their inflammation and pain attacks.

Medicines that decrease the uric acid synthesis (uricodepressive) or increase its elimination from the organism (uricosuric) are used for treatment gout.

Uricodepressive ones	Uricosuric ones	Mixed acting ones
Allopurinol	Sulphinpyrasone	Allomarone (combined)
	Colchicine	
	Benzobromarone	

Classification of medicines

The mechanism of action

Allopurinol inhibits the xanthinoxidase enzyme, disturbs the hypoxanthine transformation into xanthine and then into the uric acid. **Uricosuric** medicines increase the uric acid excretion decreasing the urates reabsorption and increasing their secretion in the kidneys. **Allomarone** alters the uric acid synthesis, inhibits its reabsorption, promotes the excretion of the uric acid.

Pharmacodynamics (ef	fects) \rightarrow Indications
Antigouty effect	Gout, hyperuricemia
Side effects	\rightarrow Contraindications
Dyspepsia, hyperthermia, eosinophilia,	Peptic ulcer, diseases of blood, liver,
leukopenia	kidneys; pregnancy, lactation

The pharmacological "face" of antigouty medicines

Medicines	Peculiarities
Allopurinol	It is also used in nephrolithiasis, arthritis, psoriasis
Sulphinpyrasone	It has also the anti-aggregant effect
Benzobromarone	It has the analgesic effect and is also used in arthritis with
	hyperuricemia, psoriasis
Colchicine	Anti-inflammatory, analgesic, antifungal effect. It is also used
	in nephrolithiasis, chondrocalcinosis, amiloidosis, Behchet's
	disease
Allomarone	It contains allopurinol and benzobromarone

The list of medicines

INN, (Trade name)	Medicinal form, dosage
Allomarone	Tabl.
Allopurinol (Alupol, Milurit)	Tabl. 0.1
Benzobromarone (Desuric, Hypuric)	Tabl. 0.1
Colchicine	Tabl. 0.1
Sulphinpyrasone (Anturan)	Tabl. 0.1

Glossary

Hyperuricemia is the increase of the uric acid level in blood. **Nephrolithiasis** is the presence of concrements in the urinary tract.

IX. MEDICINES AFFECTING THE BLOOD COAGULATION SYSTEM AND FIBRINOLYSIS

Imbalance between the functional blood coagulation and anticoagulation (fibrinolysis) systems leads to development of thrombosis or hemorrhage (bleeding).

Plasma and thrombocyte factors of blood coagulation as an object of drug affection

The natural state (fluidity and coagulation) of blood is provided by the factors of the vascular wall, proteins (proconvertin, prothrombin, fibrinogen), which are synthesized in the liver with the participation of vitamin K and blood cells thrombocytes. The mechanism of blood coagulation is performed at three (I-III) stages (phases): while damaging vascular wall the formation of the active thromboplastin (I), which promotes conversion of prothrombin to thrombin (II) that converts fibrinogen to fibrin-monomer, which, in its turn, coverts into fibrin-polymer as a result of clot retraction (III). Thus, bleeding is stopped. Thrombocyte aggregation is regulated by the thromboxane-prostacycline system. Thromboxane A_2 is thrombocytes, stimulates vasoconstriction synthesized in and thrombocyte aggregation. **Prostacycline** is formed in the endothelium of the vascular wall, inhibits adhesion of thrombocytes to the vascular wall and causes vasodilation.

Any kind of disorders of blood coagulation (hemorrhagic and thromboembolic states) requires pharmacological correction. For this purpose *anticoagulative* (*antithrombotic*) medicines, which decrease the process of blood coagulation, *or antihemorrhagic* (*hemostatic*) medicines, that intensify the process of blood coagulation are used. These two groups of medicines influence in the opposite directions on three processes that support blood homeostasis: thrombocyte aggregation, fibrin thrombus formation and their lysis.

MEDICINES DECREASING BLOOD COAGULATION (ANTITHROMBOTIC)

Direct-acting anticoagulants		Indirect-acting anticoagulants		
Resorptive-acting ones	Local-acting ones	Acenocumarol		
Heparin**	Heparin ointment	Fenindion		
Calcium nadroparin*				
*_ low molecular heparins: ** _ high molecular heparins				

Classification of medicines

*– Iow molecular neparins; *** – mgn molecular neparins

Fibrinolytics	Antiaggregants
Fibrinolysine	Dipyridamol
Urokinase	Ticlopidine
Streptokinase	Acetylsalicylic acid

The mechanism of action

Direct-acting anticoagulants have a powerful negative charge, which promotes the formation of the complex with positively charged coagulation proteins. As a result, procoagulating properties of coagulation proteins are inhibited. **Indirect-acting anticoagulants** have no influence on coagulation factors directly in the blood.

They interfere the biosynthesis of coagulation proteins (proconvertin and prothrombin) in the liver as a result of antagonism with vitamin K. **Fibrinolytics** (fibrinolysis activators) transform profibrinolysine (plasminogen) into its active form - fibrinolysine (plasmin), decrease the level of fibrinogen in the blood plasma, inhibit aggregation of thrombocytes and the activity of natural blood procoagulants, i.e. they activate the fibrinolytic system (fibrinolysis). **Antiaggregants** inhibit the synthesis of thromboxane A_2 suppressing thromboxane-synthase and cyclooxygenase enzymes.

Pharmacodynamics (effects) \rightarrow Indications		
Direct-acting anticoagulants		
Anticoagulant (inhibition of blood	Myocardial infarction, direct blood	
coagulation at all phases)	transfusion, surgery on the heart or	
	vessels. Prophylaxis and treatment of	
	embolism and vascular thrombosis	
Fibrinolysis activation, improvement of	Prophylaxis of thrombosis after coronary	
blood rheological properties	vessels shunting and prosthetics of the	
	heart valves	
Antiaggregant (inhibition of adhesion	Thrombophlebitis, trophic ulcers of the	
and aggregation of thrombocytes and	shin, hemorrhoids, subcutaneous	
erythrocytes, normalization of the blood	hematomas, hypercoagulation syndrome	
rheological properties, improvement of		
microcirculation of the brain,		
myocardium, retina, etc.)		
Hypolipidemic (decrease of the lipid	Prophylaxis and treatment of	
level in blood)	atherosclerosis	
Coronarodilating (improvement of	Myocardial infarction, stable angina of	
blood stream in the myocardium)	tension	
Immunosuppressive	Direct blood transfusion, surgery on the	
	heart or vessels, rheumatism, bronchial	
	asthma, glomerulonephritis, hemolytic	
	anemia, renal transplantation,	
	endocarditis	

Indirect-acting anticoagulants		
Anticoagulant	Prophylaxis and treatment of venous and	
	arterial thrombosis, thrombophlebitis,	
	coronary insufficiency, obliterating	
	endarteritis, hypercoagulation syndrome	
Hypolipidemic	Prophylaxis and treatment of	
	atherosclerosis	
Fibrinolytics		
Fibrinolytic (dissolution of fibrin	Venous and arterial thrombosis, acute	
filaments and recent (up to 3 days)	myocardial infarction, pulmonary	
thrombi)	embolism	

Antiaggregants	
Antiaggregant	Prophylaxis and treatment of the
	hypercoagulation syndrome, chronic
	coronary insufficiency. Prophylaxis of
	ischemic stroke and encephalopathies
Side effects	\rightarrow Contraindications
Bleedings, thrombocytopenia	Low blood coagulability, increased
	permeability of vessels, peptic ulcer,
	tuberculosis

The pharmacological "face" of anticoagulants and antiaggregants

Medicines	Route of	Onset of effect	Duration of
	administration		effect
Heparin	i/v	5 min	2-6 h
	i/m	15-30 min	2-8 h
	s/c	30-40 min	4-12 h
Nadroparin*	s/c	3-4 h	up to 6 h
Acenocumarol	per os	24-48 h	2-4 days
Fenindion	per os	10-24 h	24-72 h
Dipyridamol**	per os, i/v		
Ticlopidine**	per os	1-2 days	8-10 days
Acetylsalicylic acid	per os	20-30 min	up to 7 days

* - nadroparin is less toxic than heparin;
** - dipyridamol`s activity is similar to aspirin, and ticlopidine is more active than aspirin.

Medicines	The sources of	Affection on the	Antigenic
	obtaining	uiroindus	properties
Fibrinolysine	Donor's blood	direct outside	High
Urokinase	Human kidneys cells	indirect inside and	Practically
	culture	outside	absent
Streptokinase	Hemolytic		High
	streptococcus culture		

The pharmacological "face" of fibrinolytics

The list of medicines		
INN, (Trade name)	Medicinal form, dosage	
Acenocumarol (Sincumar)	Tabl. 0.02	
Acetylsalicylic acid (Aspirin)	Tabl. 0.3	
Dipyridamol (Curantil)	Tabl. 0.0025; sol. for inj. 0.5%	
Fenindion (Fenilin)	Tabl. 0.03	
Fibrinolysine (Plasmin)	Pwd. for inj. 20000 U	
Heparin (Vetren)	Sol. for inj. 1000 U/ml	
Heparin ointment	Oint. 100 U/g	
Nadroparin calcium (Fraxiparin)	Sol. for inj. 9500 U/ml	

Streptokinase (Streptolyase)	Pwd. for inj. 100000 U
Ticlopidine (Ticlid)	Tabl. 0.25
Urokinase	Pwd. for inj. 100000 U

accumulation is limited of blood Hematoma a in tissues. **Hemocoagulation** is coagulation of blood. **Hemophilia** is inherited insufficiency of the blood coagulation factors, it is an increased bleeding. Hypercoagulation syndrome is pathological increase of the blood coagulation ability and rate. MI (myocardial infarction) is necrosis of the myocardium part. Coronary insufficiency is insufficient supply of the myocardium with blood. Stenocardia (angina) of tension is attacks of retrosternal pain in ischemic heart because of the physical loadings. Thrombophlebitis is the inflammation of a vein with the formation of thrombi there. Thrombocytopenia is the decreased amount of thrombocytes in blood. Thromboembolism is embolism (obstruction) of a vessel by the torn thrombus. Trophic ulcer is defects of the skin or mucous membrane appeared as a result of the blood supply disorder or innervation of tissues disorder with a weak tendency to heal and a tendency of recurrences. Shunting is restoration of the blood supply when the vessel's site is excluded from the blood circulation.

MEDICINES INCREASING BLOOD COAGULATION (HEMOSTATICS, ANTIHEMORRHAGIC MEDICINES)

Medicines that increase blood coagulation promote stopping bleedings when they are used locally or as a result of the resorptive action.

Classification of meaternes			
Antifibrinolytic	Hemostatics		Coagulants of the
agents	Resorptive- Local-acting		synthetic, animal, plant
(inhibitors of	acting		origin
fibrinolysis)			
Aminocapronic	Fibrinogen	Thrombin	Carbazochrome
acid	Calcium	Hemostatic	Gelatin medical
	chloride	sponge	Water pepper herb
	Menadion		Nettle herb

Classification of medicines

The mechanism of action

Antifibrinolytic agents inhibit the action of plasminogen and the action of plasmin; suppress the kinins' system and the activity of fibrinolysis. Hemostatics are natural components of the blood coagulation system. Coagulants of the synthetic, animal and plant origin decrease permeability of the vascular wall, increase the blood viscosity, slow the blood flow, make conditions for forming thrombi.

Pharmacodynamics	$(effects) \rightarrow Indications$
	Inhibitors of fibrinolysis: bleedings caused by
	the increased fibrinolysis, thrombocytopenia,
	including ones caused by peptic and duodenal
	ulcer, postnatal bleedings
Hemostatic effect:	Hemostatics: bleedings in surgery, obstetrics,
stoppage or decrease of	traumatology caused by deficiency of blood
bleedings	coagulation system factors: capillary, from
	parenchymal organs, local bleedings (nasal,
	extraction of teeth, etc.)
	Coagulants of synthetic, animal and plant origin:
	hemorrhagic diathesis, metrorrhagia, nasal, renal,
	intestinal bleedings
Side effects	\rightarrow Contraindications
Increase of blood	Predisposition to thrombosis, thromboembolism
coagulation	

The pharmacological "face" of medicines increasing the blood coagulation

Medicines	The route of	Other effects / peculiarities
	administration	
Aminocapronic acid	per os, i/v	Anti-inflammatory, anti-allergic
Fibrinogen	i/v, locally	It is a component of the blood
Calcium chloride	per os, i/v	coagulation system
Thrombin	locally	
Menadion	per os, i/m, i/v	A synthetic water soluble
		vitamin K analogue
Hemostatic sponge	locally	A mixture of $CaCl_2$ and
		thrombin on the solid carrier
Carbazochrome	locally, s/c, i/v	A synthetic solid
Nettle herb	per os	Anti-inflammatory, capillary-
		stabilizing

The list of medicines

INN, (Trade name)	Medicinal form, dosage
Aminocapronic acid (Amicar)	Sol. for inj. 5%; tabl. 0.5
Calcium chloride	Sol. for inj. 10%; sol. 5%
Carbazochrome (Adroxon)	Sol. for inj. 0.025%
Fibrinogen	Pwd for inj. 0.8
Gelatin medical	Sol. 10%
Hemostatic sponge	Plates 10x10
Menadion (Vicasol)	Sol. for inj. 1%
Nettle herb	Pack 100.0
Thrombin	Pwd. for inj. 10 ml
Water pepper herb	Extract

Hemorrhagic diathesis is predisposition to bleedings. **Plasmin** is an enzyme that destroys clots of blood and turn fibrin to soluble elements. **Fibrinogen** is a blood plasma protein that transforms to fibrin. **Fibrinolysis** and **fibrinolytic effect** is the process of dissolution a fibrin clot as a result of enzymatic reactions.

X. MEDICINES AFFECTING BLOOD FORMATION (HEMOPOIESIS)

CORRECTORS OF ERYTHROPOIESIS

Disorders of erythropoiesis can be caused by decrease of the amount of erythrocytes and hemoglobin (anaemias) or acute increase of the amount of inferior erythrocytes in blood (erythremia). The main types of anaemias are iron deficiency, B_{12} - deficiency, and folic acid deficiency, hypoplastic and hemolytic anaemia.

Cuissification of meaternes			
Erythropoiesis stimulants		Erythropoiesis	
Iron-containing medicines	Vitamins	Erythropoietins	inhibitors
for enteral and parenteral			
administration			
Iron fumarate	$B_{12}, B_{6},$	Human	Sodium phosphate
Jectofer	B ₂ , C,	erythropoietins	solution labeled by
Ferroplex	Bc, E	(α, β, ώ)	phosphorus-32
Iron sulphate			
Iron saccharate			
Iron chloride			
Iron hydroxide			
polymaltose complex			

Classification of medicines

Erythropoiesis stimulants (antianaemic) Iron-containing medicines

The mechanism of action

Iron-containing medicines are donors of an iron ion and stimulate the synthesis of hemoglobin.

Pharmacodynamics (effects)	→ Indications
Increase of the hemoglobin amount in erythrocytes, improvement of the	Prevention and treatment of iron deficiency (hypochromic) anaemias
tissues oxygenation	
Side effects	→ Contraindications
Ulceration of the GIT, constipation, diarrhea, pain in the epigastric area,	Diseases of the GIT, anaemias that are not connected with the deficiency of iron in
intestinal colics	the organism

Vitamins

The mechanism of action

Vitamin-containing medicines promote the synthesis of the DNA; intensify the cells' division and the formation of erythrocytes.

Pharmacody	namics (effects) \rightarrow Indications
Stimulation of erythropoiesis	Anaemias (especially hyperchromic)
Side effects	\rightarrow Contraindications
Dyspepsia, tachycardia	Diseases of the GIT, tachycardia

Erythropoietins

Erythropoietin is the glycopeptide hormone produced by kidneys as a response for hypoxia of different genesis (bleedings, hypochromic and hyperchromic anaemias, the blood circulation disorders) and its role is the erythropoiesis correction. The higher level of the renal hypoxia is, the more erythropoietin is produced. Nowadays with the help of the genetic engineering **human erythropoietins** α , β , ω have been obtained.

The mechanism of action

Stimulation of proliferation and differentiation of cells of the red bone marrow because of affection the specific erythropoietin's receptors.

Pharmacod	ynamics (effects) \rightarrow Indications
Increase of erythrocytes	Anaemias caused by the chronic renal insufficiency,
and reticulocytes number,	HIV- infection, after usage of cytostatics, in preterm
the amount of hemoglobin	born infants, hypo- and aplastic anaemias
Side effe	$cts \rightarrow Contraindications$
Increase of BP	Hypertension

The pharmacological "face" of iron-containing medicines

	maimacological	fuce of non comun	ing meanenes	
Medicines	The route of	The frequency of	Composition	
	administration	administration		
Iron fumarate	per os	3-4 times a day	Iron (II) fumarate	
Jectofer	i/m	once/1-2 days	Iron (II) in the complex	
			with sorbite and citric	
			acid in dextrane water	
			solution	
Iron sulphate	per os	3-4 times a day	Iron (II) sulphate	
Iron saccharate	i/v	once/several days	Iron (III) saccharate	
Iron chloride	per os	3-4 times a day	Iron (II) chloride	
Iron hydroxide	i/m	individually	Iron (III) hydroxide	
polymaltose			polymaltose complex	
complex				
Ferroplex	per os	3 times a day	Iron (II) sulphate,	
			ascorbic acid	

II, **III** – the iron valency.

INN, (Trade name)	Medicinal form, dosage
Ascorbic acid (Vitamin C)	Sol. for inj. 5%; tabl. 0.1
Cyanocobalamine (Vitamin B ₁₂)	Sol for inj. 0.05; 0.1%
Jectofer (Ectofer)	Sol. for inj. 2ml
Iron saccharate (Ferum Lek)	Sol. for inj. 2%
Iron sulphate (Ferro-gradumet)	Tabl. 0.3
Iron fumarate (Ferronate)	Caps. 0.35
Iron chloride (Hemofer)	Sol. for inj.15.7%
Iron hydroxide polymaltose complex (Maltofer)	Sol. for inj. 5%; tabl. 0.1
Pirydoxine (Vitamin B_6)	Sol. for inj. 5%; tabl. 0.01
Riboflavin (Vitamin B ₂)	Tabl. 0.00001
Tocoferol acetate (Vitamin E)	Sol. for inj. 5%
Ferroplex	Tabl.
Folic acid	Tabl. 0.001
Human erythropoietin (Epomax)	Pwd. for inj. 1000; 5000 U

The list of medicines

Erythropoiesis inhibitors

The mechanism of action

Medicines suppress the erythrocytic part of the bone marrow.

Pharmacodynamics	$(effects) \rightarrow$	Indications		
Decrease of the erythrocytes amount	Erythremia			
in blood				
Side effects	\rightarrow Contr	raindications		
Anaemia Erythropenia, H		IV-infection		
The list of medicines				
INN, (Trade name)		Medicinal form, dosage		

Sodium phosphate solution labeled by phosphorus -32 Sol. for inj.

Glossary

 B_{12} -deficiency and folic acid deficiency anaemia is anaemia caused by the lack of vitamin B_{12} and folic acid and it leads to the disorder of the DNA synthesis and disorder of erythropoiesis. Hypoplastic anaemia is a progressive aregeneratory anaemia caused by the dysfunction of the red bone marrow. Hypochromic anaemia is a common name of anaemias characterized by the low colour index of blood. Iron deficiency anaemia is a wide-spread disease of blood characterized by the decreased amount of iron in the organism, in particular in the hemoglobin. Reticulocytes are young erythrocytes. Erythremia is an increased amount of immatured, inferior erythrocytes in blood because of their increased production by the red bone marrow. Erythropenia is the decreased amount of erythrocytes in blood. Erythropoiesis is the process of erythrocytes formation and maturation.

CORRECTORS OF LEUKOPOIESIS

Disorders of leukopoiesis are revealed both by deficient production of leukocytes and decrease of their amount in blood (leukopenia, agranulocytosis) and by an increased production of inferior leukocytes (leukosis, leukemia).

In the first case leukopoiesis stimulants and colony-stimulating factors that accelerate the formation of leukocytes in the bone marrow are used, in the second case leukopoiesis inhibitors are needed.

	Classification of medicines					
Leukopoies	sis stimulants including	Leukopoiesis inhibitors				
colony-stir	nulating factors (CSF)					
Lenograstim	Methyl-oxymethyluracil	Busulfan				
Molgramostim	Sodium nucleospermate	Mercaptopurine				
Ethyl-carboxyph	enyl-thiazolidine-acetate					

Classification of medicines

The mechanism of action

Leukopoiesis stimulants bind to specific receptors of myeloid cell-precursors of the neutrophilic group, which are necessary for the matured leukocytes formation. It leads to increase of the matured leukocytes synthesis.

Leukopoiesis inhibitors suppress the formation of leukocytes.

Pharmacodynamics (effects) \rightarrow Indications					
Leukopoiesis stimulants: the	Leukopenia including those caused by the				
increase of the matured leukocytes	therapy with antitumour medicines,				
amount in blood	radiation sickness, HIV-infection				
Leukopoiesis inhibitors: decrease of	Leukemias, lymphogranulomatosis				
the leukocytes amount in blood					
Side effects	\rightarrow Contraindications				
Leukopoiesis stimulants: dyspepsia	Diseases of the GIT				
Leukopoiesis inhibitors: inhibition	Leukopenia, anaemia, thrombocytopenia,				
of hemopoiesis, dysfunction of liver	diseases of liver and kidneys				
and kidneys					
Teratogenecity and embryotoxicity	Pregnancy, lactation				

The pharmacological "face" of leukopoiesis stimulants

Medicines	The peculiarities of	Other effects	Sources of obtaining
	the influence on		
	leukopoiesis		
Leno-	Regulates the	\uparrow the antibacterial	Recombinant human
grastim	production and	activity of leukocytes	granulocytic CSF
	maturation of		
	neutrophiles		
Molgra-	\uparrow the production of	Immune-stimulating	-//-
mostim	neutrophiles,	(increases the	
	monocytes,	phagocytosis)	
	eosinophiles,		
	macrophages		
Methyl-		↑ erythropoiesis, anti-	Synthetic
oxy-		inflammatory,	
methyl-		reparative, anabolic	
uracil			

Sodium	Increases	the	Stimulates	the	The	mixture	of
nucleo-	production	of	metabolic process	es	polyh	ydrates of	Na
spermate	neutrophiles,				salts	of DNA	and
	lymphocytes				RNA	derivatives	ob-
					tained	from	the
			sturgeor		on milts		

The list of medicines					
INN, (Trade name)	Medicinal form, dosage				
Leukopoiesis s	timulants				
Ethyl-carboxyphenyl-thiazolidine-acetate	Tabl. 0.002				
(Leukogen)					
Lenograstim	Lyoph. pwd. for inj. 33.6 mln U				
Methyl-oxymethyluracil (Pentoxyl)	Tabl. 0.2				
Molgramostim (Leukomax)	Lyoph. pwd. for inj. 0.000005				
Sodium nucleospermate (Polydan)	Sol. for inj. 1.5%				
Leukopoiesis inhibitors					
Bisulfan (Myelosan)	Tabl. 0.002				
Mercaptopurine	Tabl. 0.05				

Leukopenia is the decreased amount of leukocytes in blood. **Leukopoiesis** is the process of leukocytes formation and maturation. **Lymphogranulomatosis** is a malignant tumour of the lymphoid tissue.

XI. MEDICINES AFFECTING THE RESPIRATORY SYSTEM EXPECTORANTS AND ANTI-TUSSIVE MEDICINES. SURFACTANTS

Expectorants are medicines that dilute sputum and relieve its excretion. Expectorants are divided into medicines that stimulate expectoration (secretomotor) and bronchosecretolytic (mucolytics) ones.

Anti-tussive medicines are medicines that inhibit cough.

Surfactants are medicines, which are surface active substances, they make up the endogenous surfactant deficiency in a disorder of its formation.

Medicines stimulating	Mucolytics	Anti-tussive medicines	Sfootowta
expectoration			Surfactants
Reflex- and resorp-	Monocompo-	Central- (narcotic and	
tive*-acting ones	nent and com-	non-narcotic*),	
	bined*	peripheral**-acting ones	
Althaea* root	Ambroxol	Codeine phosphate	Colphosce-
Glycyrrhiza root	Acetylcysteine	Dimenoxadol	ryl palmitate
Mentoclar	Bromhexin	hydrochloride	Poractant
Plantain leaf	Althemix Glaucin hydrochl		alpha
Inula* root		Acetylaminonitropropoxy	
Bronchophyt		benzen**	

Classification of medicines

The mechanism of action

Medicines stimulating **expectoration** cause the reflectory (all medicines) and resorptive (Althemix, Inula root, Mentoclar, Althaea root) action on bronchi and bronchial glands. Their expectorant effect is connected with the irritation of receptors of the stomach mucous membrane, where nervous impulses transmit to bronchial glands and muscles and as a result the secretion of bronchial glands, the epithelial fibrillation, peristalsis of bronchioles increases. Sputum is diluted and its secretion is accelerated.

Mucolytics activate hydrolyzing enzymes, which decrease the sputum viscosity, and thus, relieve the secretion of sputum from the respiratory tract. Due to its sulphohydryl groups Acetylcysteine breaks disulphidic bonds of acidic glycosaminoglycans of sputum and it leads to the sputum viscosity decrease. Ambroxol, Bromhexin normalize the ratio of serous and mucous components of the bronchial secret; stimulate bronchial glands secretion and the ciliated epithelium activity and promote the removal of the mucous secret. Some mucolytics also stimulate the formation of a surfactant (Ambroxol, Bromhexin).

Anti-tussive medicines suppress the cough centre (Codeine phosphate, Dimenoxadol hydrochloride, Glaucin hydrochloride); block afferent receptors of the bronchi, trachea and lung tissue (Acetylaminonitropropoxybenzen) and, thus, inhibit cough.

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Ph		\rightarrow	In	dications			
Expectorant	(all	expectorants);	Inflan	nmatory	diseas	ses of the	respiratory
mucolytic (muc	colytics)		tract	(acute	and	chronic	tracheitis,
			bronc	hitis and	l pneur	nonia)	
Anti-tussive (all anti-tussive medicines)				lasting o	dry nor	n-productiv	ve cough
Surfactant-like (surfactants)			Respiratory distress-syndr		s-syndrome		
(surfact				ctants, E	ctants, Bromhexin, Ambroxol)		
Side effects \rightarrow C				Contra	indica	tions	
Dyspepsia, hypotension (expectorants, mucolytics,			cs, The	first ti	rimester of	pregnancy	
anti-tussive medicines)							
Pulmonary bleedings especially in newborns with			ith Pul	monary	y bleeding	8	
the marked sign	ns of the u	nripe lungs (surf	actants)			

Surfactants make up endogenous surfactant deficiency.

