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

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 3^{rd} up to the 10^{th} 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 III^{rd} 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.

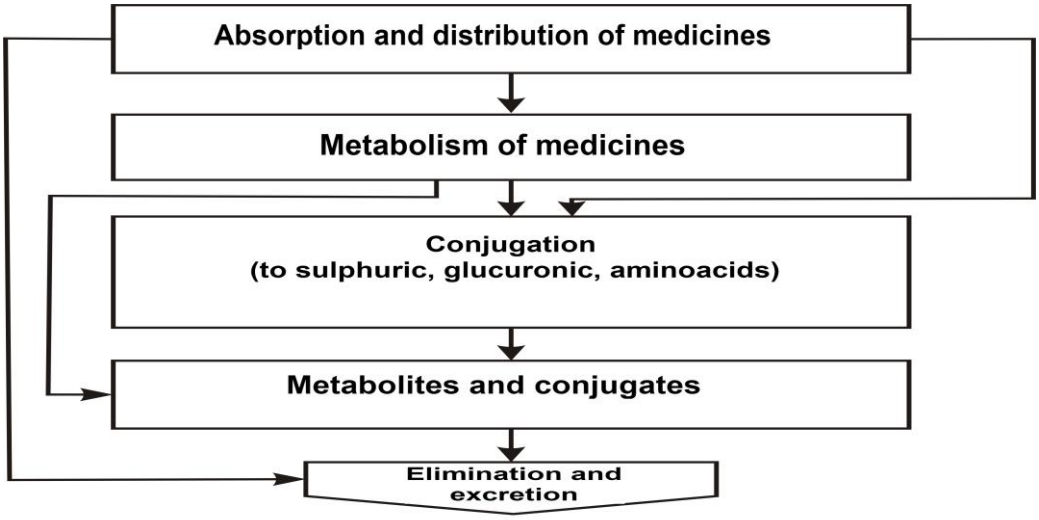

Fig. 1. Steps of pharmacokinetics

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.

Classification of medicines

Local anesthetics, expectorants, laxatives, bitters - see other chapters			
Astringent°, coating*, antacid agents**		**Adsorbents**	**Containing volatile oils**
Of plant origin:	**Salts of metals:**	Activated carbon	Menthol
Oak bark°	Aluminium phosphate***	Enterosgel	Espol
Sage leaves°	Colloidal bismuth subcitrate°**	Diosmectit	Mustard seeds
Chamomile flowers°	Almagel***		Menthol in bromisovalerianate
Tannin°	Vicalin°**		
	Anacid***		

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)	→ ***Indications***
Coating and gastro-protective (salts of metals); antacid (antacids); antimicrobial, astringent, anti-inflammatory and antiseptic (plant origin ones)	Inflammatory diseases of the gastrointestinal tract: enterites, gastrites, peptic ulcer, etc.
Astringent, anti-inflammatory, antiseptic, sudorific, wound healing (plant origin agents)	Catarrhal-inflammatory diseases: tonsillitis (fauces), laryngitis (vocal cords), 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, antiseptic (plant origin agents)	Food poisonings
Sedative, spasmolytic (menthol, validol)	Migraine, angina pectoris
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 Benzocaine	Benzofurocaine	Articaine 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) →	***Indications***
Local anesthetic	Different types of the local anesthesia
Side effects →	***Contraindications***
Hypotension, convulsions, disorders in the cardiac conduction system	Hypotension, epilepsy, 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.

The pharmacological "face" of local anesthetics

Medicines	**Anes-thesia**	**Perme-ability**	**Toxi-city**	**Effect**		
				antiar-rhythmic	*hypoten-sive*	*central analgesic*
Procaine	+	++	±	+	+	
Benzocaine	+		±			
Benzofuro-caine	++	+++	±			+
Articaine				+	+	
Lidocaine	++	+++	++	+	+	
Trimecaine	++	+++	+			

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

Normal functions of the efferent nerves are provided by such neurotransmitters (mediators) as acetylcholine, noradrenaline, adrenaline, dophamine. Medicines, which action is similar or opposite to these 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 → depolarization → 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.

Table 1

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

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

Classification of medicines

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

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) →	***Indications***
Local action: IOP decrease, myosis, the accommodation spasm	Glaucoma (except N-cholinomimetics)
Resorptive action: increase of the smooth muscles tone of the GIT, uterus, gall and urinary bladder, increase of the exocrine glands secretion; reflex stimulation of the respiratory centre (stimulation of the carotid sinus N-ChR)	Atony of the GIT, uterus, urinary bladder; radiography of the GIT (except N-cholinomimetics). Asphyxia (N-cholinomimetics only)

Side effects	→	*Contraindications*
BP decrease, bradycardia, bronchospasm		Hypotension, bradycardia, bronchial asthma (BA)

The pharmacological "face" of direct-acting cholinomimetics

Medicines	**Action**				**Peculiarities**
	Strength	*Duration*	*Resorptive*	*Local*	
Acetylcholine	+	+	+	-	not introduced iv
Carbacholine	++	++	+	+	
Pilocarpine	+	+	-	+	toxic
Aceclydine	++	++	+	+	
Cytisine	++	+	+	-	↑ respiration ↑ BP
Lobeline	++	+	+	-	

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

The pharmacological "face" of indirect-acting cholinomimetics

Medicines	**Action**				**Side effects**
	Strength	*Duration*	*Resorptive*	*Local*	
Galanthamine	+	++	+	-	+
Physostigmine	+	+	+	+	++
Neostigmine	++	+	+	+	++
Armine*	+++*	+++*	-	+	+++

*- in glaucoma only.

The list of medicines

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**.

M-cholinoblockers

Classification of medicines

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

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

The pharmacological "face" of M-cholinoblockers

Medicines	**Action**					**Peculiarities**
	Strength	Duration	Re-sorp-tive	Lo-cal	Spas-mo-lytic	
Atropine sulphate	A (refe-rence)	8 days•	+	+	+++	↓ M_1-ChR (of the stomach), M_2-ChR (of the heart), M_3-ChR (of the eyes)

Homatropine hydrobromide	<A	1,5 days•	-	+	-	↓M_3-ChR (of the eyes)
Scopolamine hydrochloride	<A	4 days•	+	+	++	Sedative, hypno-tic, inhibition of motion sickness
Platyphyllin hydrotartrate	<A	5 hours•	+	+	+++	Sedative, ↓BP
Methacine iodide	≥A		+	-	++++	Tocolytic
Ipratropium bromide	<A	8 hours*	±	+	+++