The <i>j</i>	pharmacolog	gical "f	face" oj	f expecto	orants a	nd mucol	lytics
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Medicines	Peculiarities	
Althaea root	Coating, AI effects	
Glycyrrhiza root	AI, antiulcer effects	
Mentoclar	AI effect. It contains a complex of volatile oils	
Plantain leaf	AI effect. It is also used in anorexia and hypoacidic states	
Inula root	AI, antiulcer effects	
Bronchophyt	AI, spasmolytic, bactericidal, general tonic, anti-tussive	
	effects. It contains BAS from 12 medicinal plants	
Bromhexin	A weak anti-tussive, surfactant-saving effects. It is a short-	
	acting medicine (It is inactivated quickly)	

Ambroxol	Anti-tussive, surfactant-saving effects. It is also used in the	
	RDS. It is similar to bromhexin by its structure	
Acetylcysteine	It is also used in the RDS. An antidote in poisoning by	
	paracetamol	
Althemix	AI, spasmolytic, antibacterial effects. Syrup: sodium	
	hydrocarbonate, ammonium chloride, sodium benzoate, Anis	
	oil, Althaea root extract	
Codeine	It has all the properties of OA (analgesic effect, etc.)	
Dimenoxadol	It has all the properties of OA (analgesic, cholinolytic effect,	
	etc.)	
Glaucin	Adrenolytic, hypotensive effects. It can be prescribed to	
	children	
Acetylaminonitropr	Disinfectant, local anesthetic effects. In otolaryngology it is	
opoxybenzen	used for preparating to instrumental examination	

AI – anti-inflammatory; RDS – respiratory distress-syndrome; OA – narcotic analgesics.

The list of medicines

INN, (Trade name)	Medicinal form, dosage
Ambroxol (Ambrobene, Lasolvan)	Syrup 0.6%; tabl. 0.03
Althaea root	Pwd., infusion, syrup
Althemix	Syrup 100 ml
Acetylaminonitropropoxybenzen (Falimint)	Dr. 0.025
Acetylcysteine (ACC)	Tabl. 0.1; sol. for inj. 10%
Bromhexin	Tabl. 0.008
Bronchophyt	Pack 100.0
Codeine phosphate	Pwd. 0.015
Colphosceryl palmitate (Exosurf)	Pwd. 0.108
Dimenoxadol hydrochloride (Estocine)	Tabl. 0.005
Glaucin hydrochloride (Glauvent, Tussidil)	Tabl. 0.05
Glycyrrhiza root	Pack 50.0; 100.0
Inula root	Pack 100.0
Mentoclar	Sol. 50 ml
Plantain leaf	Pack 50.0
Poractant alpha (Curosurf)	Susp. 8%

Glossary

Lung surfactant (the anti-atelectasis factor) spreads as a thin film in the inner surface of lungs, provides stability of the alveolar cells in the breathing process, protects them from negative factors, promotes the regulation of the rheological properties of the bronchopulmonary secret, improves its "glidence" along the epithelium and relieves the secretion of sputum. The **respiratory distress-syndrome** is the marked respiratory insufficiency (hypoxia), which is connected with the increase of the pulmonary capillaries permeability and with partial outcome into the pulmonary edema.

XII. MEDICINES AFFECTING THE METABOLIC PROCESSES

VITAMIN-CONTAINING MEDICINES

Vitamins are organic substances, which one needs to provide the organism's life activity. They are biologically active even in small quantities. More than 30 vitamins and vitamin-like substances are known. Some of them can be formed in the human body from the vitamin precursors (pro-vitamins) or can be synthesized by the intestinal microflora. Humans receive vitamins mainly with food products. Depending on the extent of the vitamin deficiency in an organism avitaminosis or hypovitaminosis may develop. Hypovitaminoses may be both absolute (the lack of vitamins in food, disorders in vitamin absorption, diseases of the gastrointestinal tract and liver) and relative (a daily need for vitamins increases during pregnancy, lactation, fever) ones.

Vitamin medicines are medicines, which are vitamins, their analogues or provitamins according to their chemical structure.

Classification of Vitamins				
Water-soluble vitamins				
Thiamine chlor	ride (B_1)	Folic acid (B _c)		
Riboflavin (B ₂)		Ascorbic acid (C)	
Pantothenic aci	d (B ₅)	Nicotinic acid ((PP)	
Pyridoxine hydrochloride (B_6)		Rutin (P)	Rutin (P)	
Cyanocobalamine (B_{12})		Pyridoxalphosp	Pyridoxalphosphate	
Pangamic acid (B ₁₅)		Lipoic acid	Lipoic acid	
Fat-soluble vitamins and their water-soluble analogues*			le analogues*	
Retinol (A) Tocoferol acetate (E)		tte (E)		
Ergocalciferol (D)		Menadion (K)*	Menadion (K)*	
Polyvitamin medicines				
Vitam	MultiTabs	Pregnavit	Tri-Vi Plus	
Vitrum	Oligovit	Revit	Undevit	
Hexavit	Pikovit	Taxofit	Unicap	

The mechanism of action

The vitamin-containing medicines compensate the vitamin deficiency in the organism and provide the co-enzymes functioning in the enzymatic systems and it stipulates their high activity.

Water-soluble vitamins		
Pharmacodynamics (effects) \rightarrow Indications		
Thiamine chloride (Vitamin B_1) (antineuritic)		
Cardiotrophic	Ischemic heart disease, HF, arrhythmias	
Neurotropic (regulates the activity of mediators and transmission of the nerve impulses)	Neuralgias, neuroses, beri-beri	
Hypoglycemic	Diabetes mellitus	

Riboflavin (Vitamin B ₂)		
Increase of the tissue resistance to	Acute hypoxia	
hypoxia		
Enhancement of the plasticity	Unhealed wounds, burns, hypotrophy,	
processes and energy formation	frostbites	
Normalization of vision	Conjunctivites, ceratites	
Enhancement of the erythropoietin	Anaemias, radiation sickness, leukemia	
Pantother	nic acid (Vitamin B ₅)	
Improvement of the nerve impulse conductivity	Neuritis	
Participation in the metabolism of	Diabetes mellitus, eczema, dermatites, trophic	
proteins, fats, carbohydrates in	ulcers, hepatites, atony of the intestine and	
oxidation-reduction processes	urinary bladder, hypotrophy	
Pyridoxine (Vitamin B ₆)		
Anabolic	Hypotrophy, rickets, tuberculosis	
Cardiotrophic	Myocardiodystrophy, ischemic heart disease	
Hepatoprotective	Hepatites, cholecystitis	
Detoxication	Toxicosis of pregnants, burns, radiation	
	sickness	
Hemopoietic	Anaemias	
Cyanocobalamine (Vitan	nin B ₁₂) (anti-anaemic, hemopoietic)	
Hemopoietic	Hyperchromic anaemia, radiation	
Anti-anaemic	sickness, leukemia	
Activation of the liver function	Fatty degeneration of the liver	
Activation of the nervous system	Diseases of the CNS and peripheral	
function	nervous system	
Regulation of carbohydrate and lipid	Dystrophy in children	
metabolism		
Pangamic acid (Vitamin B ₁₅) Improvement of linid metabolism		
Improvement of inpld metabolism	Allefoscierosis	
in muscles	ischemic heart disease	
Increase of the glycogen content in	Henatitis	
muscles and liver		
Antihypoxic	Нурохіа	

Folic acid (Vitamin B _c)		
Stimulation of hemopoiesis	Anaemia, radiation sickness, leukemia	
Improvement of trophism and	Tropical sprue	
regeneration of tissues		
Nicotinic acid (Vitamin PP) (antipellagric)		

Antipellagric	Pellagra
Hypolipidemic	Atherosclerosis
Reparative	Wounds that do not heal for a long time
Vasodilating	Angiospasms, endarteritis
Cardiotrophic	Ischemic heart disease
Ascorbic acid (Vitamin C) (antiscorbutic)	
Capillary-protecting, participates in	Prophylaxis and treatment of scorbutus,
blood coagulation	hemorrhagic diathesis, bleedings
Antioxidant	Atherosclerosis
Immune-stimulating	Acute and chronic infectious diseases
	(croupous pneumonia, tuberculosis)
Relief of iron absorption from the GIT	Hypochromic anaemia; states
	accompanied by the increased
	consumption of vitamin C (pregnancy,
	infectious diseases)
Rutin (Vitamin P)
Capillary-protecting	Hemorrhagic diathesis
Antioxidant, antihypoxic	Complex therapy of anaemias, IHD
Choleretic	Cholestasis
Lipoic acid	
Regulation of carbohydrate and lipid	Complex therapy of liver diseases
metabolism. Lipotropic, detoxication	(Botkin's disease, hepatic cirrhosis)
Antioxidant	IHD, atherosclerosis
Side effects	→ Contraindications
Dyspepsia	Peptic ulcer, exacerbation of gastritis
Hypervitaminosis	Hypervitaminosis

NB! Pyridoxalphosphate is derivative of pyridoxine with the similar pharmacodynamics and indications.

The list of medicines

INN, (Trade name)	Medicinal form, dosage
Ascorbic acid (Vitamin C)	Tabl.0.01; sol. for inj. 5%
Calcium pangamate (Vitamin B ₁₅)	Tabl. 0.05
Calcium pantothenate (Vitamin B ₅)	Tabl.0.01; sol. for inj.10%
Cyanocobalamine (Vitamin B_{12})	Tabl. 0.005; sol. for inj. 10%
Folic acid (Vitamin B _c)	Tabl. 0.015
Lipoic acid	Tabl. 0.025; sol. for inj. 0.5%
Nicotinic acid (Vitamin PP)	Tabl.0.05; sol. for inj. 1%
Pyridoxalphosphate	Sol. for inj. 0.5%
Pyridoxine hydrochloride (Vitamin B ₆)	Tabl. 0.05
Riboflavin (Vitamin B ₂)	Tabl.0.01; sol. for inj. 1%
Thiamine chloride (Vitamin B ₁ ; Thiamine bromide)	Sol. for inj. 6%; dr. 0.05
Vitamin P (Rutin)	Tabl. 0.02

Avitaminosis is a significant or total absence of a vitamin in the organism. **Beri-beri** is a disease caused by vitamin B_1 deficiency (polyneuritis). **Botkin's** disease is infectious hepatitis A. Hemorrhagic diathesis is a group of various diseases characterized by bleedings. Ischemia is decrease of the blood supply of an organ or a tissue. Cardiotonic effect is increase of the myocardial contractility without increase the cardiac rhythm and the oxygen consumption by the myocardium. **Cardiotrophic effect** is improvement of energy processes, trophism and metabolism in the myocardium that leads to its productivity increase. Keratitis is inflammation of the cornea. Croupous pneumonia is the acute pneumonia with rapid inflammation of the whole lung lobe and the pleura's adjacent part. Myocardial dystrophy is damage in the structure of the myocardial cells that is connected with disorder of biochemical processes in these cells. Pellagra is a disease connected with deficiency of nicotinic acid, riboflavin and tryptophan and it is characterized by disorders of the skin, GIT and mentality. Tropical sprue is an inflammatory disease of the intestine characterized by the weight loss, anaemia, polyhypovitaminosis. **Tuberculosis** is an infectious disease caused by mycobacteria. Cholestasis is congestion of bile caused by dysfunction of its outflow. Scorbutus is severe avitaminosis of vitamin C.

Pharmacodynamics (effects) \rightarrow Indications		
Retinol (Vitamin A) (antixerophthalmic)		
Regulation of the organism's growth	Complex therapy of rickets, hypotrophies,	
and development	growth disorders in children	
Normalization of vision	Eye diseases (pigmentary retinitis,	
	xerophthalmia)	
Reparative	Skin diseases (burns, wounds, eczema,	
	psoriasis, dermatitis, frostbites, etc.), liver	
	diseases, ulcerous colitis, gastritis, peptic	
	ulcer	
Increase of the organism's resistance	ARVI, chronic bronchopulmonary diseases	
and immunity		
Ergocalciferol (Vitamin D) (antirachitic)		
Participation in phosphorus and calcium	m Rickets, osteoporosis, consolidation of	
metabolism regulation	bones, hypocalcemia, spasmophilia	
Tocoferol (Vitamin E) (antisterile)		
Regulation of the reproductive organs	Menstrual cycle disorders, sterility,	
function	threatened abortion, dysfunction of	
	sexual glands in men and women	
Antioxidant, membrane-protective	Complex therapy of anaemia,	
	atherosclerosis, IHD, dermatitis, psoriasis	
Vitamin K	(antihemorrhagic)	
Hemostatic (increase of blood	Hemorrhagic diathesis, hemolytic disease	
coagulation)	of newborns, hepatitis, bleedings	

Fat-soluble vitamins

Side effects	\rightarrow Contraindications
Vita	min A
Teratogenicity	The first trimester of pregnancy
Vita	min D
Calcification of soft tissues, vascular	Heart diseases, hypercalcemia,
walls, heart valves	pulmonary tuberculosis, hepatic and renal
	diseases, peptic ulcer
Vita	min K
Increase of blood coagulation	Thromboembolism, the syndrome of
	hypercoagulation
Vitamins A, D, E, K	
Hypervitaminosis	Hypervitaminosis

The list of medicines

INN, (Trade name)	Medicinal form, dosage
Ergocalciferol (Vitamin D)	Dr. 500 IU; sol. for inj. 0.5%
Menadion (Vitamin K, Vicasol)	Tabl. 0.015; sol. for inj. 1%
Retinol (Vitamin A, Retinol acetate)	Dr. 0.00114 (3300 IU)
Tocoferol acetate (Vitamin E)	Dr. 0.15; sol. for inj. 5%

Glossary

Hemolytic disease of newborns is a congenital disease characterized by intensified lysis of erythrocytes (hemolysis), edemas and anaemia. Dermatitis is inflammation of the skin. Dyspepsia is dysfunction of digestion (nausea, vomiting, diarrhea). Bone consolidation is the process of accreation of the damaged bone. Xerophthalmia is dryness of the conjunctiva. Acute respiratory viral infections (ARVI) are the group of human acute infectious diseases with a primary damage of respiratory organs. Pigmentary retinitis is the inflammation of retina with progressive atrophy and pigmentary infiltration of its internal layers. Psoriasis and eczema are chronic skin diseases. Colitis is the inflammation of the large intestine.

Polyvitamin medicines

Abrupt changes of the organism's physiological state (physical or mental overload, change of climate, pregnancy, aging, etc.) and various pathological processes cause the increased needs in several vitamins. In these cases the states of polyhypovitaminosis can appear.

Polyvitamin medicines, as well as complex medicines containing vitamins, are used for stimulation of the organism's defensive reactions and correction of polyhypovitaminoses.

Pharmacodynamics

Polyvitamins assist renewal of the vital tone, increase the immunity, normalize the metabolism, protect the organism from unfavourable environmental affection.

Indications

Asthenic states, necessity of the organism's resistance increase to physical or mental loadings, unfavourable environmental factors. Vitrum, Multi-tabs, Picovit, Taxophyt multivitamins are used in pediatrics; elderly people are given Vitrum, Undevit, Hexavit; pregnant women are taken Pregnavit; Taxophyt, Vitrum, Picovit, Unicap M are used for treatment and prevention of rickets and caries; Tri-Vi-plus is administered for prophylaxis of cancer diseases; Taxophyt, Oligovit, Vitam are used for diseases of the cardiovascular system; Oligovit, Unicap M, Vitam are taken for treatment and prevention of anaemia; Vitrum is used for strengthening of nails and hair.

CORRECTORS OF TISSUE METABOLISM

The metabolism is a complex of biochemical processes that are the base of the vital activities of the organism.

Metabolism disorder in tissues is observed in somatic, endocrine, surgical, nervous and other diseases. It can be corrected with the help of many medicines: oxygen, dextrose, aminoacids, microelements, enzymes, anti-enzymes, biostimulants, plasma-substituting solutions, antioxidants, medicines of snake and bee poisons, hormones, vitamins, etc.

I. Medicines improving	II. Medicines improving	III. Biogenic
metabolism and energy	trophism and the tissue	stimulants
supply of tissues and	regeneration processes and	
decreasing hypoxia	causing cytoprotective* and	
Ovugan Davtraga	Actovacin Soloocorul	Aloo ovtroot
Uxygen Dexilose	Actovegin Solcoseryi	Albe extract
Inosine I rimethasidine	Cytochrome C*	Placenta suspension
Adenosine monophosphate	Rumalon **	Vitreous body
Cocarboxylase	Glucosamine **	Kalanchoe juice
IV. Medicines containing	V. Medicines for parenteral	VI. Antioxidants
snakes and bees poisons and	nutrition and aminoacids	
products of their vital		
activity		
Apilak	Methionine Cysteine	Erysod Emoxipine
Propolis	Glutaminic acid	Mexidol
Apisarthron	Cerebrolysine	Vitamins C, E, A, P
Vipraxine	Hydrolysine solution	
VII. Medicines containing	IX. Plasma-substituting	
micro- and macroelements	solutions	
Calcium chloride	Sodium chloride	
Potassium chloride	Reopolyglucine	
Calcium gluconate	Neohemodes	
Potassium iodide	Enterodes	
Sodium chloride		
Cerebrolecitin		

Classification of medicines
Medicines improving metabolism and energy supply of tissues and decreasing hypoxia

Oxygen

The mechanism of action is connected with its participation in oxidation-reduction processes providing the tissue breathing.

Pharmacody	vnamics (effects) \rightarrow	Indications
Antihypoxic	Hypoxia (but it is not use	ed in the tissue hypoxia)
Antihelminthic	Ascariasis	

Dextrose

The mechanism of action

It is the energy material that is necessary for biochemical processes, it is easily used by the organism's cells. It is absorbed and transported in tissues quickly, oxidized there with the energy formation, which is necessary for work of the skeletal muscles, the myocardium, the smooth muscles (especially the intestine) and the brain. Glucose hypertonic solutions increase the blood osmotic pressure that promote the liquid flow from the tissue into blood (the tissue dehydration); the volume of circulating blood increases and its viscosity decreases, that is why glucose decreases edema in tissues and increases the decreased BP. It increases the osmotic pressure because it is not reabsorbable in the renal tubules and that is why it decreases the water reabsorption and increases diuresis.

Pharmaco	dynamics (effects) \rightarrow Indications
The energy source	The medicines dilution, as the blood substitute
(Isotonic solution - 5%)	
Hypertensive	It is a component of the antishock liquid. Increase of
(Hypertonic solution –	the BP in collapse and shock
10-40%)	
Anti-edemic	Life threatening edemas (of lungs and brain)
Detoxication	Infectious diseases, hepatitis, intoxications
Hyperglycemic	Hypoglycemia (the insulin overdosage)

Adenosine monophosphate

The mechanism of action: it is in the composition of a number of co-enzymes that regulate oxidation-reduction processes. It takes part in the synthesis of nucleic acids and proteins. It decreases the myocardial conductivity.

Pharmacodynamics (effe	$ects) \rightarrow Indications$
Vasodilating, antihypoxic, anabolic, anti-	Obliterating endarteritis,
arrhythmic, anti-aggregant	thrombophlebitis, venous insufficiency,
	IHD, tachyarrhythmia

Inosine

The mechanism of action: it is a precursor of adenyl and guanyl nucleotides synthesis.

Pharmacodynamics (e	ffects) \rightarrow	Indic	ations	
Antihypoxic, anti-arrhythmic, anabolic	IHD,	cardiomyop	athies,	arrhythmias,
	cachexia	, hepatic	cirrhosis	, radiation-
	induced 2	leukopenia		

Trimethasidine

The mechanism of action: it supports the cellular metabolism in ischemia, corrects the ionic transport.

Pharmacodynamics (eff	$ects) \rightarrow$ Indications
Antihypoxic, antianginal, cytoprotective	IHD, giddiness and hearing disorder of
	the vascular genesis, Ménière's disease

Cocarboxylase

The mechanism of action: it takes part as a co-enzyme in oxidation-reduction carboxylation and decarboxylation of ketoacids.

Pharmacodynamics (ef	fects) \rightarrow	Indications
Cardiotrophic effect	IHD	

Medicines improving trophism and the tissue regeneration processes and causing cytoprotective and chondroprotective effects

Actovegin and solcoseryl

The mechanism of action: they improve oxidative phosphorylation, oxygen and glucose utilization, promote the accumulation of macroergic phosphates.

Pharmacodynamics (effects) \rightarrow	Indications
Regeneration stimulation and improvement of	Dysfunction of the cerebral and
the tissue trophism. Solcoseryl has also the	peripheral blood circulation,
membrane-stabilizing and cytoprotective effect	trophic ulcers

Actovegin is a deproteinased derivative from the calf blood. Solcoseryl is an extract of the cattle blood.

Cytochrome C

The mechanism of action: it is a classic cytoprotector and it stimulates oxidation-reduction reactions.

Pharmacodyna	umics (effects) \rightarrow Indication	rs
Cytoprotective, antihypoxic	IHD, hypoxia, dysfunction of	the cerebral and
	peripheral blood circulati insufficiency	on, respiratory

Rumalon

The mechanism of action: it slows down the osteoarthrosis development as it stimulates the synthesis of glycosaminoglycans and collagen of cartilage.

Pharmacodynamics (efj	fects) —	→	Indications
Chondroprotective	Diseases of	joints:	osteoarthrosis, etc.

Glucosamine

The mechanism of action: it compensates the deficiency of endogenous glucosamine that is necessary for biosynthesis of proteoglycans and the hyaluronic acid.

Pharmacodynamics ((effects) \rightarrow	Indi	cations		
Chondroprotective	Osteoarthrosis	, osteo	chondrosis		
Cardioprotective	Prevention of medicines	f the	cardiotoxic	effect	of
Gastroprotective	Peptic ulcer				

Biogenic stimulants

The mechanism of action. For the first time the name of "biogenic stimulants" was proposed by academician V.P. Filatov for substances of animal (placenta suspension, vitreous body) and plant (Aloe ectract, Kalanchoe juice) origin that are able to stimulate metabolic processes and immunity, as well as to accelerate the regeneration processes.

Pharmacodynamics (effect	ts) \rightarrow Indications
Anti-inflammatory, reparative (accelerate	Gastro-intestinal, eye diseases, wounds
the tissue regeneration)	

Medicines containing snakes and bees poisons and products of their vital activity

The mechanism of action of bee and snake poisons is not clear enough. It can be explained by the properties of the substances they contain: histamine, hyaluronidase and phospholipase enzymes, choline, tryptophan, microelements, organic acids and others. Bee poison has the reflex action because of the irritation of the skin and subcutaneous tissue receptors.

Pharmacodyna	mics (effects) \rightarrow Indications
The influence on the vascular	Apisarthron (bee poison medicine) is an ointment
permeability, microcirculation,	that is used in rheumatism, myalgia, sciatica and
the BP, the rate of the blood	sport traumas. Apilak (a dry substance of the bee
flow. Locally irritative (except	"milk") is used for treatment of hypotrophism and
Apilak), anti-inflammatory	anorexia in babies and infants. Propolis (a bee
effect	glue) is used for treatment wounds, burns
	(ointment), mouth and throat inflammatory
	diseases (an alcoholic solution). Vipraxine (a
	water solution of the adder poison) is used locally
	as analgesic and anti-inflammatory medicine in
	neuralgia, arthralgia, myalgia, myositis

Nowadays there are a lot of medicines produced on the base of propolis: **propolis** tincture, "**Propolin**" tablets, "**Propoceum**" ointment, "**Proposol**" aerosol, "**Prostopin**" suppositories, etc.

Medicines for parenteral nutrition and aminoacids

Organic acids that contain aminogroup are found in all cells of the organism both in a free state and in the composition of protein. Aminoacids are an important source of nitrogen in the organism.

Pharmacodynamics (effects)	→ Indications	
Methionine is an essential aminoacid that is	Lipid dystrophy with the	
necessary for supporting the body growth and	insufficient amount of methionine	
nitric balance in the organism	or toxic damage of the liver	
Glutaminic acid promotes the ammonium	Psychoses, mental deficiency,	
dehydration	encephalitis	
Cystein is a replaceable acid that is	Cataract (because the cysteine	
synthesized with the help of methionine	content is disordered)	
Cerebrolysine is a complex of neuropeptides	Brain traumas, ischemic stroke,	
from the swine brain. It has the neuroprotector	children mental deficiency, senile	
properties, decreases the neurotoxic effect of	dementia	
the stimulatory aminoacids (glutamate)		
Hydrolysine solution. It is obtained in the	It is a medicine for parenteral	
acid hydrolysis of the cattle blood proteins	nutrition in protein defficiency	
when adding glucose, it has a detoxication		
property and it is a source of proteins		

Antioxidants

The mechanism of action: antioxidants neutralize toxic free radicals, stimulate endogenous enzymes-antioxidants and thus, inhibit free-radical oxidation (FRO) processes. According to the mechanism of action they are divided into direct-acting antioxidants (direct interaction with free radicals, FRO inhibition) and indirect-acting antioxidants (increasing the activity of the endogenous antioxidant system).

Pharmacodynamics (effects)	\rightarrow Indications
Antioxidant is a general pharmacological	Therapy of a great number of FRO-
effect for all the medicines	induced diseases
Erysod, Cu-Zn-superoxide dismutase, has	It is used in gastroenterology,
the anti-inflammatory, anti-ulcer, hepato-,	rheumatology, dermatology
cardioprotective and other effects	
Emoxipine, is a derivative of 3-	It is used in ophthalmology,
oxypyridine, has the antihypoxic, anti-	cardiology, neurology
aggregant, stress-protective effects,	
improves microcirculation	
Mexidol (emoxipine and succinic acid salt)	Encephalopathy, acute cerebral blood
has the more marked antihypoxic and	circulation disorders
stress-protective effect, up to the	
tranquilizing effect, than emoxipine does	

Vitamins E, C, A, P; selenium, etc. are also widely used as antioxidants in medical practice.

Medicines containing micro- and macroelements

There are approximately 80 elements of D.I. Mendeleev's periodic system in human tissues. They are components of enzymes, hormones, vitamins; they are necessary for the synthesis of nucleic acids. Their mechanism of action is stipulated by substitution of their deficiency; pharmacodynamics and indications are related to the physiological role in the organism.

Pharmacodynamics (effects) \rightarrow Indications	
Cerebrolecitin is esters of glycerin,	Poor bone fracture healing, rickets,	
phosphoric and fatty acids (it is obtained	diseases of the nervous system, anaemia,	
from the cattle's brain tissue)	glaucoma	
Medicines containing iodine (iodides)	Endemic goiter, hyperthyroidism.	
are necessary for the normal functioning	Operation field preparation in surgery	
of the organism, the synthesis of	and obstetrics, for washing of wounds.	
thyroxin (the thyroid hormone) that	Skin diseases, inflammatory diseases of	
stimulates metabolism. The molecular	the respiratory tract (as expectorants).	
iodine has the antimicrobial effect; it	Syphilis, atherosclerosis. 5% iodine	
has the "resolving" effect in	alcoholic solution, complex iodine	
atherosclerosis and syphilis; the	solution are used. Potassium iodide is an	
expectorant effect	effective mucolytic	
Medicines containing sodium (the	Sodium chloride isotonic solution	
main intracellular cation) provide the	(0.9%) is a blood substituent.	
constancy of the osmotic pressure, ionic	Hypertonic solution is used for	
balance of the organism's internal	treatment wounds, ulcers, abscesses (it	
medium, acid-alkaline balance	promotes pus removal, causes	
	antimicrobial effect). Sodium	
	hydrocarbonate is an antacid	
Medicines containing potassium (the	Hypokalemia, arrhythmia, overdosage of	
main intracellular cation) participate in	cardiac glycosides, as a diuretic	
the transmission of the nerve impulses,		
increase diuresis moderately		
Medicines containing calcium provide	Hypocalcemia, osteoporosis, bone	
the endurance of the skeleton and teeth,	fractures; allergic and inflammatory	
take part in regulation of the cellular	diseases; for increase of blood	
membrane penetration for sodium and	d coagulation, the medicines are the	
potassium (thicken the membranes),), components of blood substituents. Of	
stimulate the heart work (potassium	these medicines calcium chloride (it is	
antagonists), participate in blood	introduced intravenously only) and	
coagulation	calcium gluconate are used	

Plasma-substituting and detoxication solutions

Hydrodynamic disorders in the organism appear when there are intensive bleedings and water-salt balance disorders. For their correction plasma-substituting solutions are used. The intoxication of an organism appears in alcoholism, burns, infectious and tumour diseases, toxicosis in the pregnant women. In these cases detoxication therapy is used.

The mechanism of action

By the mechanism of their action these medicines are divided into: a) hemodynamic ones (replenish the blood volume and normalize the blood circulation), b) detoxication ones (bind toxins quickly and eliminate them from the organism), c) regulators of water-salt and acid-alkaline balance.

Pharmacodynamics (effects) \rightarrow Indications
Regeneration of the normal blood	Treatment and prevention of shock, acute
circulation, decrease of intoxication	blood circulation disorders, acute blood
	loss, states accompanied by intoxication

Reopolyglucine is 10% solution of a low-molecular dextran in the sodium chloride isotonic solution.

Neohemodes is 6 % solution of a polyvinylpyrrolidone low-molecular polymer containing also sodium, potassium, calcium, chloride ions.

Enterodes is a solution of a polyvinylpyrrolidone low-molecular polymer.

Side effects and contraindications for tissue metabolism correctors

Side effects \rightarrow	Contraindications
Glutaminic acid - vomiting, diarrhea,	Fever, diseases of the liver, kidneys,
fissures on lips, excitation. With a	GIT, blood-forming organs; the
prolonged application the decrease of the	increased excitability of the CNS
hemoglobin content and leukopenia can be	
observed	
Inosine - itch, redness of the skin, with a	Gout
prolonged application – exacerbation of	
gout	
Adenosine monophosphate - headache,	Acute myocardium infarction
tachycardia, diuresis increase; in	
intravenous administration – nausea,	
redness of the face	
Liquid Aloe extract injections are painful.	Liquid Aloe extract for injections –
A feeling of burning can appear while	severe diseases of the cardiovascular
irrigating the wound with Kalanchoe juice	system and kidneys, pregnancy
Trimethasidine - nausea, pain in the	Trimethasidine – pregnancy,
epigastrium, skin itch	lactation
Solcoseryl in the form of gel can cause	Individual intolerance
burning of the skin	
Actovegin - lacrimation (while using eye	It is undesirable to use this medicine
gel)	in the period of lactation
Cytochrome C shivering with the increase	Individual intolerance
of the body temperature (with a rapid	
introduction)	

Medicines that contain poisons of bees and	Diseases of the kidneys, liver, blood	
snakes and products of their life activity	and pancreas; tumours, severe	
can cause allergic reactions. Apilak -	infectious diseases, brain and	
disorder of sleep. The feeling of a foreign	coronary blood circulation	
matter in the eye is possible when using eye	insufficiency, cardiac malformations,	
films with apilak	sepsis, cachexia, diabetes mellitus,	
-	pregnancy. Apilak – Addison's	
	disease. Propolis – eczema	
With a rapid i/v administration of	Pregnancy and severe renal	
cerebrolysine the increase of the body	dysfunction, the epileptic status	
temperature is possible		
Medicines for parenteral nutrition –	Neohemodes – bronchial asthma,	
nausea, vomiting, tachycardia, respiratory	acute nephritis, cerebral hemorrhage	
disorder (with a rapid administration of		
medicines)		
When introducing emoxipine into the eye –	Pregnancy	
pain, burning, itching, redness; in systemic		
administration – drowsiness, hypertension		
occur		
Mexidol causes nausea, dry mouth,	Marked hepatic and renal	
drowsiness	dysfunctions, allergy to pyridoxin	
	(chemical similarity to pyridoxin)	
Salt solutions – acidosis, hyperhydration,	Salt solutions – thrombocytopenia,	
increased elimination of potassium from the	insufficiency of the blood circulation	
organism	and renal failure. Sodium chloride	
	isotonic solution – hypersodemia, the	
	threat of brain and pulmonary edema;	
	treatment with high doses of	
	corticosteroids. Sodium chloride	
	hypertonic solutions should not be	
	administered subcutaneously and	
Madiainag containing notoggium nousee	The complete heart block repair	
vomiting diarrhea With a rapid i/w	dysfunction	
administration of notassium chloride	dystunction	
solution the inhibition of the heart functions		
can appear		
Medicines containing calcium when	Predisposition to thromboses, severe	
administered intravenously a feeling of	atherosclerosis, hypercalcemia.	
fever appears. With a rapid intravenous	therapy with cardiac glycosides.	
administration – bradycardia, ventricular	Calcium chloride solution should	
fibrillation, nausea appear	not be administered subcutaneously	
	and intramuscularly (the tissue	
	necrosis)	

INN, (Trade name)	Medicinal form, dosage
Actovegin	Ointment 5%, sol. for inj. 10%
Adenosine monophosphate (Adenocor)	Sol. for inj. 3%
Aloe (liquid Aloe extract)	Syrup; sol. for inj., lin.
Apisarthron	Ointment
Apilak	Ointment 3%, tabl. 0.01
Calcium gluconate	Tabl. 0.5, sol. for inj. 10 %
Calcium chloride	Sol. for inj. 5%
Cerebrolecitin	Tabl. 0.05
Cerebrolysine	Sol. for inj. 0.04 g/ml
Cocarboxylase (Berolase)	Pwd. for inj. 0.05
Cysteine	Pwd. 10.0
Dextrose (Glucose, Glucosteril)	Sol. for inj. 5%; 40%; tabl. 0.5
Emoxipine	Sol. for inj. 1%
Enterodes	Pwd. per os 5.0, pack
Erysod	Lyoph. pwd. for inj. 4 mln U
Glucosamine (Dona)	Pwd. 1.5
Glutaminic acid	Tabl. 0.5
Hydrolysine solution	Sol. for inj. 450 ml
Inosine (Riboxine)	Sol. for inj. 0.02 g/ml; tabl. 0.5
Kalanchoe juice	Alcoholic sol., vial
Mexidol	Sol. for inj. 5%, tabl. 0.125
Methionine	Tabl. 0.05
Neohemodes	Sol. for inj.
Oxygen	Inhal. sol., balloon
Placenta suspension for injections	Sol. for inj.
Potassium chloride	Tabl. 0.5, sol. for inj. 10 %
Potassium iodide	Tabl. 0.5
Propolis	Tinct. 25 ml, vial
Reopolyglucine	Sol. for infusion
Rumalon	Sol. for inj.
Sodium chloride (Saline solution)	Sol. for inj. 0.9%
Solcoseryl	Ointment 5%, sol. for inj. 10%, tabl. 0.2
Trimethasidine (Preductal)	Tabl. 0.02
Vipraxine	Sol. for inj. 1 ml
Vitreous body	Sol. for inj.

The list of medicines

Glossary

Osteoarthrosis is degeneration of a joint cartilage. **Osteochondrosis** is a disease that is characterized by a dystrophy in the bone and cartilage tissue. **Ventricular fibrillation** is the heart arrhythmia with the complete asynchronization of contraction of ventricular myofibrils. **Chondroprotective effect** is a recovery and protection of the integrity and structure of a joint cartilage.

XIII. HORMONAL AND ANTIHORMONAL MEDICINES

Hormonal medicines are medicines that are natural hormones or their synthetic analogues.

Antihormonal medicines are medicines that inhibit the production of the certain hormones or have the effects opposite to them.

MEDICINES WITH THE ACTIVITY OF THE HYPOTHALAMUS AND HYPOPHYSIS HORMONES AND THEIR ANTAGONISTS

The hypophysis (pituitary gland) and the hypothalamus form "neuroendocrine transmission system" for the signals that come from the nervous and endocrine system to different organs and tissues. For this purpose the anterior lobe of the hypophysis produces "tropic" hormones: adrenocorticotropic hormone (ACTH), thyrotropic hormone (TTH), somatotropic hormone (STH), follicle-stimulating hormone (FSH), luteinising hormone (LH) and lactotropic hormone (LTH), their synthesis is under control of the hypothalamus releasing factors. The middle lobe of the hypophysis secretes melanocyte-stimulating hormone (MCSH) and the posterior lobe produces oxytocin and vasopressin (antidiuretic hormone - ADH).

Medicines of the	Medicines of the hypophysis hormones		Antihormonal
hypothalamus	Anterior, middle* and posterior** lobe		medicines
hormones			
Prothyrelin	Corticotropin	Somatotropin	Danazol
Gonadorelin	Thyrotropin	Lactin	Bromocryptin
	Chorionic gonadotropin		
	Menopausal gonadotropin		
	Intermedin*	Oxytocin**	

Classification of medicines

The mechanism of action

Hormonal medicines of the hypothalamus and the hypophysis bind to receptors of target cells, affect the synthesis of RNA and proteins directly (activate the corresponding proteinkinases, etc.). Antihormonal medicines inhibit the secretion of the corresponding hormones of the hypophysis.

Medicines of the hypothalamus hormones

Medicines of the hypothalamus hormones have the releasing factors (liberins) activity and stimulate the secretion of tropic hormones of the anterior lobe.

Pharmacodynamics (effects) \rightarrow Indications		
Prothyrelin stimulates the secretion of	Diagnosis of the thyroid gland	
TTH, LTH	insufficiency in patients with	
	hypothyroidism, hypogalactia	
Gonadorelin stimulates the secretion of	Substitution therapy in deficiency of	
LH, FSH (promotes the maturing of	endogenic LH, in retardation of male	
follicles and ovulation, increases	and female puberty, ovarian	
spermatogenesis)	dysfunction	

Side effects \rightarrow	Contraindications
Prothyrelin increases the muscular tone	Diseases of the CNS, epilepsy,
and blood pressuse, decreases vision	ischemic heart disease, hypertension,
	pregnancy
Gonadorelin causes dyspepsia, painful	Diseases of the GIT, uterine bleedings
menstruations	

Medicines of the hypophysis anterior lobe		
Pharmacodynamics (effects) \rightarrow Indications		
Corticotropin (ACTH) stimulates the	The secondary hypofunction of the	
synthesis of glucocorticoids and partially	adrenal cortex, prevention of the	
androgens; has the anti-inflammatory,	adrenal glands deficiency after	
anti-allergic, immunosuppressive effects	glucocorticoids usage	
Somatotropin (STH) increases the	Hypophysal nanism	
skeleton growth, the body weight, has the		
anabolic effect		
Menopausal gonadotropin (FSH+LH)	Male and female sterility	
promotes the development of ovaries and		
maturing follicles there, increases		
spermatogenesis		
Chorionic gonadotropin (LH) causes the	Sexual infantilism, hypogonadism	
follicle's coming to the yellow body;	caused by hypothalamus and	
stimulates the progesterone production in	hypophysis dysfunction,	
women, activates the function of testes	cryptorchidism, the menstruation cycle	
and the testosterone synthesis in men	dysfunction, spontaneous abortion	
Lactin increases the lactation in the	Hypogalactia	
postnatal period; promotes deposition of		
fat in the body		
Side effects —	Contraindications	
Somatotropin, chorionic gonadotropin,	Oncologic diseases	
corticotropin stimulate the development		
of metostases		
Corticotropin causes hyperglycemia,	Diabetes mellitus, severe hypertension,	
edemas, blood pressure increase,	peptic and duodenal ulcer,	
ulceration of the GIT	osteoporosis, pregnancy	
Somatotropin causes hyperglycemia	Diabetes mellitus	

NB! Gonadotropins are used under the strict medical control because of the possible acute increase of the ovaries size and the increased secretion of estrogens.

Medicine of the hypophysis middle lobe

Intermedin is a medicine with the activity of the melanocyte-stimulating hormone.

Pharmacodynamics (effects) \rightarrow Ind	ications
Stimulation of the eye's retinal cones and rods, increase of	Degenerative changes
the acuity of vision, improvement of the eye's adaptation	of the eye's retina,
to darkness	pigmentary retinitis

Pharmacodynamics (eff	$ects) \rightarrow$ Indications
Stimulation of uterine contractions and	Labour induction, hypotonic uterine
development of mammary glands; in	bleedings after labour
high doses – spastic uterine contractions	
Side effects	\rightarrow Contraindications
Hypertone of the uterus, preterm	Increase of the uterine tone, anatomically
placental detachment	narrow pelvis, anomalous position of the
	fetus, uterine scar

Medicine of the hypophysis posterior lobe (oxytocin)

Hypophysal hormones secretion inhibitors

Pharmacodynamics (effects) \rightarrow Indications			
Danazol inhibits secretion of the	Endometriosis, benign mammary gland		
hypophysal gonadotropins (FSH and	tumours, gynecomastia		
LH), causes atrophy of the endometrium			
Bromocryptin inhibits the secretion of	Menstrual cycle disorders accompanied		
the hypophysal STH and LTH	by hyperprolactinemia and acromegalia		
Side effects	\rightarrow Contraindications		
Danazol – alopecia, dysmenorrhea,	Tumours of the reproductive system,		
edema, increase of the ICP	epilepsy		
Bromocryptin – orthostatic	Hypotension		
hypotension			

The list of medicines

INN, (Trade name)	Medicinal form, dosage
Bromocryptin	Tabl. 0.025
Chorionic gonadotropin (Pregnyl)	Pwd. for inj.1000 IU
Corticotropin	Pwd. for inj. 40 IU
Danazol (Danol)	Caps. 0.1
Gonadorelin	Pwd. for inj. 0.00073
Intermedin	Pwd. for inj. 0.05
Lactin	Pwd. for inj. 100 U
Menopausal gonadotropin	Pwd. for inj.75 U
Oxytocin	Sol. for inj. 5 U/ml
Prothyrelin	Pwd. for inj. 0.005
Somatotropin	Pwd. for inj. 4 IU
Thyrotropin	Pwd. for inj.

Glossary

Acromegalia is increase of extremities and features of the face connected with hypersecretion of STH after a human stops growing. Alopecia is a constant or temporary loss of hair. Gynecomastia is increase of mammary glands in males. Hypogalactia is a decreased secretion of mammary glands during the period of lactation. Hypogonadism is a decreased secretion of gonads with a weak development of genitals and secondary sexual features. Hypothyroidism is insufficient production of thyroid hormones. **Hypophysal nanism (dwarfism)** is a syndrome characterized by small stature in comparison to the sexual and age norm. **Hirsutism** is an excessive pilosis of female by male type. **Gonadotropins** are protein and peptide hormones (FSH, LH) that affect the function of female and male gonads. **Infantilism** is either mental and/or physical retardation. **Cryptorchidism** is the lack of either one or both of testicles in the scrotum, because they do not descent from the abdominal cavity. **Ovulation** is ovum's leaving from a follicle.

INSULIN-CONTAINING MEDICINES AND SYNTHETIC HYPOGLYCEMIC MEDICINES

Insulins

The endocrine part of the pancreas contains about 2 million of Langerhans islets consisting of alpha- and beta-cells that secrete glucagon and insulin, respectively.

Insulin and glucagon influence on the metabolism of carbohydrates: insulin has the hypoglycemic activity; glucagon (insulin antagonist) has the hyperglycemic activity. The physiological activity of these two hormones is directed to more complete utilization of glucose by tissues. Glucose is the most powerful and specific stimulant of the synthesis and secretion of insulin.

Absolute or relative insulin deficiency, as a result of the hypofunction of betacells of Langerhans islets, causes **diabetes mellitus** – an endocrine and metabolic disease characterized by disorders of all kinds of metabolism processes, especially it refers to disorders of the carbohydrate metabolic that leads to progressive increase of the glucose level in blood (hyperglycemia) and its excretion by the urine (glucosuria). Diabetes mellitus also develops when insulin is produced in sufficient amount but it is rapidly inactivated by insulinase. There are two types of diabetes mellitus: type I (insulin-dependent) and type II (insulin-independent).

Comatose states such as hyperketonemic coma (diabetic or hyperglycemic) and hypoglycemic coma belong to acute complications of diabetes mellitus.

Clussification of meanetics					
Human insulins and their analogues*					
Short-acting Medium-acting Long-acting					
Insulin lispro*	Human insuli	n	Human insulin		
Human insulin			Insulin glargin		
Insulin aspart*					
Insulins of animal origin					
Short-, medium- and long-acting ones					
Porcine insulin					
Combination of short- and medium-acting insulins					
Human ones Animal ones					
Human insulin Porcine insulin					

Classification of medicines

The mechanism of action

Insulin interacts with insulin receptors of cell membrane (liver, muscles, adipose tissue) forming the "insulin + receptor" complex that penetrates inside the

cell, where release of insulin takes place. Insulin regulates the protein and carbohydrate metabolism, lipid metabolism (increase of lipogenesis, decrease of lipolysis), affects the water-electrolyte exchange (reduces the loss of liquid by the organism).

Pharmacodynamics (eff	$ects) \rightarrow$ Indications
Hypoglycemic effect (decrease of	Diabetes mellitus type I, hyperglycemic
glycolysis, gluconeogenesis, increase of	coma
glycogenesis from glucose in the liver,	
muscles)	
Anabolic effect (increase of protein	Cachexia
synthesis)	
Side effects	\rightarrow Contraindications
Hypoglycemic state (feeling of hunger,	Hypoglycemia, acute hepatitis, hepatic
sweating, weakness, dizziness,	cirrhosis, hemolytic jundance,
tachycardia)	pancreatitis, cardiac malformations

The pharmacological "face" of insulins

Modicinos Origin Action				
wieurchies	Origin	Action		
		start	duration, h	
	Ultra-sh	ort-acting		
Insulin lispro	Analogue of	5-15 min	3-4	
-	human insulin			
Insulin aspart	Analogue of	10-30 min	3-5	
-	human insulin			
Short-acting				
Human insulin	Human	30 min	9	
Medium- acting				
Porcine insulin	Animal	30-60 min 8-20		
Long-acting				
Insulin glargin	Analogue of	3-4 h	24-28	
	human insulin			

The list of medicines

INN, (Trade name)	Medicinal form, dosage
Human insulin (Humulin)	Susp. for inj. 100 U/ml
Insulin lispro (Humalog)	Sol. for inj. 100 U/ml
Insulin aspart (Novorapid)	Sol. for inj. 100 U/ml
Insulin glargin (Lantus)	Sol. for inj. 100 U/ml
Porcine insulin (Pharmasulin, Monodar)	Susp. for inj. 100 U/ml

Glossary

Glycolysis is decomposition of glycogen in the liver to glucose-6-phosphate and glucose. **Gluconeogenesis** is the glucose synthesis from non-carbohydrate substances (aminoacids). **Cachexia** is the extreme degree of the organism's exhaustion and emaciation accompanied by the acute asthenia and apathy.

Peroral hypoglycemic medicines

Derivatives of				
	sulphonylurea		biguanides	thiazolidinones
1 st generation	2 nd generation	3 rd generation	Metformine	Rosiglytazone
Tolbutamide	Glybenclamide	Glymepiride	Buformine	Pyoglytazone
Carbutamide	Glyquidone			
	Glypiside			
Medicines of different groups (meglytinides, α - glycosidase inhibitors*)				
Acarbose* Repaglynide				

Classification of medicines

The mechanism of action

Sulphonylurea derivatives and meglytinides stimulate secretion of endogenous insulin by β -cells of the pancreas. Biguanide derivatives increase binding of insulin to the insulin receptors, inhibit intestinal absorption of glucose and gluconeogenesis in the liver, decrease the level of glucagon in blood. Thiazolidinones eliminate peripheral insulin resistance. α -Glycosidase inhibitors block α -glycosidase of the GIT, disturb polysaccharides breakdown to monosaccharides and their absorption.

Pharmacodynamics (effects) \rightarrow Indications			
Hypoglycemic	Diabetes mellitus type II. Diabetes		
Hypocholesterolemic	mellitus type I in patients taking insulin		
Anorectic	and suffering from obesity		
Side effects	\rightarrow Contraindications		
Hypoglycemia, meteorism, diarrhea,	Hypoglycemic coma, precomatose states,		
increase of body weight, lactacidosis	diabetes mellitus type I in children,		
	marked hepatic and renal dysfunctions,		
	pregnancy, lactation		

Medicines	Generation Hypoglycemic		$T_{1/2}, h$	Actio	on, h
		effect		start	duration
Tolbutamide	Ι	1	5-6	1	10-12
Carbutamide	— «-	++	36	5	12
Buformine	— «-		3-7	2-3	8
Metformine	— «-	++	6-17	2	16
Glybenclamide	II	150-200	4-11	1,5-2	18
Glyquidone	— «-	+++	1,5	1-2	8-12
Glymepiride	— «-	200-250	5-8	2-3	24
Glypiside	— «-		2-5	30 min	>24
Pyoglytazone	III		3-7	2-3	24
Repaglynide	— «-		1	1,5-2	12
Rosiglytazone	— «-		3-4	30-40 min	10-12

The pharmacological "face" of peroral hypoglycemic agents

INN, (Trade name)	Medicinal form, dosage		
Acarbose (Glucobay)	Tabl. 0.05		
Buformine (Glybutide)	Tabl. 0.05		
Carbutamide (Bucarban)	Tabl. 0.5		
Glybenclamide (Maninyl)	Tabl. 0.005		
Glyquidone (Glurenorm)	Tabl. 0.03		
Glymepiride (Amaril)	Tabl. 0.003		
Glypiside (Minidiab)	Tabl. 0.005		
Metformine (Glucophag)	Tabl. 0.5		
Pyoglytazone (Pyonorm)	Tabl. 0.03		
Repaglynide (NovoNorm)	Tabl. 0.0005		
Rosiglytazone (Avandia)	Tabl. 0.008		
Tolbutamide (Butamide)	Tabl. 0.05		

The list of medicines

Glossary

Hypoglycemic coma is a coma caused by abrupt decrease of glucose level in blood (for example, after insulin overdosage). **Diabetic (hyperglycemic) coma** is a coma caused by an acute deficiency of insulin in diabetes mellitus.

THYROID HORMONES MEDICINES AND ANTITHYROID AGENTS

Thyroid hormones (thyroxine, tri-iodthyronine) stimulate the growth processes, intensify the activity of the sympathetic nervous system. Thyrocalcitonin and parathyroid hormone regulate the calcium metabolism. Dysfunction of the thyroid gland can occur by either hypothyroidism or hyperthyroidism. Hypothyroidism (mixedema, cretinism, endemic goiter) can be caused by dysfunction of hypothalamic and hypophysal system or by direct dysfunctions of the thyroid gland. Hyperthyroidism occurs when the increased secretion of thyroid hormones takes place.

Thyroid ones (thyroid hormones medicines)		Antithyroid ones (thyreostatics)
Mono-component	Combined	
Thyroidine	Thyrocomb	Thiamazole
Levothyroxine sodium	Thyrotom	Propylthiouracil
Lyothyronine	Novothyral	

Classification of medicines

Thyroid medicines

The intake of thyroid medicines is one of the basic methods of hypothyroidism treatment.

The mechanism of action

The substitutive effect of thyroid medicines is stipulated by the presence of thyroxine and tri-iodthyronine in their composition. These hormones bind to receptors

of target cells and, as a result, they increase the synthesis of RNA and proteins changing the function of cells, tissues, organs and systems.

Pharmacodynamics (effects) \rightarrow Indications			
Increase of the basal metabolism,	Primary hypothyroidism, mixedema,		
growth and tissue differentiation, energy	cretinism, endemic goiter. Cancer of the		
processes, tissue need in oxygen.	thyroid gland, hypothyroid obesity.		
Anabolic, catabolic (in high doses)	Prophylaxis of goiter's recurrence after		
effects	the thyroid resection		
Side effects	\rightarrow Contraindications		
Stimulation of the CNS, perspiration,	Thyrotoxicosis, cachexia, tachycardia,		
tremor, the loss of weight, heartaches,	ischemic heart disease		
tachycardia			

The pharmacological "face" of thyroid medicines

Medicines	Efficiency	Composition/peculiarities	
Thyroidine	+	Thyroxine + tri-iodthyronine	
Levothyroxine sodium	+	Synthetic left-rotating isomer of	
-		thyroxine, has an effect in 7-12	
		days	
Lyothyronine	++	Effect develops in 6-8 h	
Thyrocomb	+++	Lyothyronine + levothyroxine +	
		iodine	
Thyrotom	+++	Lyothyronine + levothyroxine	

Antithyroid medicines

Antithyroid medicines inhibit the formation and release of the thyroid gland hormones.

The mechanism of action

They inhibit the synthesis of the thyroid gland hormones suppressing the enzymatic systems activity (peroxidases) that take part in this process.

Pharmacodynamics (effects) \rightarrow	Indications
Thyreostatic (decrease of the thyroid	Hyperthyroidism, thyreotoxicosis, diffusion
gland hormones synthesis), decrease of	toxic goiter
the basal metabolism	
Side effects \rightarrow Contraindications	
Spreading and increasing of	Hypothyroidism, nodular goiter, inhibition
vascularisation of the thyroid gland (a	of blood cells formation (leukopenia,
strumogenic effect). Leukopenia,	agranulocytosis)
agranulocytosis	

The list of medicines

INN, (Trade name)	Medicinal form, dosage
Levothyroxine sodium (L-Thyroxine)	Tabl. 0.005
Lyothyronine (Tri-iodthyronine)	Tabl. 0.0005

Novothyral	Tabl.
Propylthiouracil (Propycil)	Tabl. 0.05
Thiamazole (Mercazolyl)	Tabl. 0.005
Thyroidine	Tabl. 0.05
Thyrocomb	Tabl.
Thyrotom	Tabl.

Glossary

Toxic goiter (thyreotoxicosis, hyperthyroidism, Graves' disease, Basedow's disease) is a disease that is characterized by diffusion overgrowth of the thyroid gland and the increased secretion of thyroid hormones, which cause dysfunction of all kinds of metabolism, energy and functions of different organs. Cretinism is a syndrome of the inborn insufficiency of the thyroid gland function with the acute retardation of physical and psychic development. Mixedema is an edema (all over the body) of the subcutaneous tissue in hypothyroidism. The basal metabolism is the marker of the energy exchange intensity (kcal/24 hours or kcal/hour). Peroxidases are enzymes that catalyze the oxidation-reduction reactions. Endemic goiter is the increase of the thyroid gland due to the decreased content of iodine in water and food.

MEDICINES OF THE PARATHYROID GLANDS HORMONES AND MEDICINES REGULATING CALCIUM LEVEL IN THE BODY

Normal calcium concentration in the body is controlled by parathormone (that stabilizes the calcium ions concentration in blood if it is decreased); by calcitonin (that normalizes the calcium level in blood if it is increased); by the active form of vitamin $D - D_3$ (that restores the calcium absorption in the intestine if its concentration decreases in the blood plasma).

Parathyroid glands take part in the exchange of calcium and phosphorus producing parathormone. When decreasing the calcium concentration in blood the parathormone secretion intensifies. The excess of calcium in blood leads to inhibition of the parathormone release.

The list of medicines		
Parathyroidine	Calcitonin	

The mechanism of action

They interact with target-organs (bone tissue, intestine, kidneys) and stabilize the calcium level in blood and bones: calcitonin inhibits bone resorption; parathyroidine (parathormone) increases bone resorption.

Pharmacodynamics (effects)	\rightarrow Indications
Parathyro	idine
It promotes calcium release from bones and	Prophylaxis of tetany in hypo-
increase of its amount in blood, intensifies	parathyroidism, diseases caused by
the calcium absorption by the intestinal	disorder of the phosphorus-calcium
mucous membrane, its reabsorption in renal	exchange (spasmophilia, hypo-
tubules; retains reabsorption of phosphates	calcemic convulsions, etc.)

Calcitonin			
It regulates calcium and phosphates	Osteoporosis, hypercalcemia, pain in		
exchange in the body, promotes the	bones, Paget's disease, osteomyelitis,		
transition of phosphates and calcium from	paradontosis, hypervitaminosis D,		
blood to the bone tissue	slow inosculating of fractures		
Side effects \rightarrow	Contraindications		
Parathyroidine			
Hypercalcemia	Increased amount of calcium ions in		
	blood		
Calcitonin			
Hypocalcemia	Decreased amount of calcium ions in		
	blood		

The	list	of m	edicines
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INN, (Trade name)	Medicinal form, dosage
Calcitonin (Calcitrin)	Sol. for inj. 50 U
Parathyroidine (Parathormone)	Sol. for inj. 20 U/ml

Glossary

Paget's disease is deforming osteitis. **Hypoparathyroidism** is hypocalcemia when parathormone is insufficient. **Osteoporosis** is dystrophy of the bone tissue with the complete resolution of some bone cross-pieces. **Spasmophilia** is the combination of the increased neuro-muscular excitability with the laryngospasm. **Tetany** is attack of tonic convulsions.

MEDICINES OF ADRENAL GLANDS CORTEX HORMONES

Mineral corticoids (MC)			
Desoxycorticosterone acetate			
Glucocorticoids (GC)			
Systemically- Local-acting ones			
acting ones	for inhalation	for external and	combined
		intranasal use	medicines
Hydrocortisone	Budesonide	Hydrocortisone	Aurobin
Dexamethasone	Dexamethasone	Budesonide	Trimistine
Mazipredone	Triamcinolone	Dexamethasone	
Triamcinolone	Flunisolide	Triamcinolone	
		Fluocinolone acetonide	

Mineral corticoids

The mechanism of action

Penetrating into the cellular cytoplasm of the renal distal tubules MC bind to the cytoplasm receptors forming the hormone-receptor complex. This complex penetrates into the nucleus and stimulates the synthesis of permease protein that promotes the reabsorption of Na^+ from urine.

Pharmacodyna	mics	es (effects) \rightarrow Indications
Regulation of water-s	salt	Primary and secondary insufficiency of
metabolism: increase of the blo	bod	adrenal cortex (hypocorticism, Addison's
pressure, retention of Na ⁺ , H ₂ O a	and	disease)
elimination of K ⁺		
Normalization of the tone a	and	Myasthenia
improvement of the skele	etal	
muscles activity		
Side effects		\rightarrow Contraindications
Edema, increase of I	BP,	Hypertension, heart failure, treatment with
hypokalemia, increase	of	loop and thiazide diuretics, glaucoma
intraocular and intracranial press	ure	

Glucocorticoids

The mechanism of action

The mechanism of action of glucocorticoids (GC) is similar to the mechanism of action of other steroid hormones. The hormone-receptor complex penetrates into the nucleus where influencing on the genetic apparatus it affects the protein synthesis processes. The metabolic effects of GC such as the influence upon all kinds of metabolism in the body (protein, carbohydrate, lipid, water-salt ones) are determined by the activation of the synthesis of some proteins and the inhibition of the synthesis of others.

Pharmacodynamics (effects) \rightarrow	Indications
Protein metabolism: increase of the	Substitution therapy of chronic and
protein disintegration, inhibition of their	acute adrenal insufficiency
synthesis	(hypocorticism, Addison's disease)
Carbohydrate metabolism: decrease of	
glucose coming to cells, hyperglycemia	
Lipid metabolism: stimulation of the	
lipid synthesis from glucose and the fat	
deposition in the region of face, the upper	
part of the trunk and in the lower	
extremities, increase of appetite.	Collagenoses, glomerulonephritis, acute
Anti-inflammatory, immunosuppressive,	pancreatitis, organ transplantation, severe
anti-allergic, antishock, antitoxic effects	allergic reactions, shock
Side effects	\rightarrow Contraindications
Water retention, <i>†BP</i> , "steroid" diabetes,	Severe hypertension, diabetes mellitus,
ulcer, psychosis; muscle weakness,	peptic ulcer, osteoporosis, psychic
gastric bleedings, osteoporosis, increased	dysfunctions, predisposition to thrombo-
blood coagulability, body weight increase	ses, Itsenko-Cushing disease, pregnancy

NB! GC taking as anti-inflammatory medicines are administered only in the case when all other possible therapies do not give result. Fluorine-containing medicines are the most effective GC for local application. A sudden stoppage of usage of GC provokes the syndrome of "rapid discontinuation" and that is why it is

necessary to decrease their dose gradually under doctor's supervision. The term of a gradual withdrawal can last for some months. Corticotropin is administered 3 days before the stoppage of medicines usage.

Medicines	The duration of action	Anti- inflammatory effect	Na ⁺ retention	Other peculiarities		
Hydro-	Short	1	1	It is used both		
cortisone	(5-12 h)			systemically and locally		
Flunisolide	Short -//-	200-300	0	Aerosol		
Fluocinolone	Short -//-	25-30	0	Ointment (is used on the		
acetonide				limited sites of the skin)		
Aurobin	Short -//-	4	0	Ointment (mazipredone,		
				lidocaine, triclosan) for		
				hemorrhoid treatment		
Mazipredone	Middle	4-5	0.8	Water soluble synthetic		
	(12-30 h)			prednisolone derivative		
Budesonide	Middle	4	0	It is similar to		
	//			triamcinolone		
Triamcino-	Long	5	0	It is used systemically		
lone	(36-72 h)			and locally		
Dexametha-	_//_	25-30	0	A strong anti-allergic		
sone				effect		

The pharmacological "face" of glucocorticoids

The list of medicines

INN, (Trade name)	Medicinal form, dosage	
Aurobin	Ointment, tube 20.0	
Budesonide (Apulein, Pulmicort)	Tabl. 0.0005; sol. 0.025%; oint. 0.025%	
Desoxycorticosterone acetate (DOCSA)	Tabl. 0.005; sol. for inj. 2.5%	
Dexamethasone (Dexalone)	Tabl. 0.004; sol. 0.4%	
Flunisolide (Ingacort)	Aerosol 0.25 mg/day; gel 0.25 mg/g	
Fluocinolone acetonide (Sinalar,	Gel 0.025%	
Synaflan, Flucinar)		
Hydrocortisone (Hydrocort, Locoid)	Cream 2.5%; sol. for inj. 2.5%	
Mazipredone (Depersolone)	Sol. for inj. 3%; ointment 0.25%	
Triamcinolone (Kenalog)	Tabl. 0.008; sol. for inj. 4%; cream 0.1%	
Trimistine	Ointment, tube 10.0	

Glossary

Itsenko-Cushing disease is a hyperproduction of endogenous cortisol in adrenal hyperplasia (obesity, diabetes, hypertension, amenorrhea in women, osteoporosis, etc.). Collagenoses are autoimmune diseases with diffusive damage of the connective tissue and vessels. Myasthenia is the muscular weakness. "Steroid" diabetes, ulcer, psychosis are development of hyperglycemia, ulcerations of the GIT, disorders of the CNS caused by GC administration.

MEDICINES OF THE SEXUAL HORMONES. ANABOLIC STEROIDS. ANTAGONISTS OF THE SEXUAL HORMONES

Fei	nale	Male	Anabolic
Estrogens	Gestagens	(androgens)	steroids
Estron	Allylestrenol	Testosterone	Nandrolone decanoate
Estradiol	Progesterone	Methyltestosterone	Methylandrostendiol
Hexestrol			

Classification of medicines

MEDICINES OF THE FEMALE SEXUAL HORMONES Medicines of estrogens

Estrogens are medicines containing the female sexual hormones produced by follicles and their synthetic analogues.

The mechanism of action

Estrogenic medicines accumulate selectively in target organs: uterus, vagina, mammary glands, anterior lobe of the hypophysis, liver where they bind to specific extranuclear protein – estrophyllin, receptors of plasmatic membranes of target cells forming hormone-receptor complexes, which penetrate into the nucleus, influence on the protein synthesis (activating the DNA and RNA synthesis).

Pharmacodynamics (effects)	\rightarrow Indications		
Estrogenic effect:	The insufficient function of		
- stimulation of development of the sexual	1 ovaries (amenorrhea, dysmenor-		
organs and the secondary female sexua	l rhea, climacterium, sterility),		
characters;	hypoplasia of the genitals and		
- proliferation of the endometrium during th	e underdevelopment of the		
first part of the menstrual cycle;	secondary sexual characters		
- increase of the uterine contractility and tone	Labour induction		
Side effects \rightarrow	Contraindications		
Cystic degeneration of ovaries, Tume	ours of uterus and ovaries, cystic		
carcinoma of the uterus and the mastopathies, uterine bleedings, sev			
mammary gland, uterine bleedings, form	s of hypertension, pregnancy,		
edema, hypertension lactat	ion		

The pharmacological "face" of estrogenic medicines

Medicines	Activity	Duration of action	Other peculiarities
Estron	+	+	It is obtained from female and animal urine
Estradiol	++	+++	It is used once per 2 days
Hexestrol	+		It has the non-steroid structure

Medicines of gestagens

Gestagens are medicines containing the female sexual hormones produced by the yellow body, placenta, as well as their synthetic analogues.

The mechanism of action

Gestagens interact with progestine receptors located in target organs (the reproductive organs) and in the brain. It leads to changes in the synthesis of DNA, RNA, proteins and appearance of the gestagenic effect.

Pharmacodynamics (ej	(fects) \rightarrow Indications
Gestagenic effect:	Endocrine forms of infertility, dysfunction
-stimulation of the endometrium's	of the menstrual cycle, habitual abortions,
secretory phase in the second part of	threatened preterm labour, peroral
the menstrual cycle;	contraception
-preparation of the endometrium to	
implantation of the impregnated ovum;	
- inhibition of the hypophysis	
gonadotropic function (in high doses);	
- decrease of the uterine contractility	
Side effects	\rightarrow Contraindications
Increase of BP, acne, hirsutism, libido	Hypertension, uterine bleedings, hormone-
changes, body weight increase	dependent cancer of the mammary gland
	and the genitals

The pharmacological "face" of gestagenic medicines

Medicines	Activity	Peculiarities
Allylestrenol	++	It is a medicine for peroral use
Progesterone	+	A short-acting, as it is quickly destroyed

MEDICINES OF THE MALE SEXUAL HORMONES

Androgens

Androgens are medicines containing hormones produced by the male sexual glands, adrenal cortex, and their synthetic analogues.

The mechanism of action

The mechanism of action of **androgens** is based on their interaction with cytosol testoid receptors located in target organs (the prostate, testis and their epoophorons, skeletal muscles, etc.). After binding to androgens the receptor conformation changes and the changes in DNA and RNA functions take place leading to the synthesis of different functional proteins (enzymes, etc.).

Pharmacodynamics (effects)	\rightarrow Indications		
Androgenic effect:	Infertility, infantilism, impotency,		
-stimulation of development of the genitals	pathological male climacterium,		
and the secondary male sexual characters;	malignant tumours of the mammary		
- providing the reproductive function;	gland and ovaries in women (up to		
-regulation of spermatogenesis, potency,	60 years old)		
libido after puberty of the organism			
Moderate anabolic effect			

	Side effects		> Contraindic	cations		
Edema, BP inc	rease, prostate hy	perplasia,	Hypertension,	prosta	te	cancer,
hypercalcemia,	spermatogenesis	dysfunc-	hypercalcemia,	renal	and	hepatic
tion, muscul	inisation (in	women),	insufficiency, pr	egnancy,	for 1	nen over
hepatotoxicity			65 years old			

The pharmacological "face" of androgens

Medicines	Activity	Origin	Peculiarities
Testosterone	+++	natural	It is introduced parenterally
Methyltestosterone	+	synthetic	It is stable in the GIT

Anabolic steroids

Anabolic steroids (AS) are synthetic derivatives of the male sexual hormones that unlike the natural androgens have a significantly decreased androgenic and a high anabolic effect.

The mechanism of action

AS penetrate into the cytoplasm of target organs cells (skeletal muscles, myocardium, kidneys, liver, lungs, etc.), are transported into the nucleus interacting with DNA and RNA, regulate the protein synthesis, as well as hormones with the polypeptide structure. Under the influence of anabolic steroids the increase of the cell breathing intensity and oxidative phosphorylation, accumulation of macroergic phosphates, secretion of the STH are observed.

Pharmacodynamics (eff	$ects) \rightarrow$ Indications		
Anabolic effect (stimulation of the	Cachexia, hypotrophy; radiation and		
protein synthesis, retention of nitrogen,	glucocorticoid therapy, burns, myocardial		
calcium, phosphorus in the body)	infarction, osteoporosis, traumas		
Moderate androgenic effect			
Side effects	\rightarrow Contraindications		
Hepatotoxicity, cancerogenic effect,	Liver and kidney diseases, prostate		
edema, BP increase, hypercalcemia,	cancer, hypertension, hypercalcemia,		
hyperglycemia, hyperlipidemia	epilepsy, pregnancy, lactation, for		
	children		

The	pharmacol	ogical	"face"	of	anabolic	steroids
Inc	primiticoi	vs icui	Juce	v .	anaoono	Siel olus

Medicines	Activity	The duration of action
Nandrolone decanoate	++	+++
Methylandrostendiol	+	+

The list of medicines

INN, (Trade name)	Medicinal form, dosage
Allylestrenol (Turinal)	Tabl. 0.005
Estradiol (Proginova)	Tabl. 0.001; TTS 25 mcg
Estron (Folliculin)	Sol. for inj. 0.1%
Hexestrol (Synestrol)	Tabl. 0.001
Methylandrostendiol (Methandriol)	Tabl. 0.01
Methyltestosterone	Tabl. 0.01

Nandrolone decanoate (Retabolil)	Sol. for inj. 5%
Progesterone	Caps. 0.1
Testosterone propionate	Caps. 0.04; sol. for inj. 1%

Glossary

Amenorrhea is the absence of menstruations. Hirsutism is an excessive hairiness in women by the male type. Musculinisation (syn. virilization) is the appearance of the male features in women while using androgens (gruff voice, increased hairiness, etc.).

Antagonists of the sexual hormones

Classification of medicines				
Anti-estrogenic Antigestagenic Anti-androgenic				
Clomiphencitrate	Miphepristone	Cyproterone		

The mechanism of action

Anti-estrogens bind to estrogen receptors competitively in the hypothalamus and ovaries and it leads to the more intensive release of gonadotropins (according to the negative feedback principle) causing maturation of follicles. In addition, by binding to estrogenic receptors in a tumour cell they block the activity of estrogens.

Antigestagens block progestin receptors in the uterus and prevent progesterone's influence on them.

Anti-androgens (in particular, Cyproterone) inhibit competitively cytoplasmic androgenic receptors in target cells, decrease the action of the male sex hormones.

Pharmacodynamics (effects) \rightarrow Indications					
Α	nti-estrog	gens			
Ovulation stimulation, inhibition	Anovulat	ory steri	lity, breast cancer,		
of estrogen-dependent tumours	endometr	iosis, dysfur	nctional uterine bleedings		
A	ntigestag	ens			
Antigestagenic (in particular,	, Interrup	otion of pro-	egnancy at early stages		
uterotonic) effect	(medica	al abortion)			
A	nti-andro	gens			
Anti-androgenic (decrease of potence	cy, decreas	se Androge	nization in women,		
of spermatogenesis, inhibition of	androgen	n- preterm	puberty in boys, non-		
dependent tumours growth) effect operative prostate carcinoma					
Side effects \rightarrow Contraindications					
Anti-estrogens					
Thromboses, hypercalcemia, edema	a, ovarian	Thromboe	mbolic states, hypercalce-		
hyperstimulation syndrome, metrorr	hagia	mia, uterine bleedings, pregnancy			
Antigestagens					
Dizziness, weakness, fever, dyspeps	ia, metror	rhagia Bleeding, pregnancy			
Anti-androgens					
Changes in body weight and	Spermatogenesis disorder, pregnancy,				
depression, gynecomastia, spermatogenesis		edema, thromboses, liver function			
disorder, edema, thromboses, hepato	disorders, age under 18				

NB! With a low level of endogenous estrogens in the organism anti-estrogenic medicines have a moderate estrogenic effect, while with a high level they have the anti-estrogenic effect.

The use of medicines					
INN, (Trade name)	Medicinal form, dosage				
Clomiphencitrate (Clomiphene)	Tabl. 0.05				
Cyproterone (Androcur)	Tabl. 0.01				
Miphepristone (Penkrofton)	Tabl. 0.2				

The list of medicines

Glossary

Metrorrhagia is the uterine bleeding. **Endometriosis** is a benign prolifiration of the endometrium tissue outside the uterus. **Ovulation** is the process when a mature ovum comes from the follicle.

CONTRACEPTIVES

Contraceptives are medicines used to prevent undesirable pregnancy.

Comb	Microdoses of gestagens						
monophasic biphasic		tri-phasic	(mini-pills)				
Ovidon	Antiovin	Tri-regol	Linestrenol				
Logest		Triquilar					
Post	tcoital	Vaginal contraceptives (spermicides)					
Levonorgestrel		Benzalkonium chloride					

Classification of medicines

The mechanism of action

By the negative feedback principle **combined estrogen-gestragen contraceptives** block the release of hypothalamus hormones and the gonadotropic hormones of the hypophysis anterior lobe (FSH and LH), and, therefore, they inhibit the central regulation mechanism of the ovule maturation. Gestagens suppress development of follicles in the ovary, cause the thickening of the cervical mucus that prevents spermatozoons penetrating into the uterine cavity; besides, they cause changes in the endometrium preventing the implantation of the fertilized ovum.

The contraceptive effect of **mini-pills** is based on the following factors:

- the "**cervical**" factor is decrease of the amount of the cervical mucus and change of its physical and chemical properties (increase of viscosity), as a result the spermatozoons penetrating ability decreases;

- the "**uterine**" factor is inhibition of the endometrium proliferation, ovum implantation altering;

- the "**tubal**" factor is inhibition of the peristaltic contractions of the Fallopian tubes that hamper the ovum's transport.

The inhibiting influence of gestagens microdoses on the hypothalamus and hypophysis system is less compared to that of the combined peroral contraceptives.

Postcoital contraceptives inhibit ovulation, change the normal course of the secretory phase of the menstrual cycle, cause temporary atrophic changes in the ovaries.

Spermicides disturbing the cell membrane cause fragmentation and destruction of spermatozoons.

Pharmacodynamics (effects) \rightarrow Indications					
Contraceptive (for all medicines), and	ti-ovulatory (for Contraception				
hormonal medicines); spermicidal (for spe	ermicides) effect				
Side effects –	Side effects \rightarrow Contraindications				
Estrogen-dependent complications	Thromboembolism, hypertension, ische-				
include thromboses, increase of the blood	mic heart disease, diabetes mellitus in a				
pressure, edema, headache, nausea,	severe form, hormone-dependent tu-				
vomiting, chloasma.	mours, epilepsy, neuroses, psychoses,				
Gestagens cause fatiguability, depress-	pregnancy and lactation, progressive				
sion, body weight increase, libido	diseases of liver and kidneys, diseases				
decrease, painfulness of mammary	of the brain vessels, marked hyper-				
glands, intermenstrual bleedings lipidemia					
Spermicides may cause the development of vaginal dysbiosis Vaginal dysbiosis					

NB! Before using contraceptives it is necessary to examine mammary glands, to check blood pressure, to determine the glucose level in urine and to check the hepatic function, to take a vagina smear test. In the case of the prolonged administration of oral contraceptives the medical examination should be taken every 6 months. The administration of contraceptives should be stopped three months before a planned pregnancy.

Medicines	The peculiarities of	Other indications
	contraception	
	For women:	
Ovidon	With the phenotype of the	Dysfunctions of the menstrual
	estrogen character	cycle
Logest	Over 35 years old, after	Dysfunctions of the menstrual
	abortion, with	cycle + juvenile uterine
	hyperandrogenisation	bleedings
Antiovin	With the phenotype of the	
	gestagen character	Dysfunctions of the menstrual
Tri-regol	Young women, adolescents	cycle
Triquilar		
Levonorgestrel	In lactation, irregular sexual life	
	(high doses); concomitant	
	diabetes mellitus, hypertension,	
	obesity (mini-pills)	
Benzalkonium	Any age, in irregular sexual life	Prevention of some sexually
chloride		transmitted diseases,
		endometriosis

The pharmacological "face" of contraceptives

INN, (Trade name)	Medicinal form, dosage
Antiovin	Tabl. № 21
Benzalkonium chloride (Farmatex, Erotex)	Vaginal cream 2%
Levonorgestrel (Postinor)	Tabl. 0.00075
Linestrenol (Exlutone)	Tabl. 0.00075
Logest	Tabl. №21
Ovidon	Dr. №21
Tri-Regol	Tabl. №21
Triquilar	Dr. № 21

The list of medicines

Glossary

Ovum implantation is the introduction of the fertilized ovum into the mucous membrane of the uterus. **Libido** means sexual desire. **Postcoital contraceptive** is contraceptive used immediately after a sexual intercourse. **Spermatozoon fragmentation** is the destruction of spermatozoons by the medicine affection. **Folliculogenesis** is the process of the follicle's maturation. **Chloasma** is the skin hyperpigmentation in the form of yellowish-and-brownish patches.

MEDICINES AFFECTING MYOMETRIUM

These medicines are the medicinal agents that increase (uterotonics) or decrease (tocolytics) the uterine tone and contractions.

Classification of medicines						
Uterotonics			Uterolytic	cs (tocolytics)		
Oxytocin	Dinoprost	Estron	Fenoterol	Salbutamol		

Pachycarpine hydroiodide

Ergotal

Classification of medicines

Uterotonics

Progesterone

The mechanism of action

The mechanism of action of **Oxytocin** is connected with the stimulation of oxytocin receptors of the uterine smooth muscle cells, which leads to the increase of the calcium level in a cell and intensification of the uterine contractions. Being progesterone antagonist **Dinoprost** stimulates prostaglandin receptors of the myometrium cell membranes and intensifies the uterine contractions. **Pachycarpine hydroiodide** increases the sensitivity of the M-cholinoreceptors of the uterus to endogenous acetylcholine, as a result the uterine contractility intensifies. **Ergotal** stimulates α_1 -adrenoreceptors of the uterus and it leads to the increase of its tone. **Estron** increases the sensitivity of the uterus (in the end of pregnancy) to endogenous stimulators: oxytocin and prostaglandins.

Pharmacodyna	mics (effects) —	> Indications
Uterotonic effect	Labour induction	on, hypotonic uterine bleedings
Side effects	\rightarrow	Contraindications
Myometrium hypertone	Pregnancy	

Tocolytics *The mechanism of action*

Fenoterol, Salbutamol stimulate inhibitory β_2 -adrenoreceptors of the uterus and it leads to its relaxation. **Progesterone** decreases the sensitivity of the myometrium to endogenous oxytocin.

Pharmacodynamics (eff	$Tects) \rightarrow Indications$
Tocolytic effect	Threatened preterm labour
Side effects	\rightarrow Contraindications
β_2 -adrenomimetics – tachycardia,	Arrhythmias, hypotension, diabetes
blood pressure decrease, hyperglycemia	mellitus
Gestagens – hypertension, thromboses	Hypertension, predisposition to
	thrombosis

The pharmacological "face" of medicines affecting the myometrium

		UTEROTONICS			
Medicines	affecting primarily on uterine:		The action in:		Belong to the group of
	tone	contractility	labour	stopping bleedings	
Oxytocin	++	+++	++++	+	hormones of the hypophysis posterior lobe
Dinoprost	+	++	+++	-	analogues of prostaglandins
Estron	+	++	+	-	estrogens
Ergotal	+++	-	-	++	Claviceps purpurea alkaloids
Pachycarpine	+	++	++	-	Ganglionic blockers
TOCOLYTICS					
		Belong to the group of		0	ther effects
Fenoterol Salbutamol		β_2 -adrenomimetics		В	roncholytic
Progesterone		gestagens Gestagenic		Gestagenic	

The list of medicines

INN, (Trade name)	Medicinal form, dosage
Dinoprost (Prostine $F_{2\alpha}$)	Sol. for inj. 0.5%
Ergotal	Sol for inj. 0.05%
Estron (Folliculin)	Sol for inj. 0.1%
Fenoterol (Berotec, Partusystene)	Aerosol 0.1 mg/1dose
Oxytocin	Sol. for inj. 10 U/ml
Pachycarpine hydroiodide	Sol. for inj. 3%
Progesterone	Caps. 0.1

Salbutamol (Ventoline)	Sol. for inj. 0.1%; tabl. 0.002
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Glossary

Tocolytic (uterolytic) effect is decrease of the uterine tone and contractility. **Uterotonic** effect is intensification of the uterine tone and contractility.

XIV. ANTIMICROBIAL, ANTIVIRAL AND ANTIPARASITIC MEDICINES

ANTISEPTICS AND DISINFECTANTS

Antiseptics are antimicrobial medicines, which disturb the normal course of biochemical processes in microbes due to inhibition of the enzymatic systems activity and have mainly bacteriostatic type of action. Antiseptics act selectively to certain types of microorganisms. **Disinfectants** are medicines, which cause irreversible changes in the protoplasm of microbial cells and lead to their rapid death, i.e. they have bactericidal type of action. They do not have a marked selective action to microorganisms.

Classification of medicines					
Haloids	Oxidants	Alkalies	Salts of	heavy	Acids
			meta	als	
Chloramine B	Hydrogen	Sodium	Merc	ury	Salicylic acid
Chlorhexidine	peroxide	tetraborate	dichlo	oride	Benzoic acid
Povidone-	Potassium		Silver r	nitrate	
iodine	permanganate				
Phenols	Dyes	Nitrofurans	Derivat	ives of	Aldehydes and
			8-oxyqu	inoline	alcohols
Phenol	Brilliant green	Nitrofural	Nitroxoline		Formaldehyde
Tricresol	Methylene	Furadonine			Hexamethylen-
	blue				tetramine
					Ethanol
Tars and resins		Antibacterial		Detergents	
		medicines of	natural		
		origii	n		
Ichthammol		Novoimanine		Ethonium	
Medical	edical ozokerite Chloroph		Ullipt Decamethox		ecamethoxine
		Ecteric	ide		Miramistine

Classification of medicines

The mechanism of action

They cause the protein coagulation in microbes, alter the permeability of their cell wall, inhibit the enzymatic activity.

Pharmacodynamics (effec	ets) \rightarrow Indications
Antiseptic, bacteriostatic	Treatment of wounds, burns, ulcers, disinfection of the
	operational field and syringes, washings in gynecology,
	urology, stomatology
Disinfectant, bactericidal	Disinfection of hands and instruments, sterilization of
	instruments, patient's ejecta and excrements, premises,
	furniture and clothes

INN, (Trade name)	Medicinal form, dosage
Benzoic acid	Pwd.
Brilliant green	Sol. 1; 2%
Chloramine B	Pwd. 10.0
Chlorhexidine	Pwd.
Chlorophyllipt	Sol. 1%
Decamethoxine (Septefril)	Tabl. 0.1, sol. 0.02%
Ectericide	Sol. 250 ml
Ethanol	Sol. 70%, 96%
Ethonium (Ethonium ointment)	Ointment 1%
Formaldehyde (Formalin)	Sol. 100 ml
Furadonine	Tabl. 0.05
Hexamethylentetramine	Sol. for inj. 40%, tabl. 0.5
Hydrogen peroxide	Sol. 3%
Ichthammol	Ointment 100.0
Medical ozokerite	Bars 2 kg
Mercury dichloride	Tabl. 0.5
Methylene blue	Sol. 1%
Miramistine	Sol. 0.01%
Nitroxoline (5-NOC)	Tabl. 0.05
Nitrofural (Furacilin)	Tabl. 0.1, ointment 0.2%
Novoimanine	Sol. 1%
Phenol (Carbolic acid)	Sol. 10, 15, 25 ml
Potassium permanganate	Pwd. 15.0
Povidone iodine (Betadine, Polyiodine)	Sol. 10%
Salicylic acid	Sol. 1%
Silver nitrate	Pwd.
Sodium tetraborate (Bura)	Sol. 20%
Tricresol	Sol. 2.5%

The list of medicines

Glossary

Bacteriostatic type of action is the action directed to inhibition of the growth and reproduction of microorganisms. **Bactericidal type of action** is the action leading to the rapid death of microorganisms.

ANTIBIOTICS

Antibiotics are substances of biological origin synthesized by microorganisms or isolated from plant and animal tissues, as well as their semi-synthetic and synthetic analogues selectively suppressing the viability of microorganisms sensitive to them.

Classification of antibiotics

Antibiotics are classified according to the origin, chemical structure, mechanism (fig. 5) and peculiarities of their action (type and spectrum) to microorganisms.

By the chemical structure antibiotics are divided into:

- β -lactams (with the β -lactam ring in the structure: penicillins, cephalosporins, monobactams, carbapenems); tetracyclines (with four condensed six-membered heterocycles in the structure); macrolides and azalides (with the macrocyclic lactone ring in the structure); aminoglycosides (containing aminosugars in the molecule); lincosamides, chloramphenicols (derivatives of dioxyaminophenylpropane); rifamycines, polymyxines (cyclic polypeptides); fusidines, glycopeptides, antibiotics of other chemical groups.

Bactericidal			Bacteriostatic
		Disturbing	
the synthesis of the microbial cell wall components	the structure and function of the cytoplasmatic membrane	the protein synthesis at the level of ribosomes* (irreversibly), nucleic acids	the protein synthesis at the ribosome level (reversibly)
β-lactams Glycopeptides Phosphomycine Cycloserin	Polymyxines Gramicidine Antimycotic antibiotics	Aminoglycosides* Rifamycines Fluoroquinolones• Griseofulvin	Macrolides Azalides Oxazolidinones Fusidines Lincosamides Tetracyclines Fusidines Chloramphenicols

Classification of antibiotics by the mechanism and type of action

• they are not classical antibiotics, but they are synthetic antimicrobial medicines that are close to antibiotics in their pharmacological properties.

There are also antitumour antibiotics.

By the spectrum of the antibacterial action, antibiotics can be of **wide** (**broad**), **moderate** and **narrow** spectrum of action. Antibiotics of the wide spectrum of action are prescribed in the case of severe course of disease, before obtaining the results of the antibiogram and in mixed infections. When determining the causative agent of the disease it is expedient to use antibiotics with the narrow spectrum.



Fig. 5. The main mechanisms of the antibiotics antimicrobial action

By the type of the antibacterial action there are antibiotics with the **bacteriostatic** and **bactericidal** (they have a fast therapeutic effect in severe infections, their use is rarely accompanied by recurrences of the disease and the cases of bacteria-carrying) action. Antibiotics with the bacteriostatic type of action are rather effective for diseases of the average severity and in the cases of the prolonged treatment of the patient. There are antibiotics of the **first** and the **second therapy line**. Medicines of the second line are less active than the first line medicines and they are prescribed in the case when medicines of the first line are non-effective or when the strain of the pathogen isolated is more sensitive to these medicines. There is also a separate group of **reserve medicines** that are prescribed only in special cases when the Ist and the IInd line medicines are not effective.

Typical side effects of antibiotic therapy

Resistance of microorganisms to antibiotics. **Superinfection** is development of a new infection following the previous unfinished infectious process, especially when caused by microorganisms that are resistant or have become resistant to the antibiotics used earlier. **Dysbacteriosis (dysbiosis)** is suppression of the normal microflora of macroorganism accompanied by reproduction of conditionally pathogenic microorganisms that are previously either absent or present in insufficient amounts in the organism and suppressed by the normal microflora. **Allergic reactions** are typical for most antibiotics. There may be an immediate (acute), as well as delayed type responses.

The main principles of the rational antibiotic therapy

1. Antibiotics should be prescribed only taking into account the type of causative agent isolated and antibiogram. Choose the most active and the least toxic medicine.

2. Determine the optimal doses of antibiotics and their scheme of administration taking into consideration the drug pharmacokinetics, the severity of the disease, the condition of the liver and kidneys, as well as the age of the patient.

3. The concentration of the antibiotics should exceed the minimal inhibiting concentration for the pathogen isolated 3-4 times.

4. Take into account side effects of the antibiotics, especially in the case of hepatic and renal insufficiency.

5. Determine the presence of hypersensitivity of a patient to the definite antibiotic.

6. Begin the treatment timely and take the whole course of the antibiotic treatment.

7. Take into account a cross-sensitivity to antibiotics. Combine antibiotics of different groups to broaden the spectrum of their action and to enhance their antibacterial effect.

8. Prescribe concomitantly antifungal agents to prevent dysbacteriosis.

Antibiotics of the β-lactam structure

The group of β -lactam antibiotics includes medicines of the following groups: penicillins, cephalosporins, carbopenems and monobactams. All these groups of antibiotics contain the β -lactam ring, which determines their antimicrobial activity, in the nucleus of the molecule.

 β -lactam antibiotics differ from each other by their resistance to hydrochloric acid of the gastric juice and it determines the route of their administration. Natural penicillins (excluding phenoxymethylpenicillin), anti-pseudomonal penicillins, most of cephalosporins, as well as carbopenems, monobactams are decomposed in the stomach and are administered only parenterally. β -lactam antibiotics are evenly distributed in an organism accumulating therapeutic concentrations in many organs, tissues and biological fluids. **Crossed allergic reactions** between penicillins and other β -lactam antibiotics are observed.

The mechanism of action

The mechanism of action of all β -lactam antibiotics is similar. It is based on the inactivation of enzymes that participate in the synthesis of peptidoglycan mureine, the main component of the external membrane (cell wall) of microorganisms, and it leads to the death of the microbial cell.

Penicillins

Peculiarities of penicillins

1. The greatest effect on gram-positive (G^+) microorganisms, which cellular wall contains from 40 to 90% of peptidoglycans (gram-negative (G^-) ones – only 5%).

2. The effect only to divisible cells because the growing microbial cells need the material to build the cellular wall.

3. A low toxicity.

4.A broad spectrum of the therapeutic action.

5. A good absorption, distribution and penetration into tissues.

	Natural				
Short-acting			Depo-medicines		
Sodium and p	otassium salts of be	nzylpenicillin	Bicillin-5		
	Semi-synthetic				
Antistaphylococcal	Aminopenicillins	Antipseudomonal	Combined		
Oxacillin	 Ampicillin 	Carbenicillin	 Amoxiclav 		
 Cloxacillin 	 Amoxicillin 	Azlocillin	(Amoxicillin+		
			clavulanic acid)		
			 Helicocin 		
			(Amoxicillin+		
			Metronidazole)		

Classification of medicines

• -resistant to β -lactamases, • -acid resistant

Pharmacodynamics (e	effects) \rightarrow Indications
Antibacterial effect.	Rheumatism, syphilis, angina,
The type of action is bactericidal.	pneumonia, meningitis, abscess, otitis,
The spectrum of action is mo	oderate diphtheria, gas gangrene, peptic ulcer,
(natural penicillins) and broad ((semi- anthrax
synthetic penicillins), including G	G ⁺ and
G^- cocci, G^+ bacilli, anae	erobes,
spirochetes	
Side effects	\rightarrow Contraindications
Neurotoxicity (tremor,	, Epilepsy (especially in endolumbal
convulsions, hallucinations),	, administration). High doses during pregnancy
bleeding	should be administered with care

Antipseudomonal penicillins have a broader antibacterial spectrum comparing to other penicillins. The spectrum of action of semi-synthetic penicillins considerably expands (they are active against such G⁻ microorganisms as Klebsiella, Proteus vulgaris, anaerobes, bacteroids) due to their combination with inhibitors of βlactamases, i.e. clavulanic acid, sulbactam and tazobactam. The simultaneous administration of penicillins with bacteriostatic antibiotics and sulphonamides should be avoided since they decrease the efficiency of penicillins. Penicillinase is administered as an antidote in poisoning (allergy) by penicillins.

The list of medicines

INN, (Trade name)	Medicinal form, dosage
Azlocillin (Securopen)	Pwd. for inj. 1.0
Amoxiclav (Amoxicillin + clavulanic acid)	Tabl. 0.625
Amoxicillin (Quiconcil)	Tabl. 0.5
Ampicillin (Ampicillin trihydrate)	Tabl. 0.5, pwd. for inj. 0.5
Benzylpenicillin sodium and potassium salts	Pwd. for inj. 1000000 U
(Penicillin)	
Bicillin-5	Pwd. for inj. 1500000 U
Carbenicillin	Pwd. for inj. 1.0

Cloxacillin (Cloxapen)	Tabl. 0.5, pwd. for inj. 0.5
Oxacillin (sodium salt of oxacillin)	Tabl. 0.5, pwd. for inj. 0.5
Helicocin (Amoxicillin + Metronidazole)	Tabl. № 36

Cephalosporins

The group of cephalosporins is the class of natural and semi-synthetic β -lactam antibiotics, which contain 7-aminocephalosporanic acid (7-ACA).

The I st	The II nd	The III rd	The IV th
generation	generation	generation	generation
Cephazolin	Cefuroxime	Cephtriaxone	Cephepim
 Cephalexin 	 Cephaclor 	 Cephixim 	Cephpirom

Classification of medicines

acid resistant

Peculiarities of cephalosporins

1. Close to penicillins in their structure and pharmacological properties.

2. A low toxicity and a good pharmacokinetics.

3. A good combinability with other antibacterial agents.

4. A high resistance to the affection of Staphylococcal β -lactamases comparing to penicillins.

Cephalosporins of different generations differ in the spectrum of their antibacterial action (table 5).

Table 5.

Generation of	Effectiveness against	
cephalosporins	Gram-positive bacteria	Gram-negative bacteria
The first	+++	+/-
The second	++	+
The third	+	+++
The fourth	++	+++

Pharmacodynar	nics (effects) \rightarrow Indications
Antibacterial effect.	Infections of respiratory tract, skin and soft tissues,
The type of action is	bones and joints, urinary tract, heart; prevention of
bactericidal.	infections after surgery. Meningitis and blue pus
The spectrum of action is	(pseudomonal) infection -cephalosporins of the III-
broad	IV generations
Side effec	ets \rightarrow Contraindications
Bleeding, hemato-, nephro-,	Porphyria, epilepsy, severe disorders of kidneys and
neuro-, hepatotoxicity	liver functions, pregnancy, lactation

The list of medicines

INN, (Trade name)	Medicinal form, dosage
Cefuroxime (Zinaceph, Zinnat)	Pwd. for inj. 0.5
Cephazolin (Kefzol, Reflin)	Pwd. for inj. 0.5
Cephaclor (Ceclor)	Caps. 0.5

Cephalexin	Caps. 0.5
Cephepim (Maxipim)	Pwd. for inj. 0.5
Cephixim	Caps. 0.1
Cephpirom (Keyten)	Pwd. for inj. 0.5
Cephtriaxone (Longaceph)	Pwd. for inj. 0.5

Carbapenems and monobactams

The peculiarity of these classes of antibiotics is the fact that their structure is based on the simple β -lactam ring, which is not bound to a thiazolidine ring in contrast to penicillins and cephalosporins.

Classification of medicines

Carbapenems	Monobactams
• Imipenem-cylastatin	• Aztreonam
• Meropenem*	
• – resistant to β –lactamases *	resistant to renal dehydropeptidase-1

Carbapenems Peculiarities of carbapenems

1. A marked resistance to the affection of β -lactamases.

2. A slow development of microorganisms resistance (exceptions are blue pus bacilli and staphylococci).

3. A super broad spectrum of action.

4. Strong post-antibiotic effect.

5. Antibiotics of a super deep reserve (second choice)!

6. Antibiotics have relatively low toxicity and are well-tolerated.

Pharmacodynamics (effects)	\rightarrow Indications
Antibacterial effect.	Severe hospital infections caused by a
The type of action is bactericidal.	multi-resistant strains of microor-
The spectrum of action is extremely	ganisms; infections of bones and joints,
broad covering the majority of aerobic and	skin and soft tissues, abdominal cavity,
anaerobic G^+ and G^- bacteria. Chlamydia,	female reproductive organs, urinary
mycoplasmas, tuberculous and leprosy	tract; bacterial endocarditis (imi-
mycobacteria, pseudomonads (except blue	penem), pneumonia, septicemia, me-
pus bacillus) have a natural resistance to	ningitis (meropenem)
carbapenems	
Side effects \rightarrow	Contraindications
Hemato-, neurotoxicity	Blood disorders, epilepsy, pregnancy,
	lactation

Imipenem is metabolized in the epithelium of renal tubules by renal dehydropeptidase-1 with the formation of nephrotoxic metabolites. To prevent this process imipenem is co-administered with cylastatin, an inhibitor of the enzyme, in the ratio of 1:1. A combined medicine imipenem-cylastatin has a trade name Tienam.
Monobactams Peculiarities of monobactams

- 1. A second choice group.
- 2. A high resistance to the affection of β -lactamases of the gram-negative flora.
- 3. The absence of the cross-sensitive allergy with penicillins and cephalosporins.
- 4. A slow development of microorganisms' resistance.
- 5. A possible use for newborns treatment.

Pharmacodynamics (effects) \rightarrow Indications
Antibacterial effect.	Severe infections of different location
The type of action is bactericidal.	caused by gram-negative flora that is
The spectrum of action is narrow (G ⁻	resistant to the 3 rd generation of
aerobes, gonococci, meningococci,	cephalosporins, to the 2^{nd} and 3^{rd}
Salmonellas, Shigellas, Klebsiellas,	generations of aminoglycosides, and
Proteus, E. coli and blue pus bacilli)	antipseudomonal penicillins
Side effects \rightarrow Contraindications	
Bleeding, hepatotoxicity	Bleeding, dysfunctions of the liver and
	kidneys. They should be used carefully in
	pregnancy and lactation
The list of medicines	

I ne list of mealcines

INN, (Trade name)	Medicinal form, dosage
Aztreonam (Azactam)	Pwd. for inj. 0.5
Imipenem-cylastatin (Tienam)	Pwd. for inj. 0.5
Meropenem (Meronem)	Pwd. for inj. 0.5

Glossary

Anaerobes are microorganisms that are capable to exist without oxygen. Aerobes are microorganisms that need free oxygen to survive. Meningitis is the inflammation of brain and spinal cord membranes. Post-antibiotic effect is a phenomenon of the antibacterial effect presence after discontinuation of the antibiotics' administration. Erysipelas is an infectious and inflammatory disease of the skin and soft tissues often caused by streptococci. The spectrum of action is the list of microorganisms that are sensitive to a medicine. β -lactamases are enzymes of microorganisms produced for protection and that destroy a β -lactam ring of antibiotics.

Tetracyclines

The group of tetracyclines includes natural and semi-synthetic antibiotics. Their chemical structure is based on 4 condensed six-membered rings.

Natural	Semi-syr	nthetic
Tetracycline	Methacycline	Doxycycline

Classification of medicines

By duration of their effect tetracyclines are divided into short-acting medicines (6-8 hours and they are administered 4 times per 24 hours) – tetracycline; long-acting ones (12-24 hours and they are administered 1-2 times per 24 hours) – methacycline, doxycycline.

Peculiarities of tetracyclines

1. The bacteriostatic type of action.

2. A broad spectrum of antibacterial activity, but a high level of secondary resistance of many bacteria.

3. A good absorption from the gastrointestinal tract.

4. Frequent side effects.

The mechanism of action

They bind to 30S-subunit of bacterial ribosomes and it prevents inclusion of aminoacids into the protein peptide chains (only in the phase of microorganisms active growth), i.e. it disturbs the protein synthesis.

Pharmacodynamics (effects) \rightarrow	Indications
Antibacterial effect.	Infections of respiratory tract,
The type of action is bacteriostatic.	biliary tract, abdominal and
The spectrum of action is broad (including G ⁺	intestinal infections, syphilis,
and G ⁻ cocci, bacilli, intracellular pathogens,	Helicobacter pylori eradication
anaerobes).	
Side effects \rightarrow Con	<i>traindications</i>
Dysbiosis, dyspepsia, decrease of the body weig	ght, Severe diseases of the liver
hepato-, hemato-, nephro-, neurotoxicity, muto-	and and kidneys, pregnancy,
teratogenecity, photodermatitis, growth disorder	of lactation, myasthenia, age
bones and teeth	under 8

Food and antacids reduce bioavailability of **tetracyclines** considerably because of their formation of poor soluble chelate complexes with aluminium, calcium, magnesium. That is why these medicines should be taken on an empty stomach an hour before meals or two hours after meals. They should not be taken with milk.

The list of medicines		
INN, (Trade name)	Medicinal form, dosage	
Doxycycline (Vibramycine)	Caps. 0.1, sol. for inj. 2%	
Methacycline (Rondomycine)	Caps. 0.3	
Tetracyline (Imex)	Caps. 0.12, oint. 3%	

The list of medicines

Glossary

Helicobacter pylori is a Gram-negative bacterium causing development of peptic ulcer. Photodermatitis is allergic skin disease caused by hypersensitivity to the sun light.

Macrolides and azalides

It is a group of antibiotics containing a macrocycle lactone ring bound to carbohydrate part.

Macrolides and azalides*			
The I st	The II nd	The III rd	Combinations of
generation	generation	generation	macrolides with
			tetracylines and other*
			medicines
Erythromycine	Roxythromycine	Azythromycine*	Oletetrin
	Clarythromycine		Zynerit*

Classification of medicines

A group of azalides is close to macrolides group, they are sometimes considered as the III^{rd} generation of macrolides.

Peculiarities of macrolides

1. The bacteriostatic action with the primary activity to G^+ (streptococci, staphylococci) microorganisms.

2. Activity against intracellular microorganisms (Chlamydia, mycoplasmas, legionellas).

3. One of the least toxic antibiotics.

- 4. A good absorption from the gastrointestinal tract.
- 5. Capable to accumulate in the site of inflammation.

The mechanism of action

They bind to ribosomes of microorganisms, inhibit the RNA synthesis and the protein synthesis in the microbial cell. Thus, the growth and reproduction of microorganisms are blocked.

Pharmacodynamics (effects)	\rightarrow Indications
Antibacterial effect.	Infections of respiratory, urinary, biliary
The type of action is bacteriostatic.	tract; reproductive system; diphtheria,
The spectrum of action is broad	syphilis, skin infections
(including G ⁺ , G ⁻ cocci, intracellular	
microorganisms)	
Side effects	\rightarrow Contraindications
Seldom: hepatotoxicity, photo-	Dysfunctions of the liver, kidneys, heart
dermatitis, arrhythmias	

The list of medicines

INN, (Trade name)	Medicinal form, dosage
Azythromycine (Sumamed)	Caps. 0.25
Clarythromycine (Clacid)	Tabl. 0.5
Erythromycine (Meromycine)	Tabl. 0.1, oint. 2%
Oletetrin	Caps. 0.25
Roxythromycine (Rulid)	Tabl. 0.1
Zinerit (Erythromycine + Zinc acetate)	Pwd. 30.0

Aminoglycosides

Aminoglycosides are antibiotics of oligosaccharide structure.

Classification of medicines			
Aminoglycosides (AG)			
The I st and	l II nd * generation	The .	III rd generation
Streptomycine	Neomycine	Amycacine	Tobramycine
Gentamycine*	Canamycine		

Classification of medicines

Peculiarities of aminoglycosides

1. A broad spectrum of action and a powerful bactericidal effect, especially on G^{-} microflora.

2. A high toxicity, but rare allergic reactions.

3. Medicines of the II^{nd} and the III^{rd} generations potentiate the effect of penicillins and cephalosporins.

The mechanism of action

Aminoglycosides suppress the protein synthesis in the microbial cell irreversibly as the result of binding to ribosomes.

Pharmacodynamics (effects	$) \rightarrow Indications$
Antibacterial effect.	Hospital infections; sepsis, peritonitis,
The type of action is bactericidal.	endocarditis, pneumonia, infections of
The spectrum of action is broad	small pelvis organs (pyelonephritis,
(including aerobes, G ⁻ microflora: E.	urosepsis), osteomyelitis, meningitis of the
coli, Proteus, Salmonellas, Klebsiella,	unclear etiology
Enterobacter, Shigellas). Medicines of	
the II^{nd} and the III^{rd} generations affect	
blue pus bacillus	
Side effects \rightarrow Contraindications	
Nephro-, oto-, neurotoxicity	Dysfunction of the kidneys, hearing and
	vestibular apparatus disorder, the CNS
	diseases, concomitant administration of
	muscle relaxants
The list of medicines	

The list of medicines

INN, (Trade name)	Medicinal form, dosage
Amycacine (Amycine)	Sol. for inj. 5 %
Gentamycine (Garamycine)	Sol. for inj. 1; 4 %
Canamycine	Sol. for inj. 5 %
Neomycine	Ointment 2 %
Streptomycine	Pwd. for inj. 0.5
Tobramycine	Sol. for inj. 1; 4 %

Glossary

Osteomyelitis is the inflammation of the bone marrow and relating bone tissue. **Sepsis** is a severe disease caused by continuous or periodical coming of microorganisms into the blood.

Glycopeptides Medicines

Vancomycine

Teicoplanine

Peculiarities of glycopeptides

1. Highly active against G^+ microflora, especially to methycillin-resistant staphylococci and enterococci.

2. The bactericidal type of action.

3. A slow development of microbes resistance and the absence of cross resistance with all other antibiotics.

The mechanism of action

Like β -lactam antibiotics, glycopeptides suppress the synthesis of the cellular wall peptidoglycane.

Pharmacodynamics (e	ffects) \rightarrow Indications
Antibacterial effect.	Severe hospital infections caused by resistant
The type of action is bactericidal.	strains of staphylococci; enterococci,
The spectrum of action is broad	streptococci resistant to penicillins; sepsis,
(including G ⁺ aerobic and	pneumonia, meningitis, endocarditis, infections
anaerobic microorganisms: strepto-	of the skin and soft tissues, bones and joints,
cocci, pneumococci, enterococci)	pseudomembranous colitis
Cida affaata	Contugin digations

Side effects	\rightarrow Contraindications
Nephrotoxicity	Dysfunction of the kidneys
Ototoxicity	Hearing disorders
Syndrome of "a red person"	Allergic reactions

The list of medicines

INN, (Trade name)	Medicinal form, dosage
Teicoplanine (Targocide)	Pwd. for inj. 0.2
Vancomycine (Vancocine)	Pwd. for inj. 0.5

Glossary

Syndrome of "a red person" is a syndrome accompanied by the rush of blood (and redness) to the face, neck, BP decrease, pain in the chest and back, dyspnea, rash (because of release of a great amount of histamine). This syndrome appears with a fast intravenous injection of glycopeptides.

ANTIBIOTICS OF DIFFERENT GROUPS

		Clubbi	jicanon oj i	<i>icultics</i>	
Lincosamides	Fus	idines	Chlorar	nphenicols	Rifamycines
Lincomycine	Fusi	dic acid	Chlora	mphenicol	Rifampicine
hydrochloride			Levosin	Levomecol	
Phosphomyc	ines	Poly	myxines	Oxazoli	dinones* and others
Phosphomycine		Polymyxi	ne B sulpha	te Linezolide *	^k Fusafungin
				Gramicidine	

Classification of medicines

The mechanism of action

Lincosamides, fusidic acid, chloramphenicols, oxazolidinones disturb the synthesis of bacterial proteins; rifamycine inhibits the synthesis of RNA; phosphomycines break the formation of a cellular wall. Polymyxines and gramicidine break the structure and function of cytoplasmatic membranes. Fusafungin suppresses colonization and adhesion of microorganisms on the mucous membrane of the upper respiratory tract.

Lincos	amides
Pharmacodynamics (effects) \rightarrow Indications
Antibacterial effect.	Reserve antibiotics in treatment severe
The type of action is bactericidal and	staphylococcal, streptococcal, anaerobic
bacteriostatic.	infections
The spectrum of action is broad (including	
G ⁺ microorganisms, anaerobes)	
Side effects –	Contraindications
Dyspepsia, pseudomembranous colitis.	Colitis. Liver diseases. Leukopenia,
Hepatotoxicity. Leukopenia, neutropenia,	neutropenia, thrombocytopenia
thrombocytopenia	
Chloran	phenicols
Pharmacodynamics (effects) \rightarrow Indications
Antibacterial effect.	Infections of the GIT, meningitis, gas
The type of action is bacteriostatic.	gangrene, plague, rickettsioses, typhoid,
The spectrum of action is broad (including	g abdominal and pelvis infections
G ⁺ microorganisms, anaerobes)	
Side effects –	Contraindications
Accumulation in the bone marrow. Pregna	ncy, lactation, children under 10, anaemias,
Inhibition of blood formation leukop	enia, HIV-infection
Fusi	dines
Pharmacodynamics (effects) \rightarrow Indications
Antibacterial effect.	Staphylococcal infections when
The type of action is bacteriostatic.	staphylococci are resistant to other
The spectrum of action is narrow	antibiotics and if there is allergy to β -
(staphylococci, anaerobes)	lactams
Side effects –	Contraindications
Dyspepsia	Diseases of the GIT
Oxazol	idinones
Pharmacodynamics (effects) \rightarrow Indications
Antibacterial effect. The type of action is	bacteriostatic. Pneumonia, endocarditis,
The spectrum of action is broad (including	ng G^+ aerobes, severe infections caused by
anaerobes, resistant to other antiobiotics)	enterococci
Side effects –	Contraindications
Anaemia, thrombophlebitis	Pregnancy, lactation
Increase of bilirubin level	Liver diseases

]	Polymyxi	nes			
Pharmacodynamics (effects)	\rightarrow	Indication	IS	
Antibacterial effect.		Severe G ⁻	infections ca	used by n	nulti-
The type of action is bactericidal.		resistant	hospital	strains	of
The spectrum of action is na	rrow (G ⁻	microorga	nisms		
bacteria, including Salmonellas,	cholera				
vibrion, blue pus bacillus)					
Side effects	\rightarrow	Contraindi	cations		
Nephrotoxicity Hepa	tic insuffic	ciency			
Neurotoxicity Myas	thenia,	pregnancy,	children	under	12,
admin	nistration of	of muscle re	laxants		

NB! Polymyxines are used only by vital indications because of their toxicity.

Rifamycines

Pharmacodynamics (effects)	\rightarrow Indications
Antibacterial effect.	Tuberculosis, leprosy, pneumonia,
The type of action is bactericidal.	infections of urinary and biliary tract,
The spectrum of action is broad	osteomyelitis, meningitis
(including G ⁻ microorganisms, chlamydia,	
tuberculous mycobacteria)	
Side effects \rightarrow	Contraindications
Hepato-, hematotoxicity Liver diseases. F	Pregnancy, age under 1 year old

Phosphomycines

Pharmacodynamics (effects)	\rightarrow Indications
Antibacterial effect.	Acute non-complicated infections
The type of action is bactericidal.	of urinary and biliary tract, sepsis,
The spectrum of action is broad (including G	meningitis
microorganisms)	
Side effects \rightarrow (Contraindications
Dyspepsia Child	lren under 5

Gramicidine

Pharmacodynamics (effects) \rightarrow Indications
Antibacterial effect.	Purulent inflammatory processes of the
The type of action is bactericidal.	skin and mucous membranes
The spectrum of action is moderate	
(including G ⁻ microorganisms)	
Side effects –	Contraindications
Contact dermatitis	Dermatitis

Fusafungin

Pharmacodynamics (effects) \rightarrow	Indications
Antibacterial effect.	Infections of the upper
The type of action is bacteriostatic.	respiratory tract

The spectrum of	of action is bro	oad (includin	$ng G^+$ and G	r-			
microorganisms	, anaerobes)						
	Side effec	ets —	→ Contra	indicatio	ns		
Nasopharynx	irritation,	laryngo-,	Children	under	2.5	years	old,
bronchospasm			laryngospa	ısm			

Comparison of the pharmacological "face" of antibiotics of different groups

Medicines	Spect-	Type of	Resistance	Toxi-	Peculiarities of
	rum	action		city	action
Lincosamides	В	Bs, bc	slowly	++	Accumulation in
					bones and joints
Polymyxine B	N(G)	Bc	_//_	++++	It is not absorbed
sulphate					from the GIT
Gramicidine	М	Bc	no	+++	Only local admi-
					nistration
Chloramphenicol	В	Bs	_//_	++++	GIT infections.
					Reserve A!
Fusidines	N	Bs	rapidly	++	Reserve A! 90% of
					bioavailability
Rifamycine	В	Bc	rapidly	++	Microsomal
					enzymes inductor. It
					is effective in TB
Phosphomycines	В	Bc	slowly	++	Infections of urinary
	$G^+ < G^-$				tract
Oxazolidinones	В	Bs	slowly	++	Severe infections
	$G < G^+$				
Fusafungin	В	Bs	no	+	Anti-inflammatory
					effect

A – antibiotic; B – broad, N – narrow, M – moderate; bc – bactericidal, bs – bacteriostatic; TB – tuberculosis

|--|

INN, (Trade name)	Medicinal form, dosage
Chloramphenicol (Levomycetine)	Tabl. 0.5, sol. 3 %
Fusafungin (Bioparox)	Aerosol 0.125 mg/dose
Fusidic acid	Tabl. 0.25, sol. 1 %
Gramicidine	Oint. 4 %
Levomecol	Oint. 30.0
Levosin	Oint. 40.0
Linezolide (Zyvox)	Tabl. 0.6, sol. for inj. 0.2 %
Lincomycine hydrochloride	Caps. 0.5, sol. for inj. 30 %
Phosphomycine	Pwd. 3.0
Polymyxine B sulphate (Polymyxine B)	Pwd. for inj. 0.05
Rifampicine (Rifadine)	Tabl. 0.6, caps. 0.6, syrup 2 %

Glossary

Colitis is an inflammatory disease of large intestine. **Rickettsiosis** is a disease caused by Rickettsiae (G⁻ microorganisms).

FLUOROQUINOLONES

By the chemical structure fluoroquinolones are synthetic antibacterial medicines, derivatives of quinolone, containing fluorine atoms in their structure. Nowadays fluoroquinolones are considered to be a serious alternative to highly active antibiotics of the broad spectrum of action when treating severe infections.

Classification of medicines

The I st generation	The II nd generation	The Ш rd generation
Norfloxacine	Levofloxacine	Moxifloxacine
Ofloxacine	Sparfloxacine	
Cyprofloxacine		

Peculiarities of the group

1. A unique mechanism of action and a strong bactericidal effect.

2. A super broad spectrum of the antibacterial action.

3. A good pharmacokinetics (a high bioavailability, the long period of elimination, all medicines are stable to acid).

4. A slow development of resistance in microorganisms.

5. The presence of the post-antibiotic effect.

6. A high efficiency in treatment infections of any location and a good tolerance in patients.

7. A possibility of application as empirical therapy in severe infections at hospital.

The mechanism of action

Fluoroquinolones inhibit DNA-gyrase (topoisomerase) of bacteria and it leads to disturbance of biosynthesis of DNA, RNA, and then of protein in a microbial cell.

Pharmacodynamics (effects	$s) \rightarrow Indications$
Antibacterial effect.	Infections of urinary and respiratory tract,
The type of action is bactericidal.	bones and joints, skin, soft tissues;
The spectrum of action is super broad	intestinal infections, sepsis; gonorrhea,
(including G^+ and G^- aerobic and anaerobic microorganisms, chlamydia, mycoplasmas, legionellas, mycobac- teria)	meningitis, chlamydiasis, tuberculosis
Side effects -	→ Contraindications
Chondrotoxicity	Persons under 18

Comparison of the pharmacological "face" of antibiotics (A) and fluoroquinolones

Antibio- tics group	Spect- rum	Type of action	Toxi- city	PAE	ICA	Resis- tance	Other peculiarities/ indications
Р	M*/B	bc	+	-		q	For peptic ulcer. A cross allergy with CS
CS	В	bc	++	+**			A cross allergy with P . A high resistance to β -lactamases
С	SB	bc	+++	+		S	A high resistance to β -
Μ	Ν	bc	+++	+		5	lactamases
Т	В	bs	+++	-	+	q	It is used for peptic ulcer
ML	В	bs	+	-	+		For peptic ulcer. The prolonged action
GP	В	bc	+++	+		n	They are used for pseudomembranous colitis
AG	В	bc	++++	+**			For tuberculosis treatment
F	SB	bc	+++	+	+	S	They have immuno- modulating effect

P – penicillins, CS – cephalosporins, C – carbapenems, M – monobactams, T – tetracyclines, ML – macrolides, GP – glycopeptides; AG – aminoglycosides; F – fluoroquinolones; B – broad; N – narrow, M – moderate, SB – super broad; bc – bactericidal, bs – bacteriostatic; PAE – post-antibiotic effect; ICA – intracellular activity; s – slowly, q – quickly, n – no; * - a moderate spectrum of action for natural penicillins; ** - only medicines of the III-IV generations.

J	
INN, (Trade name)	Medicinal form, dosage
Cyprofloxacine (Cyfran)	Tabl. 0.25
Levofloxacine	Tabl. 0.5
Moxifloxacine	Tabl. 0.4
Norfloxacine	Tabl. 0.4
Ofloxacine (Floxal)	Tabl. 0.2
Sparfloxacine	Tabl. 0.2

The list of medicines

Glossary

Chondrotoxicity is ability of medicines to cause pathological changes in a cartilage tissue (it is especially dangerous for children). **Gonorrhea** is an infectious venereal disease caused by gonococci with the primary affection of mucous membranes of urinary and genital organs. **Tuberculosis** is an infectious disease caused by mycobacteria with the formation of specific granulomas in tissues and organs, more often in lungs. **DNA-gyrase** is an enzyme, which provides superspiralisation of DNA.

ANTITUBERCULOUS MEDICINES

These are the medicines used for specific antituberculous therapy, which inhibit the growth and development of mycobacteria or cause their death. Antituberculous medicines are divided into first-line (main) medicines, which are highly effective and have low toxicity and second-line (reserve) medicines, which are less effective and more frequently cause side effects, but which are used in case of mycobacterial resistance to first-line medicines.

Classification of medicines				
First-line medicines				
Isonicotinic acid hydrazide and para-	Antibiotics and isonicotinic acid			
aminosalicylic acid* derivatives	thioamide derivatives*			
Isoniazide Phthivazide	Rifampicine Streptomycine sulphate			
Para-aminosalicylic acid (PASA)* Ethionamide*				
Second-line medicines				
Antibiotics and other drugs*				
Capreomycine sulphate Florimycine				
Cycloserine Ethambutol*				

There is also efficacy-based classification of antituberculous medicines: group A (most effective) – isoniazide, rifampicine; group B (effective) – streptomycine sulphate, ethambutol, ethionamide, cycloserine; group C (least effective) – PASA.

Mechanism of action

Isonicotinic acid hydrazide and isonicotinic acid thioamide derivatives form complexes with heavy metal ions, inhibit breathing and development of tuberculosis bacilli, disturb the synthesis of mycolic acid, which is the main structural component of cell wall of given pathogen. Para-aminosalicylic acid derivatives compete with PABA, which is essential for the growth and reproduction of mycobacteria. Antibiotics inhibit synthesis of mycobacterial proteins.

Pharmacodynamics (effects) \rightarrow Indications					
Tuberculostatic or tuberculocidal effect	Tuberculosis of various forms and				
	location				
Side effects \rightarrow (Contraindications				
Dyspepsia, CNS disorders	Peptic ulcer, acute gastritis, erosive-				
	ulcerous colitis; CNS diseases				

Pharmacological "face" of antituberculous medicines						
Medicine	Type of	Type of action		n of action	Activity	Toxicity
	Ts	Тс	Broad	Narrow		
Isoniazide	+	+		+	S	+++
Phthivazide	+			+	<s< td=""><td>+++</td></s<>	+++
PASA	+			+	<s< td=""><td>++</td></s<>	++
Rifampicine*	+	+	+		=s	++
Ethionamide*	+			+	<s< td=""><td>+</td></s<>	+
Streptomycine	+	+	+		<s< td=""><td>+++</td></s<>	+++
Capreomycine	+			+	<s< td=""><td>++</td></s<>	++

Ethambutol	+		+	<s< th=""><th>++</th></s<>	++
Florimycine	+	+		<s< td=""><td>++</td></s<>	++
Cycloserine	+	+		<s< td=""><td>++</td></s<>	++

* – are also used to treat leprosy; s – standard medicine; Ts – tuberculostatic action; Tc – tuberculocidal action.

The list of medicines				
INN, (Trade name)	Medicinal form, dosage			
Capreomycine sulphate	Pwd. 1.0			
Cycloserine	Caps. 0.25			
Ethambutol (Mycobutol)	Tabl. 1.0			
Ethionamide	Tabl. 0.25			
Florimycine	Sol. for inj. 0.5			
Isoniazide	Sol. for inj. 10%			
PASA (Aminacyl)	Sol. for inj. 3%			
Phthivazide	Tabl. 0.5			
Rifampicine	Sol. for inj. 5%			
Streptomycine sulphate	Pwd. 0.5			

The list of medicines

Glossary

Tuberculocidal type of action is an action resulting in tuberculosis mycobacteria death. **Tuberculostatic type of action** is an inhibition of growth and reproduction of tuberculosis mycobacteria.

SULPHONAMIDE MEDICINES

Sulphonamides are synthetic antibacterial medicines (sulphanylic acid amides) having the identical spectrum of the antimicrobial action and differing in the pharmacokinetic properties.

MONOCOMPONENT					
1. Resorptive-acting (absorbed in the intestine)					
Short-acting	Long-act	ing	Super long-acting		
Sulphanylamide	Sulphadimetho	oxine	Sulphamethoxipyrazine		
Sulphathiazole					
2. Acting in the intestine	3. Derivatives of		4. For external use		
(poorly absorbed from	sulphonamides and 5-				
the GIT)	aminosalicylic acid				
Phthalylsulphathiazole	Salazosulphap	yridine	Sulphacetamide		
			Silver sulphathiazole Maphenide		
COMBINED					
1. Resorptive-acting		2. For e.	xternal use		
(Sulphonamide+Trimethoprim)					
Co-trimoxazole		Algimaf	Streptonitol		

Classification of medicines

The mechanism of action

Sulphonamides are competitive antagonists of para-aminobenzoic acid (PABA) owing to their structural similarity. Imitating PABA sulphonamides in the certain concentration inhibit the synthesis of folic acid blocking dihydrofolate-synthetase enzyme and formation of dihydrofolic acid. Folic acid in the reduced form (tetrahydrofolic acid) participates in the synthesis of purine and pyrimidine bases that are necessary for formation of nucleic acids. As the result of disorder of the protein synthesis the process of the cellular division is slowed down, the bacteriostatic action develops.

Trimethoprim breaks the folic acid metabolism blocking dihydrofolatereductase enzyme and formation of tetrahydrofolic acid. When combining trimethoprim with sulphonamides stronger inhibition of nucleic metabolism and development of the bactericidal action take place.

The silver ion binds to DNA, accumulates on the surface of the bacteria nucleus and inhibits their growth and division, and when combining with sulphonamides it provides also the bactericidal action (silver sulphathiazole).



Fig. 6. The mechanism of the sulphonamide action

Pharmacodynamics (effects) \rightarrow	Indications
The antibacterial effect.	Infectious diseases: quinsy,
The type of action is bacteriostatic or bactericidal.	bronchitis, pneumonia, intes-
The broad spectrum of action: microorganisms that	tinal infections, cystitis,
synthesize the folic acid - staphylococci, strep-	urethritis, prostatitis, chole-
tococci, pneumococci, gonococci, meningococci,	cystitis, meningitis, otitis,
causative agents of intestinal infections	wound infection, malaria
(Salmonellas, Cholera vibrion, E.coli), chlamydias,	
protozoa (malarial plasmodium, toxoplasms)	

Side effects \rightarrow	Contraindications
Crystaluria, agranulocytosis, leukopenia;	Renal insufficiency, blood formation
teratogenicity	disorders; pregnancy, lactation

The principles of sulphonamides dosing include the intake of **loading doses** followed with **maintaining** ones, that is connected with the mechanism of their action. Breaking the dosing principles for sulphonamide medicines (the absence of loading doses and reduction or interruption of the course of treatment) leads to development of the microorganisms strains resistant to sulphonamides.

The antibacterial action of sulphonamides decreases in the presence of pus, blood, decomposed tissues where PABA and folic acid are in sufficient amount. That is why sulphonamides for external use are applied only on the preliminary cleaned wound. However, **maphenide**, the medicine that does not change its activity in the acid medium, is not inactivated by PABA and has the activity in an uncleaned wound. For crystaluria prevention sulphonamides should be taken with a plenty of weak alkaline drink decreasing the acidity of urine. The alkaline medium also promotes the sulphonamides transition in the ionic state and it facilitates the capture and assimilation of medicines by a microbial cell. Medicines should be taken on the empty stomach or between meals (in 2 h after the previous meal and 2 h before the following meal).

Medicines	Action		Absorption	Bs/Bc	Dose,
	duration	strength	in the GIT		g/day
Sulphanylamide	S	r	+++	+/-	3-6
Sulphathiazole	S		+++	+/-	3-4
Phthalylsulphathiazole	S		+	+/-	6
Sulphadimethoxine	1	≥r	+	+/-	1
Salazosulphapyridine	1		+	+/-	2
Sulphacetamide	sl		+++	+/-	
Silver sulphathiazole	sl	>r		+/+	
Co-trimoxazole	sl	>r		+/+	
Maphenide **	sl			+/-	
Algimaf**(C)	sl			+/-	
Streptonitol (C)		>r		+/-	

The pharmacological "face" of sulphonamides

S – short (to 8 h), 1 – long (8-12 h), sl – super long (24-48 h); r – reference; Bs – bacteriostatic, Bc – bactericidal, * - anti-inflammatory effect; ** - it can be used for treatment of an uncleaned wound; C – combined medicine.

INN, (Trade name)	Medicinal form, dosage
Algimaf	Gel
Co-trimoxazole (Bactrim, Biseptol)	Tabl. 0.48, syrup 48 mg/ml
Maphenide	Ointment 10 %
Phthalylsulphathiazole (Ftalazole)	Tabl. 0.5
Salazosulphapyridine (Sulphasalazine)	Tabl. 0.5

The list of medicines

Silver sulphathiazole (Argosulphan)	Cream 2%
Streptonitol	Ointment 15.0
Sulphacetamide (Sodium sulphacyl, Albucide)	Sol. 30%, ointment 30%
Sulphadimethoxine	Tabl. 0.5
Sulphamethoxipyrazine (Sulphalen)	Tabl. 0.2
Sulphanylamide (Streptocide)	Tabl. 0.5, ointment 10%
Sulphathiazole (Norsulphazole)	Tabl. 0.5

Glossary

Crystaluria is formation of crystals of insoluble acetylated derivatives of sulphonamides in kidneys with the further risk of stones formation (nephrolithiasis).

ANTIMALARIAL MEDICINES

Antimalarial (malariacidal) medicines is a group of antiprotozoal medicines used for prevention and treatment of malaria.

Malaria is collective name for the group of infections of the protozoal etiology. The cyclic course with changing the periods of acute fever attacks and interictal states (recurrences and remissions), splenohepatomegalia, anaemia, severe damage of the nervous system and other organs is characteristic for malaria. The causative agent (pathogen) of malaria is malarial plasmodium (P.), a representative of protozoa. Depending on the type of plasmodium, which causes the disease, and different time of the internal erythrocytic cycle of its development malaria can be defined as three days malaria caused by P.vivax and P. ovale, four days malaria caused by P. malariae and tropical one caused by P. falciparum. Any type of plasmodia has two cycles of development: asexual reproduction (schizogony) - in the human organism and sexual one (sporogony)- in the body of a female mosquito of the Anophales genus.

Classification of medicines					
Medicines acti (schizontocides	ng on schizogony s, schizontotropic)	Medicines acting on	Combined		
Affecting the tissue Affecting the		sporogony (agmontocides	medicines		
(histoschizontocides) erythrocytes)		<i>(gamontotropic)</i>			
	(hematoschizontocides)				
Pyrimethamine	Pyrimethamine	Pyrimethamine	Fansidar		
Proquanyl h/chl.	Proquanyl h/chl.	Proquanyl h/chl.	(Pyrimethamine +		
Quinocide	Chloroquine	Quinocide	sulphadoxine)		
Fansidar	Mefloquine	Mefloquine			
	Fansidar				

Classification of medicines

The mechanism of action

The main link in the mechanism of action of antimalarial medicines is disturbance of the nucleic acids synthesis and functions of the plasmodia.

Pharmacodynamics (effe	$ects) \rightarrow$	Indications
Antimalarial effect	Treatment and	d prevention of malaria

Side effects	\rightarrow Contraindications
Hepato- and nephrotoxicity	Diseases of the liver and kidneys
Teratogenicity	Pregnancy (especially the 1 st trimester)

Antimalarial medicines have their own peculiarities in usage. So, hematoschizontocides are used for stopping acute attacks of malaria and for treatment in the case of the chronic course of the disease. Histoschizontocides are taken for chemoprophylaxis of malaria recurrences. *Gamontotropics* (sporocides) are medicines for the total or epidemiological prevention of malaria.

When malarial plasmodia are stable to the main antimalarial medicines these medicines are prescribed in combination with sulphonamides or sulphones and it allows reducing their dose and the toxic effects, as well as increasing their efficiency.

Medicines	Resis- tance	Acti- vity	The rate of the	Accu- mula-	Other indi	ications	
	deve- lopment		effect's deve- lopment	tion	Protozoal infections	Non-infectious diseases	
Pyrimethamine	rapidly	>Q*	+	+	Toxo- plasmosis		
Proquanyl	rapidly		++	no			
Quinocide		>Q					
Chloroquine	slow	>Q	++	++		RA, SLE, TA	
Mefloquine			+	++			

The pharmacological "face" of antimalarial medicines

*-activity relating to the reference medicine of the group – quinine (Q), **RA** - rheumatoid arthritis, **SLE** - systemic lupus erythematosus, **TA** – tachyarrhythmia.

The list of medicines					
INN, (Trade name)	Medicinal form, dosage				
Chloroquine (Delagil, Quingamine)	Tabl. 0.25, sol. for inj. 5%				
Fansidar (Pyrimethamine + sulphadoxine)	Tabl., sol. for inj.				
Mefloquine	Tabl. 0.25				
Pyrimethamine (Chloridine)	Tabl. 0.01				
Proquanyl h/chl. (Bigumal)	Tabl. 0.1				
Quinocide	Tabl. 0.01				

The list of medicines

Glossary

Gamontotropic medicines (gamontocides, sporocides) are medicines that act on the sexual cycle of plasmodia development in the human body (from a mosquito gets in the human body and the sexual cycle completion). **Schizontocides** are medicines that act on non-sexual forms of plasmodia, which develop in the human body. They are divided into **hemato-** and **histoschizontocides,** i.e. medicines that act on erythrocytic and tissue non-sexual forms of plasmodia, respectively.

ANTISYPHILITIC MEDICINES

Antisyphilitic medicines act to the pale spirochete and are used for syphilis treatment.

	Bismuth-				
Penicillins	Penicillins Cephalosporins Macrolides and Tetracyclines				
		azalides*		medicines	
Benzylpenicillin	Cephaloridine	Erythromycine	Tetracycline	Biyoquinol	
sodium and		Azythromycine			
potassium salts					

Classification of medicines

The mechanism of action

Penicillins, cephalosporins inhibit the synthesis of the components of the spirochete cell wall (see "Antibiotics").

Macrolides, azalides, tetracyclines disturb the protein synthesis in the microbial cell (see "Antibiotics").

Bismuth-containing medicines block sulphohydryl groups of thiolic enzymes of the spirochetes and it causes inhibition of their tissue breathing resulting in death.

Pharmacodynamics (effects)	\rightarrow Indications
Antibacterial (antispirochetal) effect	Syphilis (all forms and stages)
Side effects \rightarrow	Contraindications
Bismuth-containing medicines: salivation,	Dysfunctions of the liver, kidneys,
"bismuth border" on the gums, stomatitis,	blood formation organs; pregnancy,
colitis, nephrotoxicity, leukopenia, pain in the	lactation
site of injection	

The pharmacological "face" of antisyphilitic medicines

Medicines	Type of		Type of		Type of H		Peculia-	Toxi-	Route of	Other
	action		rities of	city	administ-	peculiarities				
	Bc	Bs	action		ration					
Benzylpenicillin	+		All stages	+	p/e	AB of the medium				
			of syphilis			spectrum				
Cephaloridine	+			+	p/e	AB of the broad				
						spectrum				
Azythromycine	+	+	I, II stages	+	p/o	AB of the broad				
			of syphilis			spectrum				
Tetracycline		+		+++	p/o	AB of the broad				
						spectrum				
Biyoquinol			All stages	++	p/e	Anti-inflammatory				
			of syphilis			effect, used in non-				
						syphilitic diseases of				
						the CNS				

p/e- parenteral, **p/o** – peroral, **AB** – antibiotic.

The usi of medicines				
INN, (Trade name)	Medicinal form, dosage			
Azythromycine (Sumamed, Azythrocine)	Tabl. 0,5			
Benzylpenicillin sodium and potassium salts (Penicillin)	Pwd. for inj. 1000000 U			
Biyoquinol	Susp. 8%			
Cephaloridine	Pwd. for inj. 0.25			
Erythromycine	Tabl. 0.2			
Tetracycline	Tabl. 0.1			

The list of medicines

Glossary

Syphilis is an infectious disease caused by the pale spirochete. **Stomatitis** is inflammation of the mucous membrane of the oral cavity.

ANTIHELMINTHIC MEDICINES

Antihelminthic (helminthicide) medicines are used to treat and prevent helminthiases (helminthic invasions).

The majority of helminthiasis pathogens belong to nemathelminths (round worms, nematodes), flatworms (cestodes), flukes (trematodes). Helminthiases are respectively divided into nematodoses, cestodoses and trematodoses. Helminths parasitize in GIT (intestinal helminths), other organs: liver, gall bladder, blood and lymphatic vessels, subcutaneous fat (extraintestinal parasites).

Ascarids, seatworms, hookworms, whipworms are nematodes that most frequently parasitize human intestines and cause ascariasis, enterobiasis, ancylostomiasis and trichocephaliasis respectively.

Medicines used in intestinal nematodoses	Medicines used in intestinal cestodoses and	Medicines used in extraintestinal
(*-broad spectrum ones)	trematodoses*	helminthiases
Mebendazole*	Aminoacrichine	Prasiquantel
Albendazole*	Prasiquantel	Mebendazole
Pyrantel	Mebendazole	Albendazole
Levamisole	Ethylene tetrachloride*	
Prasiquantel*		
Tansy flowers		

Classification of medicines

Mechanism of action

Pyrantel, levamisole, aminoacrichine disturb the neuromuscular system functions in helminths. **Albendazole** and **mebendazole** disturb metabolic processes in helminths. **Prasiquantel** increases calcium ion permeability of cell membranes of helminths promoting the increase of their muscular tone turning into spastic paralysis. **Ethylene tetrachloride** has paralizing effect on helminths. Antihelminthic effect of **Tansy flowers** is caused by volatile oils present there.

Pharmacodynamics (effects) \rightarrow Indications		
Antihelminthic effect	Helminthiases (according to spectrum of action)	

Side effects \rightarrow Contraindications		
Dyspepsia	Ulceration of GIT, liver diseases	

Effective and safe use of antihelminthic medicines requires strict dosing regimen, special diet, simultaneous administration of laxatives, proper treatment scheme. As a rule, dosing and administration methods of any given antihelminthic medicine differ depending on the kind of helminthiasis. Mebendazole, Pyrantel, Prasiquantel do not require any preparation and special diet, administration of laxatives is also unnecessary. However, use of Ethylene tetrachloride and Tansy flowers requires special diet and administration of laxatives.

As a rule, helminths do not develop resistance to medicines, and even in cases of recurrent invasions administration of the same medicine leads to full recovery. In the majority of cases in treatment of intestinal helminthiases it is recommended to use medicines on empty stomach to ensure maximal contact of the medicine with the parasite.

Medicines	Indications				
	Ascaria-	Entero-	Cesto-	Trichocepha-	Ancylo-
	sis	biasis	doses	liasis	stomiasis
Albendazole	+	+	+	+	+
Aminoacrichine			+		
Levamisole*	+				
Mebendazole	+	+	+	+	+
Pyrantel	+	+			+
Prasiquantel			+		

Pharmacological "face" of antihelminthic medicines

* - it has immunostimulating effect.

The list of medicines				
INN, (Trade name)	Medicinal form, dosage			
Albendazole	Tabl. 0.2			
Aminoacrichine	Tabl. 0.3			
Ethylene tetrachloride				
Levamisole (Decaris)	Tabl. 0.05			
Mebendazole (Vermox)	Tabl. 0.1			
Prasiquantel (Drontsit)	Tabl. 0.6			
Pyrantel (Combantrin)	Tabl. 0.25, susp. 5%			
Tansy flowers	Pack 75.0			

The list of medicines

ANTIFUNGAL MEDICINES

Antifungal medicines are medicines used to treat fungous diseases (mycoses) and which in therapeutical dose, depending on pathogen kind, have fungicidal and/or fungistatic effect.

Classification of medicines					
Antifungal antibiotics					
Polyene structure ones and others*					
Amphoterycine B Nystatin					
Natamycine	Griseof	ulvin*			
Antifungal medicines of synthetic origin					
Azoles (imidazole	N-methylnaphtha-	Undecylenic acid	Combined		
and triazole*	lene derivatives,	derivatives	medicines		
derivatives)	pyrimidines*				
Clotrimazole	Terbinafine	Zincundan	Clion D		
Ketoconazole	Flucytosine*		Pimafucort		
Miconazole					
Fluconazole*					
Itraconazole*					

Mechanism of action

The majority of antifungal medicines inhibit the main enzymes of ergosterol synthesis. Ergosterol is the main component of fungous cell wall, whereas in human cells cholesterol is the main steroid.

Pharmacodynamics (effects) \rightarrow Indications					
Antifungal effect.	Systemic	and local			
Type of action: fungicidal and/or fungistatic	mycoses				
Side effects \rightarrow Contraindications					
Dyspepsia, teratogenicity (associated with resorp	otive GIT	diseases,			
effect)	pregnano	су			

Amphoterycine B, itraconazole, fluconazole, ketoconazole have broad spectrum of antifungal activity.

Pharmacological "face" of antifungal medicines

Medicines	Effects		Mycoses		Absorption	
	fc	fs	antimicrobial	local	systemic	in GIT
Amphoterycine	+			+	+	+
Nystatin	+			+	+	Ŧ
Natamycine	+			+		
Griseofulvin		+		+		
Clotrimazole	+	+	+	+		
Ketoconazole	+	+	+	+	+	+
Miconazole	+	+	+	+		
Fluconazole	+	+	+	+	+	+
Itraconazole	+	+	+	+	+	+
Terbinafine		+	+	+		
Flucytosine		+	+	+		
Zincundan		+	+	+		
Clion D	+	+	+	+		

 \mathbf{fc} – fungicidal effect, \mathbf{fs} – fungistatic effect.

INN, (Trade name)	Medicinal form, dosage
Amphoterycine B (Amphocyl)	Tabl. 0.01
Clion D	Vaginal tabl.
Clotrimazole (Antifungol)	Cream 1%, sol. 1%
Fluconazole (Diflucan)	Caps. 0.1
Flucytosine (Ancotil)	Tabl. 0.5
Griseofulvin	Tabl. 0.5
Itraconazole (Orungal)	Caps. 0.1
Miconazole (Dactarin)	Cream 2%
Natamycine (Pimafucine)	Cream 2%
Nystatin (Mycostatin)	Tabl. 500000 IU; ointment 100000 U/g
Pimafucort	Ointment 15.0
Terbinafine (Lamisil)	Cream 1%
Zincundan	Ointment

The list of medicines

Glossary

Local mycoses are fungous diseases developing in the site of pathogen invasion, e.g. skin (dermatomycosis), nail (onychomycosis), hairy area of the head (trichomycosis), mucous membranes mycoses. **Systemic mycoses** are fungous diseases, in which the pathogen while circulating in blood affects different organs simultaneously (e.g. generalized candidiasis, histoplasmosis, blastomycosis etc.). **Fungicidal effect** is the ability of the medicine to cause death of a fungous cell. **Fungistatic effect** is the ability of the medicine to inhibit growth and reproduction of a fungous cell.

ANTIVIRAL MEDICINES

Antiviral medicines are medicines used to prevent and treat viral diseases.

Anomalous nucleosides	Adamantane and other groups* derivatives	Pyrophosphate analogues
Acyclovir	Remantadine	Sodium foscarnet
Ribavirine	Amantadine	
Gancyclovir	Oxolin*	
Famcyclovir		
Interferons and	Interferon synthesis	HIV- proteinase and
immunoglobulins*	inducers	reverse transcriptase
_	(interferonogens)	inhibitors*
Interferon-(α -1, α -2B,	Cycloferon	Saquinavir
β-1Β)	Amixin	Nelfinavir
Normal human	Inosine pranobex	Didanosine*
immunoglobulin*	_	Zidovudine*

Classification of medicines

Mechanism of action

The main mechanism of the drug antiviral action is to inhibit an early stage of specific viral replication after their penetration into a human cell. Adamantane derivatives inhibit viral RNA release from protein, altering RNA penetration into cell nucleus. Anomalous nucleosides inhibit viral RNA and DNA synthesis. Pyrophosphate analogues inhibit viral DNA-polymerase. Interferons block viral-specific protein synthesis. Interferon synthesis inducers stimulate synthesis of endogenous interferon in human body. Interferon synthesis in human cells is human organism's natural mechanism of protection against viruses. HIV-proteinase inhibitors inhibit viral proteinase through binding to specific receptors. Reverse transcriptase inhibitors disturb the process of replication and viral DNA formation through reverse transcriptase inhibition.

Pharmacodynamics (effects) \rightarrow Indications				
Antiviral effect (all drugs).	ARVI, herpes, influenza A, B;			
Immune-stimulating effect (interferons,	encephalomyelitis, cytomegaloviral			
immunoglobulins, interferon synthesis	infections, viral pneumonias, chickenpox,			
inducers)	conjunctivitis, viral hepatitis (A, B, C),			
	chlamydiasis			
Antiretroviral effect (antiviral effect	HIV-infection			
against HIV-infection)				
Side effects \rightarrow (Contraindications			
Nephro- and hepatotoxicity,	Renal and hepatic failure, pregnancy and			
teratogenicity, CNS disorders (tremor,	lactation, epilepsy			
hallucinations, convulsions)				

Medicines	Herpes simplex and herpes zoster	Influenza	Cytome- galoviral infection	Hepatitis	Oncoviruses	Dissemina- ted sclerosis	Tickborne encepha-litis	HIV-infec- tion
Acyclovir	+		+	A, B, C				
Remantadine		А						
Amantadine		А						
Foscarnet	+		+					
Ribavirine	+	A, B						
Gancyclovir		А, В,	+					
		Р						
Famcyclovir	+							
Oxolin	+	А						
Interferon-α-		A, B		Β, C, Δ	+	+	+	
2B								
Immunoglo-	+			A				
bulin								

Pharmacological "face" of antiviral medicines

Cycloferon	+	A, B,	+	A, B,	+	+	+	+
		Р		C, Δ				
Amixin	+	A, B,	+	A, B, C		+		
		Р						
Inosine	+		+	B, C		+		
Saquinavir								+
Nelfinavir								+
Didanosine								+
Zidovudine								+

P – para-influenza, Δ – delta.

INN, (Trade name)	Medicinal form, dosage		
Amantadine (Midantan)	Tabl. 0.1		
Amixin	Tabl. 0.125		
Acyclovir (Aclovir, Herpex, Zovirax)	Tabl. 0.4, pwd. for inj. 0.25, ointment 5%		
Cycloferon (Neovir)	Sol. for inj. 0.125 g/ml		
Didanosine (Videx)	Tabl. 0.025		
Famcyclovir (Famvir)	Tabl. 0.25		
Gancyclovir	Caps. 0.25		
Inosine pranobex (Groprinosine)	Tabl. 0.5		
Interferon β -1B (Betaferon)	Lyoph. pwd. for inj. 9600000 U		
Interferon α -2B (Viferon)	Supp. 150000 IU		
Interferon-α-1	Sol. for inj. 6000000 IU		
Normal human immunoglobulin	Sol. 1.5 ml		
Nelfinavir (Virasept)	Tabl. 0.25		
Oxolin	Ointment 3%		
Remantadine (Flumadine)	Tabl. 0.05, syrup 10 mg/ml		
Ribavirine	Tabl. 0.2		
Saquinavir (Invirase)	Caps. 0.2		
Sodium foscarnet (Triapten)	Cream 2%		
Zidovudine (Azatidine, Zidosan,	Tabl., caps. 0.1, 0.25		
Retrovir)			

The list of medicines

Glossary

Chickenpox is an infectious disease characterized by fever and vesicular rash. **HIV-infection** is a disease developed as a result of human immunodeficiency virus contamination and causing a state called "acquired immunodeficiency syndrome, AIDS". **Herpes** is a viral disease caused by herpes viruses and characterized by vesicular rash appearing on skin and/or mucous membranes (herpes simplex) and along the nerve (herpes zoster). **Influenza** is a severe viral respiratory disease. **Interferons** are endogenous species-specific low-molecular proteins produced in cells as a response to viral, antigenic affection on the organism and protecting organism from being contaminated. **Teratogenic effect** is a negative effect of a medicine on a fetus resulting in possible severe abnormalities development. **Encephalomyelitis** is a brain or cerebrospinal inflammation.

XV. ANTITUMOUR MEDICINES

Antitumour (antiblastic, antineoplasm, etc.) medicines are medicines that suppress the development of atypical cells of true tumours (cancer, sarcoma, etc.) and hemoblastoses (leukemia, etc.).

Antitumour medicines are widely used in the oncological practice supplementing surgery and radiation therapy, and they are the only method of treatment in some tumourous processes (leukemia, lymphogranulomatosis).

Classification of medicines								
			1. A	lkylating comp	ounds			
Deriva	itives	of	D	erivatives of	Derivatives of	Derivatives of		
chloret	hylam	ine	e	thylenimine	sulphonic acid	nitrosourea,		
						hydroxyurea		
Chlorethylaminouracil		Thio	phosphamide	Busulphan	Nimustine			
Cyclophosph	namic	le	Phos	phemide		Hydroxycarba-		
				_		mide		
N	letal-	organic c	отроі	unds	Other alkylati	Other alkylating compounds		
Cisplatin					Dacarbazine			
			2	2. Antimetaboli	tes			
Antagon	ists o	of the		Antagonist	s of the	Antagonists of		
folio	c acid	!		purine b	ases	pyrimidine		
Methotrexate	e		Merc	captopurine		Fluorouracil		
		3.	Cytos	statics of the pla	ant origin			
Alkaloids of	f Vin	ca rosea		Alkaloids of Po	odophyllum	Alkaloids of		
(vinca a	lkalo	oids)		(podophyll	otoxins)	Colchicum		
						speciosum		
Vincristine		Podo	Podophylline		Colchamine			
Terpenoids of Taxus tree (taxozides)								
Paclitaxel								
4. Hormonal and antihormonal medicines								
Gestagens		Estrogens	1	Antiestrogens	Androgens	Antiandrogens		
Megestrol	Ethy	ynylestrad	liol	Tamoxyphen	Testosterone	Ciproterone		
					propionate	acetate		
A	nalog	gues of go	nadoli	iberin	Inhibitors of	Inhibitors of adrenal cortex		
					hormones	hormones biosynthesis		
Gozerelin					Aminoglutetim	ide		
5	. Ant	titumour	antibi	iotics	6. Inhi	bitors of		
				-	topoisomeras	e I, aromatase*		
Actinomyci	nes	Anthi	a-	Phleomycines	Topothecan	Anastrozol *		
		cyclin	es					
Dactinomyci	ine	Doxorub	icine	Bleomycine				
		7. Cytok	kins		8. Ei	8. Enzymes		
Aldesleukin					L-asparaginase	L-asparaginase		
	9. Recombinant monoclonal antibodies							
				Trastusumab				

The mechanism of action

Alkylating medicines are nitrogenous compounds, whose mechanism of action is connected with transferring the alkyl radical to the receptor of other molecule. Quaternary ammonium derivatives with a high reactivity, which are forming, react (alkylate) with such physiologically important groups of the cell molecules as amino-, sulphohydryl-, hydroxyl-, phosphatic ones. As a result, the latter ones lose their possibility to participate in metabolic processes. Besides, alkylating medicines suppress the biosynthesis of nucleic acids and the ability of tumour cells to divide, damage mitochondrial membranes, alter the processes of oxidation and phosphorylation, break irreversibly the structure and the functions of tumour cells in any functional stage.

Antimetabolite medicines are similar to metabolites by their chemical structure: they are modified molecules of aminoacids, purines and pyrimidines, i.e. precursors of nucleic acids, folic acid, vitamins and hormones. The mechanism of action of antimetabolites is an ability to form competitively the bonds with receptors instead of the normal metabolites. Antimetabolites substitute them in biochemical reactions but they cannot perform their functions. As a result, the course of the vital biochemical processes in the cell, in particular the DNA and RNA synthesis inside a tumour cell, becomes slow. Thus, antimetabolites become pseudometabolites for the cells, metabolically inactive or even toxic substances. Sometimes this process is called "the lethal synthesis".

The action of **cytostatics** of the plant origin is explained by their ability to block the cell mitosis in the phase of metaphase and inhibit the DNA synthesis. Medicines bind to tubuline, the protein of microtubules, inhibit the formation of the mitotic spindle and as a result the cell division is blocked.

Camptothecines – irinothecan and topothecan – have been obtained from the plant Camptothecana acuminata for the first time. According to their mechanism of action they are **inhibitors of topoisomerase I**, which takes part in the DNA synthesis and provides its spacious configuration, reparation if damaged, replication and transcription. As a result, the growth of tumour cells is inhibited.

Hormonal medicines form complexes with hormonal receptors, penetrate into the cell nucleus, bind to chromatin and break the synthesis of nucleic acids in target cells (sensitive to a certain hormone).

So, gestagens and androgens suppress the production of the pituitary gonadotropins and it leads to the inhibition of the estrogen synthesis. The analogues of gonadoliberin turn off the hormone-synthesizing function of testes and ovaries (i.e. cause the pharmacological castration). Antiestrogens bind specifically to estrogen receptors of the mammary gland tumours. As a result, the stimulating effect of the endogenous estrogens disappears. Antiandrogens block competitively androgen receptors in target tissues and it leads to the suppression of the physiologic activity of endogenous androgens. Inhibitors of aromatase block the enzyme aromatase in the peripheral tissues and it leads to the decrease of the estradiol amount. Aminoglutetimide inhibits the biosynthesis of corticosteroids, as well as estrogens and androgens.

Antitumour antibiotics form stable complexes with the cell DNA that leads to disorder of the DNA-dependent synthesis of RNA and replication of the tumour cell.

The mechanism of their cytotoxic action is related with the introduction (intercalation) between two DNA filaments, inhibition of topoisomerase II, and formation of free radicals. Hence, another name of these medicines is **intercalants**.

Cytokins stimulate cytotoxic T-killers and natural killers and it is accompanied by the release of γ -interferon, interleukin-2 (mediators of immune reactions).

The enzymatic medicine **L-asparaginase** decreases the L-asparagine synthesis, which is important for the growth of tumour cells.

Trastusumab, which contains recombinant humanised monoclonal antibodies to the receptor of the epidermal growth factor, inhibits selectively the proliferation of malignant cells.

Pharmacodynamics (effects) \rightarrow Indications				
Antitumour medicines have cytosta	tic, cytotoxic and Tumours of different			
immune-suppressive effects (all, exce	ept hormonal and location			
antihormonal ones).				
Hormonal and antihormonal med	icines retard the			
division of hormone-dependent tumour	cells and promote			
their differentiation, have androge	enic (androgens),			
antiandrogenic (antiandrogens, estro	gens), estrogenic			
(estrogens), antiestrogenic (gestagen	ns, antiestrogens,			
inhibitors of the adrenal glands horm	ones biosynthesis)			
effects; inhibit hormone synthesizing function of testes				
and ovaries - cause the pharmacological castration				
(analogues of gonadoliberin); cause th	e pharmacological			
andrenalectomy (aminoglutetimide)				
Side effects \rightarrow Contraindications				
Inhibition of the blood formation	n, Inhibition of the hemopoiesis, immune			
immune suppression, dyspepsia	a; deficiency, peptic ulcer (with caution);			
mutagenicity, teratogenicity	pregnancy, lactation			

The pharmacological "Jace" of	aniiumour meaicines (A)
Indications	Medicines
Leukosis (leukemia)	1, 2, 3, 4, 5, 10, 11, 13, 16, 26, 27, 30
Cancer of the uterus	2, 7, 8, 9, 10, 11, 12, 13, 17, 19, 20, 24,
	25, 26
Cancer of the stomach	8, 12, 24, 25, 26
Mammary gland cancer	1, 2, 8, 10, 12, 13, 16, 17, 19, 20, 22, 23,
	25, 28, 30, 31
Lung cancer	2, 6, 7, 8, 10, 13, 24, 25, 26
Lymphogranulomatosis	1, 2, 7, 8, 9, 13, 24, 25, 26, 30
Tumours of the brain	6, 7, 27, 26
Melanoma	6, 7, 9, 13, 24
Cancer of the esophagus	6, 14, 16
Cancer of the penis	26
Cancer of the thyroid gland	25, 26
Cancer of the ovaries	2, 7, 8, 10, 12, 17, 19, 20, 21, 22, 23, 25,

The pharmacological "face" of antitumour medicines (A)

	26
Cancer of the prostate	2, 8, 10, 12, 17, 19, 20, 24, 25, 26
Sarcoma	2, 8, 9, 10, 13, 24, 25, 26
Cancer of the urinary bladder	2, 8, 12, 13, 16, 25
Skin cancer	15, 26
Cancer of the pancreas	12, 25
Cancer of the liver	25
Cancer of the testicle	2, 8, 24, 26
Cancer of the kidney	2, 10, 13, 29, 24, 26
Cancer of the head, neck	7, 8, 10, 12, 13, 16, 25, 26, 27
Cancer of the adrenal cortex	8
Ewing's tumour	2, 10, 9
Myeloma	2, 9, 10, 25, 29
Lymphosarcoma, T-cells lymphoma,	30, 7*
ervthremia*	

Numbers 1-31 are the numbers of medicines in classification.

I ne pnarmac	ological face of antitumour medicines (B)	
Medicines	Peculiarities	
Chlorethylaminouracil	Hypocholesterolemic effect	
Cyclophosphamide	It is a "premedicine", also used in autoimmune diseases	
Bisulphan	Resistance to the medicine can appear	
Nimustine	They penetrate through the blood-brain barrier	
Hydroxycarbamide		
Cisplatin	It doesn't penetrate through the BBB	
Methotrexate	Anti-inflammatory effect, it is used in dermatosis,	
	rheumatoid arthritis	
Mercaptopurine	It is used in autoimmune diseases, resistance develops	
	quickly	
Fluorouracil	It is quickly inactivated and it requires frequent intakes	
Podophylline	Laxative, choleretic effects	
Paclitaxel	Treatment of multiple idiopathic hemorrhagic sarcoma in	
	AIDS patients	
Megestrol	It is used in anorexia and cachexia	
Ethynylestradiol	It is used in hormonal disorders of non-tumour origin	
Testosterone		
Cyproterone acetate	Male hypersexuality, female hyperadrogenisation	
Gozerelin	Depo-medicine (introduced once a month)	
Aminoglutetimide	Anticonvulsant effect, decreases the synthesis of GC, MC	
	It is used in hypocorticism, hypertension	
Doxorubicine	Cardiotoxicity	
Bleomycine	It increases the sensitivity of a tumour to radiation therapy	
Aldesleukin	It has the immune-modulating effect	

The pharmacological "face" of antitumour medicines (B)

INN, (Trade name)	Medicinal form, dosage
L-asparaginase	Pwd. for inj. 10000 U
Aldesleukin (Proleukin)	Pwd. for inj. 0.0012
Aminoglutetimide (Mamomit)	Tabl. 0.25
Anastrozol (Arimidex)	Tabl. 0.001
Bleomycine (Bleocine)	Pwd. for inj. 0.015
Busulphan (Myelosan)	Tabl. 0.002
Chlorethylaminouracil (Dopan)	Tabl. 0.002
Cisplatin (Platidiam)	Sol. for inj. 0.1%
Colchamine	Tabl. 0.002, ointment 0.5%
Cyclophosphamide	Tabl. 0.05, pwd. for inj. 0.5
Cyproterone acetate (Ciprostat)	Tabl. 0.01, sol. for inj. 10%
Dacarbazine (Biocarbazine)	Pwd. for inj. 0.1
Dactinomycine	Sol. for inj. 0.05%
Doxorubicine (Adriablastin)	Pwd. for inj. 0,01
Ethynylestradiol (Microfollin)	Tabl. 0.01
Fluorouracil (Flurox)	Sol. for inj. 5%
Gozerelin (Zoladex)	Tabl. 0.0036
Hydroxycarbamide	Caps. 0.5
Megestrol	Tabl. 0.04
Mercaptopurine	Tabl. 0.05
Methotrexate (Trexan)	Tabl. 0.005, sol. for inj. 1%
Nimustine	Pwd. for inj. 0.05
Paclitaxel (Taxol)	Concentrate for inj. 6%
Phosphemide	Pwd. for inj. 0.02
Podophylline	Pwd. 100.0
Tamoxyphen	Tabl. 0.02
Testosterone propionate (Andriol)	Sol. for inj. 5%
Thiophosphamide (Thiotepa)	Pwd. for inj. 0.01
Topotecan (Gicamptine)	Sol. for inj. 0.004
Trastusumab	Pwd. for inj. 0.44
Vincristine (Onkovin)	Sol. for inj. 0.1%

The list of medicines

Glossary

Adrenalectomy is the removal of the adrenal glands. Immune-suppressive effect is inhibition of the antibody production and the immune response. Cytostatic effect is the action that precedes the cytotoxic effect and is revealed as retardation of the tumour cell growth. Cytotoxic effect is destruction of the nucleus and death of growing tumour cells in the state of division.

XVI. IMMUNOSTIMULANTS

Immunostimulants are used in the states of immune deficiency, chronic infections, in some cancer diseases, etc.

Medicines Group **Origin**/ Pharmacological «face» composition They normalize T-lymphocytes and Polypeptide Thymalin Tactivin fractions their ratio with B- lymphocytes, from the catcellular immunity reactions; increase tle's thymus activity of natural killers. the intensify phagocytosis and production of lymphokins. They are used in burns, trophic ulcers, inhibition of hemopoiesis, immunity, in radiation **Endoge**and chemotherapy nous It stimulates proliferation and the Myelopid polypep-Cell culture functional activity of T- and B-killers. tides of bone marrow of calves. It is used in secondary immune deficiency states (the humoral pigs immunity), for prevention of complications after operations and traumas Immunofan Synthetic It stimulates interleukin-2 formation. hexopeptide decreases the production of the tumour necrosis factor, regulates the production of immunity mediators and immunoglobulins. It is used in immune deficiency states Levamisole **Synthetic** Imidazole It regulates differentiation of Tmedicines derivative lymphocytes, promotes the synthesis of immunoglobulins (see "Antihelmint hic medicines") Polyoxydo-**Synthetic** Immune-stimulating, detoxication nium polymer effects **Microbial** It stimulates the humoral and cellular Broncho-Bacteria munal medicines immunity, increases the amount and lyophylic lysate activity and their of lymphocytes and analogues immunoglobulins A, G, M, cytokins in the mucous membrane of the respiratory tract. It is used in infections of respiratory tract. resistant to the antibiotic therapy

Pharmacological description

Prodigiosan		Complex from microorganis ms <i>B.</i> prodigiosum	It increases non-specific and specific resistance of an organism (activates B- lymphocytes, interferons, lysocim, complement). It is used in chronic in- flammations, poor healing of wounds, radiation therapy
Interferon α, β*, α-2a, β- 1b*	Interfe- rons	Natural and recombinant*	It has antiviral, anti-inflammatory, immune-stimulating effects. It is used in herpes, hepatitis B, C, HIV- infection, influenza and ARVI, etc.
Amixin	Interfe- ron synthesis inducers	Low- molecular synthetic agent	A broad spectrum of the antiviral action against DNA- and RNA- containing viruses (see "Antiviral medicines")
Poludan		The biosynthetic polyribonucle ic complex	It affects viruses of a simple herpes (herpes conjunctivitis, keratitis, iridocyclitis, etc.)
Cycloferon		Low- molecular compound	Antiviral (see "Antiviral medicines"), anti-inflammatory, immune-stimula- ting, antichlamydial, radioprotective effects. It is used in tick-borne encephalitis, herpes, cytomegalovirus and HIV-infections; in collagenoses
Roncoleukin	Inter- leukins	Recombinant analogue of interleukin-2	Immune-stimulating, antitumour effects. It increases proliferation of T-lymphocytes and interleukin-2-dependent acids, cytotoxicity of lymphocytes and killers of tumour cells, production of γ -interferon, interleukin-1, the tumour necrosis factor. It is used in cancer of kidneys
Betaleukin		Recombinant human interleu- kin-1	Increases leukopoiesis and immunity. Used in chemo- and radiation therapy of tumours, immune deficiencies
Molgra- mostim, Filgrastim, Lenograstim	Colony- stimula- ting factors	Recombinant human colony- stimulating factors	See "Leukopoiesis stimulants"

Normal hu-		Immunoglobulin G	It is used in immune
man immuno-			deficiency states,
globulin			thrombocytopenic purpura,
	Human		etc.
Pentaglobin	immuno-	Immunoglobulin G en-	It is used in severe bacterial
	globulins	riched by im-	infections (sepsis), immune
		munoglobulins M, A	deficiencies
Cytotect		Specific hyperimmune	It is used in cytomegaloviral
		immunoglobulins G	infections
Hepatect		against the certain	It is used in hepatitis B
		pathogens	

The list of medicines

INN, (Trade name)	Medicinal form, dosage
Amixin	Tabl. 0.125
Betaleukin	Lyoph. pwd. for inj. 0.001
Bronchomunal	Caps. 0.0035
Cycloferon	Sol. for inj. 12.5%, tabl. 0.15
Cytotect	Sol. for inj. 10%
Hepatect	Sol. for inj. 50 U/ml
Immunofan	Sol. for inj. 0.005%
Interferon α	Lyoph. pwd. for inj. 1 mln U
Interferon β	Lyoph. pwd. for inj. 1 mln U
Interferon-α-2a (Roferon A)	Lyoph. pwd. for inj. 3 mln U
Interferon-β-1b (Betaferon)	Lyoph. pwd. for inj. 9600000 U
Myelopid	Lyoph. pwd. for inj. 0.003
Normal human immunoglobulin	Sol. for inj. 5%
Pentaglobin	Sol. for inj. 5%
Poludan	Lyoph. pwd. 100 U
Polyoxydonium	Lyoph. pwd. for inj. 0.003
Prodigiosan	Sol. for inj. 0.005%
Roncoleukin	Lyoph. pwd. for inj. 0.001
Tactivin	Sol. for inj. 0.01%
Thymalin	Lyoph. pwd. for inj. 0.01

Glossary

Interleukins (IL) is a group of lymphokins acting as growth and differentiation factors of lymphocytes (approximately 20 of them have been described) and they perform complex of intercellular interactions involved into the immune response. **Immunoglobulins (Ig)** is the class of proteins structurally related that participate in immune reactions (being antibodies by their functions). **The tumour necrosis factor (TNF)** is a cytotoxin produced by macrophages that causes necrosis of some tumours and activates neutrophils stimulating the synthesis of cytokins.

XVII. MEDICINES FOR DYSBIOSIS TREATMENT

Up to 90% of microbes of the large intestine are bifidobacteria, which have a positive effect on the activity of GIT organs, cardiovascular system, blood formation, immunity; improve digestion of proteins, carbohydrates, fats; provide absorption of vitamins E, K, B, PP, D and the synthesis of aminoacids, antibodies, immunoglobulins, interferon and cytokins. The normal microflora of the large intestine supports pH=5.3-5.8 and because of this the pathogenic putrefactive and gas-forming microflora perishes. Decompensated dysbiosis (dysbacteriosis) (indication for these medicines), dysfunction of the normal microflora composition (in particular, the intestinal) is the result of a severe intestinal infection or use of the incorrect scheme of chemotherapeutics administration.

Medicines					
normalizing the flora:	stimulating the normal	inhibiting the conditional			
probiotics -	flora growth:	pathogenic microflora:			
monocomponent,	prebiotics and symbi-	bacteriophages and			
polycomponent *,	otics*	others*			
combined **					
Lactobacterin	Potassium permanganate	Staphylococcal and			
Bactisubtil	Hilak-forte	pseudomonal			
Linex*	Lactulose	bacteriophages			
Bificol*	Bifiform*	Fluconazole*			
Bifidumbacterin forte*		Natamycine*			
		Ketoconazole*			

Classification of medicines

The mechanism of action						
Promote the formation of	Decrease pH of the large	Destroy the conditional-				
the acetic, lactic acids in	intestine. Contain the	pathogenic flora;				
the intestine inhibiting the	components necessary for	fungicidal and fungistatic				
putrefactive and gas- nutrition and reproduction		effects against Candida				
forming flora	of bifidobacteria and	fungi				
	lactobacteria					

Pharmacodynamics

	in macouy munnes	
Support the balance of the normal	Stimulate the growth and	Antibacterial,
microflora; reduce meteorism,	reproduction of the	antifungal
normalize digestion and	normal microflora of the	effects
absorption in the intestine;	intestine, strengthen the	
promote the organism's resistance	peristalsis of the GIT	
to infection		

Side effects	\rightarrow Contraindications	
Seldom – dyspepsia (all); meteorism	Infants before 6 months (Bificol); liver	
(Lactulose, Fluconazole);	diseases, pregnancy, lactation	
hepatotoxicity (Fluconazole)	(Ketoconazole); porphyria (Natamycine);	
	intestinal obstruction	

Side effects and contraindications have not been determined for Bactisubtil, Bifidumbacterin forte, Bificol, Bifiform, Potassium permanganate, Lactobacterin and Linex.

Medicines	Dysbiosis			Other indications		
	Com-	Subcom- Decom-		Acute	Diarrhea	Chronic
	pensa-	pensated	pensated	intestinal	in	entero-
	ted			infections	children	colitis
All, except	+	+	+	+**	Hilak-	+*
Fluconazole [@] ,					forte,	
Natamycine [@] ,					Lactobac	
Ketoconazole [@]					-terin	

The pharmacological "face" of medicines for dysbiosis treatment

* - except bacteriophages inhibiting conditional pathogenic flora; ** - only probiotics; [@] - except dysbiosis it is used in mycoses.

INN, (Trade name)	Medicinal form, dosage
Bactisubtil	Caps. 0.035
Bificol	Packs
Bifidumbacterin forte	Packs
Bifiform	Caps.
Fluconazole	Tabl. 0.2
Hilak-forte	Liquid 100ml
Ketoconazole	Tabl. 0.2
Lactobacterin	
Lactulose	Pwd. 10.0
Linex	Caps.
Natamycine	Tabl. 0.1, cream 30.0, supp. 2.5%
Potassium permanganate	Pwd. 3.0
Staphylococcal and pseudomonal	
bacteriophages	

The list of medicines

Glossary

Probiotics are medicines, which contain living weak microorganisms. **Prebiotics** are substances of non-microbial origin, which promote the growth and development of the normal intestinal microflora. **Symbiotics** are combined medicines containing probiotics and prebiotics.

XVIII. ANTI-ALLERGIC MEDICINES

Anti-allergic medicines are medicines for prevention and treatment of allergic diseases.

Traditionally allergic reactions (hypersensitivity reactions) are divided into: **immediate type reactions** (they develop in some minutes after the repeated contact with an allergen): anaphylactic shock, angioneurotic edema, serum disease, urticaria, pruritus, pollen fever; **retarded** (slow) **type reactions** (they are revealed in 2-3 days

and more): reaction of graft rejection, contact dermatitis, autoimmune diseases. Histamine takes the specific place in the pathogenesis of allergic reactions. It is contained mainly in the Erlich mastocytes (located along the tiny vessels, in the bronchial tissue, in the intestine), as well as in basophiles, leukocytes and it is inactivated by histaminase. Histamine is the natural ligand of 4 subtypes of histamine receptors: H₁-, H₂-, H₃- and H₄-receptors. Allergic reactions are connected with stimulation of H₁-receptors located in the smooth muscles of the bronchi, intestine, biliary and urinary tracts, heart and blood vessels. In ordinary conditions histamine is found in the inactive (bound) state, but in allergic reactions the quantity of free histamine sharply rises, and it leads to activation of H₁-histamine receptors, which is revealed in the increase of the smooth muscles tone of the bronchi, intestine and uterus; decrease of the blood pressure (partially), increase of the capillaries permeability with the edema development, hyperemia and pruritus development. Serotonin together with histamine takes part in the development of all allergic reactions. The peripheral action of serotonin is connected with the stimulation of serotonin receptors, that leads to contraction of the smooth muscles of the uterus, intestine and bronchi, and contraction of blood verssels; increase of the thrombocytes aggregation.

Cussification of meaternes					
Blockers of H ₁ -histamine receptors		Blockers of serotonin [*] receptors,			
		combined**	^a gents		
Promethazine	Clemastine	Ciproheptad	ine*		
Terfenadine	Loratadine	Clarinase**			
Diphenhydramine					
Membrane stabilizers	Glucocorticosteroids		Selective antagonists of		
			leukotriene receptors		
Cromoglycic acid	Prednisolone	e	Zafirlucast		
	Triamcinolo	ne acetonide			

Classification of medicines

The mechanism of action

Medicines of this group cause their anti-allergic effect affecting different links of the allergy pathogenesis.

Antihistaminic medicines (blockers of H_1 -histamine receptors) block H_1 -receptors due to competitive antagonism with histamine and eliminate the increased sensitivity of the cell membranes (especially smooth muscles) to the free histamine. **Ciproheptadine** blocks histamine and serotonin receptors and decreases production of cytokines. **Membrane stabilizers** block the calcium ions flow into mastocytes inhibiting their degranulation and, thus, preventing the release of the mediators of allergy and inflammation: histamine, bradykinin, serotonin and other biologically active substances. The mechanism of action of **glucocorticosteroids** in the allergic inflammation is decrease of histamine and serotonin synthesis; potentiation of the catecholamines effects; inhibition of cholinergic effect; inhibition of plasma and granulocytes leaving from capillaries; decrease of the amount of leukocytes, eosinophils, neutrophils, lymphocytes in the site of inflammation; inhibition of the phospholipase A_2 activity (as a result the release of the arachidonic acid and the

formation of its metabolites are prevented, in particular leukotrienes and a slow reacting substance of anaphylaxis). Selective antagonists of leukotriene receptors are competitive antagonists of LTC_4 -, LTD_4 - and LTE_4 - receptors (components of a slow reacting substance of anaphylaxis). Clarinase is a combined medicine containing pseudoephedrine and loratadine. Loratadine blocks H_1 -histamine receptors, pseudoephedrine reduces edema of the mucuos membranes.

Pharmacodynamics (effec	ts) \rightarrow Indications
Anti-allergic effect	Allergic reactions (anaphylactic shock,
	bronchial asthma, dermatitis, angioneurotic
	edema, etc.)
Side effects	\rightarrow Contraindications
Inhibition of the CNS (decrease of	The activity that requires attention,
attention, sedative effect), cardiotoxic	craniocerebral trauma, hypertension, liver
effect, hypotension	diseases, pregnancy, lactation

Medicines	Recep-	Effects			Duration	Other effects
	tors blockers	Spas- mo-	Seda- tive	Anti- inflam-	of action	
		lytic		matory		
Promethazine (I)	H ₁ +H ₂	+	+	+	8-12	Local anesthetic, potentiating,
C_1 (I)					C 10	пурнонс
Clemastine (1)	H_1+H_2	+	+	+	6-10	
Ciproheptadine	H_1+H_2	+	+	+	8-12	Appetite increase
Terfenadine (II)	H ₁	+			12-24	
Loratadine (II)	H ₁	+		+	12-24	Antipruritic
Cromoglycic acid		+		+	2-4	
Prednisolone		+		+	8-12	Immunity decrease
Triamcinolone acetonide		+		+	8-12	Immunity decrease, antipruritic
Zafirlucast				+	12	Incompatible with food. A strict doctor's control is necessary
Diphenhydramine (I)	H ₁ +H ₂	+	+	+	4-6	Potentiating, hypnotic

The pharmacological "face" of anti-allergic medicines

I, II –generations of histamine-blockers

INN, (Trade name)	Medicinal form, dosage
Ciproheptadine (Peritol)	Tabl. 0.004
Clarinase	Tabl.
Clemastine (Tavegil)	Tabl. 0.001
Cromoglycic acid (Intal)	Aerosol 2%, sol. 2%
Diphenhydramine (Dimedrol)	Tabl. 0.05, sol. for inj. 1%
Loratadine (Claritine)	Tabl. 0.01
Prednisolone	Tabl. 0.001, ointment
Promethazine (Diprasine, Pipolfen)	Tabl. 0.005, sol. for inj. 2.5%
Terfenadine	Tabl. 0.06
Triamcinolone acetonide (Fluorocort)	Ointment 0.025%
Zafirlucast (Acolat)	Tabl. 0.02

The list of medicines

Glossary

Allergy (in Greek *allos* is "other" and *ergon* is "action") is a state of the organism's increased sensitivity to the repeated affection of allergens. Leukotrienes are the class of biologically active substances synthesized in the arachidonic acid cascade, which take part in the development of allergic and inflammatory reactions. A slow reacting substance of anaphylaxis is substances produced by mastocytes during an allergic reaction (the mixture of leukotrienes C_4 , D_4 , E_4) causing a slow contraction of smooth muscles, which is more prolonged than that caused by histamine.

XIX. MEDICINES THAT USED IN POISONINGS (ANTIDOTES)

Antidotes are medicines that are able to make a poison (which is in blood or bound to biological substrates) harmless in case of intoxication and/or remove the toxic effects of a poison or accelerate its elimination.

Medicines	The	Pharmacodynamics	Indications
	mechanism of		(poisonings)
	action		
Activated	Absorption of a	Decrease of the poison	Food toxical infection,
carbon,	poison	absorption in the GIT,	poisoning by orally
Polyphepan		its elimination	administered poisons
Dipyroxim,	Restoration of	Normalization of the	Poisoning by irreversible-
Isonitrosine	the	cholinergic	acting anticholinesterase
	cholinesterase	neurotransmission	medicines, FOC
	activity		
Unithiol	Formation of	Reduction of the	Poisoning by heavy
	low toxic water	thiolic enzymes	metals, cardiac
	soluble	activity, binding to	glycosides, arsenic
	complexes with	thiolic poisons	
	thiolic poisons		
Calcium	Formation of	Elimination of a	Poisoning by metals
trisodium	chelate	poison in form of	
pentetate, Sodium Calcium edetate, Sodium edetate	complexes with 2-, 3-valency metals	stable poorly dissociated non-toxic complexes	
---	--	--	--
Sodium nitrite, Amylnitrite	Conversion of hemoglobin into methemoglobin, which reacts cyanides well with	Binding of cyanides	Poisoning by cyanides
Methylene blue	Depending on the dose it plays the role of donor or acceptor of electrons	Conversion of methemoglobin into hemoglobin in small doses, transfering of hemoglobin into methemoglobin in high doses	Poisoning by cyanides, nitrates, aniline and carbon monoxide
Ethyl alcohol (ethanol)	Retardation of the methanol	Decrease of formation of highly toxic formaldehyda	Poisoning by methanol
Atropine sulphate	Blockade of M- cholinorecep- tors	Decrease of parasympathetic effects	Poisoning by direct-acting cholinomimetics
Neostigmine methylsulphate	Reversible inhibition of acetylcholine- esterase	Increase of parasympathetic effects on the internal organs	Poisoning by atropine, belladonna-containing medicines, antidepola- rizing myorelaxants
Nalorphine	Antagonism with opiate receptors	Removal of the narcotic analgesics effects	Poisoning by narcotic analgesics (the group of morphine)
Bemegride	Direct stimulation of the respiratory and vasomotor centres	Stimulation of breathing, increase of the blood pressure	Poisoning by hypnotics (barbiturates), other CNS depressants
Protamine sulphate	Antagonism with heparin	Increase of blood coagulation	Overdosage of heparin
Flumazenyl	Competitive blockade of benzodiazepine receptors	Removal of the tranquilizers effects; anticonvulsant effect	Overdosage of benzodiazepine tranquilizers

FOC- phosphorus-containing organic compounds (insecticides).

Besides the medicines mentioned diuretics, plasma substituted medicines, methods of hyperbaric oxygenation and hemodyalysis are used in poisonings. To restore the life important functions, if it is necessary, analeptics, hypertensive, antiarrhythmic and other medicines, as well as apparatuses for artificial ventilation of lungs are used.

INN, (Trade name)	Medicinal form, dosage	
Activated carbon (Carbolong)	Tabl. 0.25	
Amylnitrite	Sol., amp.	
Atropine sulphate	Sol. for inj. 0.1%	
Bemegride	Sol. for inj. 0.5%	
Calcium trisodium pentetate (Pentacine)	Sol. for inj. 5%	
Dipyroxim	Sol. for inj. 15%	
Ethyl alcohol (Ethanol)	Liquid, vial 50 ml (as antiseptic)	
Flumazenyl	Sol. for inj. 0.01%	
Isonitrosine	Sol. for inj. 40%	
Methylene blue	Sol. for inj. 1%	
Nalorphine	Sol. for inj. 0.5%	
Neostigmine methylsulphate (Proserin)	Sol. for inj. 0.05%	
Polyphepan (Entegnine)	Pwd., packs 10.0	
Protamine sulphate	Sol. for inj. 1%	
Sodium calcium edetate (Tetacine-calcium)	Sol. for inj. 10%	
Sodium nitrite	Sol. for inj. 1%	
Sodium edetate (Trilon B, EDTA)	Sol. for inj. 5%	
Unithiol	Sol. for inj. 5%	

The list of medicines

Glossary

Phosphorus-containing organic compounds (insecticides: chlorophos, dichlophos and others) are substances of agricultural and household chemistry, however, they are similar to irreversible-acting anticholinesterase medicines by the mechanism of action and the symptoms of poisoning.

XX. MEDICINES OF DIFFERENT PHARMACOLOGICAL GROUPS

Since therapy of many diseases is complex, and many medicines have a wide spectrum of pharmacological action, there are pharmacological groups or separate medicines, which belong to several pharmacological groups simultaneously. Along with the main effects that are characteristic for the certain group, they have some additional pharmacological properties used for pharmacological correction of various diseases. Besides, modern classification of medicines often forms the so-called «combined groups» where there are medicines, representatives of different pharmacological groups. Therefore, it is necessary to systematize these medicines in one section (see tables).

Group	It is described in the corresponding groups or in table 2*
Hypertensive	Analeptics, psychomotor stimulants, adaptogens,
medicines	adrenomimetics (α_1 , $\alpha + \beta$). Dophamine*,
	Angiotensinamide*
Gastroprotectors	Antiulcer medicines (bismuth-containing medicines,
	astringents, covering medicines, cytoprotectors –
	prostaglandins analogues)
Inhibitors of	Enzymatic and anti-enzymatic medicines (Aprotinine);
proteases (anti-	medicines increasing blood coagulation (Aminocapronic
enzymatic)	acid)
Prokinetics	Domperidone*, Methoclopramide*
Anti-aggregants	Medicines decreasing blood coagulation (Aspirin,
	Dipyridamol, Ticlopidine). Abcyximab*
Cholelitholytic	Hepatoprotectors (Ursodeoxycholic acid).
medicines	Chenodeoxycholic acid*
Cholagogue	Hepatoprotectors (Flamine). Allochol*, Himechromone*
(choleretic)	
medicines	
Normothymics	Anticonvulsants (Carbamazepine, valproates), calcium
	antagonists (Verapamil, Dilthiazem, etc see anti-anginal,
	hypotensive, anti-arrhythmic medicines). Salts of lithium*
	(carbonate, gluconate, chloride, etc.)
Antidiarrheal	Inhibitors of hypophysis hormones secretion (Synthetic
medicines	somatostatin*). Nifuroxaside*, Hilac forte *, Smekta*,
	Loperamide*
Enzymatic medicines	Pancreatic enzymes; medicines decreasing blood
	coagulation (fibrinolytics). Hyaluronidase*, Trypsin*,
	Cytochrome C *, Penicillinase*, Deoxyribonuclease*
Immunotropic:	- glucocorticosteroids, antitumour medicines (alkylating
- immunodepressants	medicines, antibiotics, etc.), antibiotics. Thymoglobulin*,
	Azathioprin*, Daclizumab*, Cyclosporin*
- immunostimulants	- Antihelminthic (Levamisole), antiviral (interferons and
	their inducers), leukopoiesis stimulants, immunostimulants,
	hypotensive medicines (bendazole)

Table 2

The pharmacological "face" of medicines

Hypertensive (stimulant of dophamine receptors, α , β -AR). It acts
dose-dependently: in small doses it dilates vessels of the kidneys and
intestine; in average ones it has the cardiostimulating effect, increases
the coronary blood flow; in high doses - \uparrow TPVR, constricts renal
vessels. It is used in hypotension, shock of different etiology

Angiotensi-	Hypertensive (amide of the natural angiotensin II). \uparrow TPVR,
namide	secretion of adrenaline and aldosterone. It is used in shock and
	related vasomotor collapse
Domperi-	Prokinetics (D ₂ -dophamine receptors blocker). It intensifies the GIT
done	peristalsis, has anti-emetic effect. It is used in dyspepsia with the
	gastro-enteral reflux, esophagitis: nausea and vomiting of various
	genesis
Metho-	Prokinetics (blocker of dophamine and serotonin receptors). It
clopramide	regulates the tone and peristalsis of the GIT. It has anti-emetic.
	antinausea effects. It is used in intestinal paresis, nausea and
	vomiting after operation, radiation and chemotherapy
Abcyximab	Anti-aggregant (contains monoclonal antibodies). It inhibits non-
	competitively binding of fibring on to glycoproteins IIb/IIIa in the
	membrane of thrombocytes, disturbs their aggregation. It is used to
	prevent thromboses
Chenode-	Cholelitholytic. It decreases the synthesis, absorption of cholesterol
oxycholic	and formation of cholesterol stones in the gallbladder. It is used in
acid	cholelithiasis
Allochol	Cholagogue (choleretics). It contains bile, extracts of garlic and
	belladonna, activated carbon. It intensifies formation and excretion of
	bile. It is used in hepatites, cholecystitis
Himechro-	Cholagogue (synthetic choleretics). It intensifies reflexively bile
mone	secretion, prevents formation of stones, has spasmolytic effect on the
	biliary tract. It is used in dyskinesia of the billiary tract, cholecystitis,
	hepatitis with cholestasis
Lithium	Normothymics. They correct the mood disorders, have antimaniac
salts	and antidepressant effects. They are used during phasic psychotic
	mood disorders
Synthetic	Antidiarrheal. It decreases secretion of somatotropin and insulin,
somatosta-	production of gastric juice, inhibits the GIT peristalsis. It is used in
tin	intractable diarrhea, acromegalia, tumours of the gastro-entero-
	pancreatic system
Nifuroxa-	Antidiarrheal (synthetic antibacterial). It is used in bacterial
side	diarrhea
Hilac forte	Antidiarrheal (embryoless water substrate of metabolism products of
	the normal intestinal microflora). It normalizes the microflora in
	dysbiosis, diarrhea
Smekta	Antidiarrheal (adsorbing agent). It stabilizes the mucous bicarbonate
	barrier of the mucous membrane of intestine and stomach, protects it
	from aggression of food, microbial toxins, hypersecretion; prevents
	the affection of digestive enzymes on it. It is used in diarrhea
Loperamide	Antidiarrheal (agonist of the peripheral opiate receptors). It is used
	in diarrhea
Trypsin	Enzymatic (proteolytic enzyme). It dilutes viscous secretions,

	exudates, blood clots, splits, necrotized tissues due to the destruction		
	of peptide bonds in protein molecules. It is used for expectoration, in		
	burns, purulent wounds, commissure processes, iridocyclitis		
Deoxyri-	Enzymatic (proteolytic enzyme). See "Trypsin" + antiviral effect. It		
bonuclease	is used in bedsores, keratitis, conjunctivitis		
Hyaluroni-	Enzymatic medicine . It increases tissue permeability decreasing		
dase	viscosity of hyaluronic acid; softens scars, removes contractures in		
	joints, hematomas. It is used in hematomas, contractures in joints,		
	rheumatoid arthritis		
Cytochrome	Enzymatic. It improves tissue breathing, restores oxidative processes.		
C	It is used in asphyxia of newborns, chronic pneumonia, HF, IHD,		
	hypoxia		
Penicilli-	Enzymatic . It inactivates penicillins destroying the β -lactam ring. It		
nase	is used in acute allergy caused by penicillins		
Thymoglo-	Immunodepressant (polyclonal antibodies, antithymocytic		
bulin	immunoglobulin). It is used in rejection of the transplant,		
	transplantation of organs, aplastic anaemia		
Azathioprin	Immunodepressant (synthetic cytostatic-antimetabolite). It is used		
	for prevention the tissue incompatibility when transplanting organs, in		
	autoimmune diseases (rheumatoid arthritis, systemic lupus		
	erythematosus, etc.)		
Daclizumab	Immunodepressant (monoclonal antibodies to interleukin-2		
	receptors). It suppresses interleukin-2-dependent proliferation of T-		
	lymphocytes, inhibits the immune response to antigens. It is used to		
	prevent rejection of a kidney while transplantation		
Cyclosporin	Immunodepressant (antibiotic). Cyclic peptide that inhibits		
	production of interleukin-2, and it leads to decrease of differentiation		
	and proliferation of T-lymphocytes. It is used in transplantation of		
	organs, the bone marrow transplantation, autoimmune diseases		

Ethyl alcohol (Ethanol)

Pharmacodynamics	(effects) —	> Indications
Locally:		
Antibacterial, antiseptic	Disinfection of	the injection's site, instruments
	and hands	
Irritating	As a part of rub	bing, compresses in inflammatory
	diseases of the	locomotor organs
Resorptively:		
Foam-extinguishing		Pulmonary edema (as inhalation)
Antishock		Shock (seldom)
Antidote in poisonings by methanol (inhibition		Poisoning by methanol
of highly toxic formaldehyde formation)		

Ethyl alcohol is of the limited interest for medical practice. It is applied mainly as a preservative in the pharmaceutical industry and as an antiseptic. High concentrations of the alcohol locally cause protein denaturation of the skin and mucous membranes. Its negative resorptive action is connected with the influence on the central nervous system as it causes dose-dependent action: the CNS stimulation (euphoria) \rightarrow the CNS inhibition (hypnotic effect, analgesia) \rightarrow narcosis. The alcohol is not used as general anesthetic and analgesic because of the narrow interval of the therapeutic action. It causes addiction, mental and physical dependence, chronic poisoning (alcoholism). As the result of inhibition of antidiuretic hormone formation, diuresis increases. It influences on the thermoregulation (increase of heat emission, vasodilation, heat loss, feeling of heat), increases salivary and digestive glands secretion (reflex and direct action on glands), decreases the stomach motility

THE LIST OF ABBREVIATIONS

aer.	Aerosol
ACE	Angiotensin-converting enzyme
ACh	Acetylcholine
ACTH	Adrenocorticotropic hormone
ADH	Antidiuretic hormone
AIDS	Acquired immune deficiency syndrome
amp.	Ampoules
AR	Adrenoreceptors
ARVI	Acute respiratory viral infections
ASA	Acetylsalicylic acid
ATP	Adenosine triphosphate
BA	Bronchial asthma
BAS	Biologically active substances
BBB	Blood-brain barrier
CG	Cardiac glycosides
BHP	Benign hyperplasia of prostate
cAMP	Cyclic adenosine monophosphate
caps.	Capsules
ChR	Cholinoreceptors
CS	Cholesterol
CNS	Central nervous system
COG	Cyclooxygenase
СОМТ	Catechol-O-methyltransferase
BP	Blood pressure
CSF	Colony-stimulating factor
DNA	Deoxyribonucleic acid
dr.	Drage
EH	Essential hypertension
extr.	Extract
for inj.	For injections
FSH	Follicle-stimulating hormone
GABA	Gamma-aminobutyric acid
GC	Glucocorticosteroids
GIT	Gastro-intestinal tract
HC	Hypertensive crisis
h/chl.	Hydrochloride
HDLP	High density lipoproteins
	Heart failure
	Human immunedeficiency virus
	Intracranial pressure
	Iscnemic neart disease
	International name
1/m	intramuscularly

IOP	Intraocular pressure	
i/v	Intravenously	
LDLP	Low density lipoproteins	
LH	Luteinizing hormone	
LTH	Lactotropic hormone	
lyoph.	Lyophilised	
MAO	Monoamine-oxidase	
MC	Mineral corticosteroids	
MCSH	Melanocyte-stimulating hormone	
MI	Myocardial infarction	
NA	Noradrenaline	
NNA	Non-narcotic analgesics	
NSAIDs	Non-steroidal anti-inflammatory drugs	
OA	Opioid analgesics	
OR	Opiate (opioid) receptors	
PABA	Para-aminobenzoic acid	
PASA	Para-aminosalicylic acid	
PG	Prostaglandins	
pwd.	Powder	
RNA	Ribonucleic acid	
s/c	subcutaneous	
sol.	Solution	
STH	Somatotropic hormone	
supp.	Suppository	
susp.	Suspension	
tabl.	Tablets	
TG	Triglyceride	
tinct.	Tincture	
TPVR	Total peripheral vascular resistance	
TTH	Thyrotropic hormone	
VLDLP	Very low density lipoproteins	
\downarrow	Decrease	
↑	Increase	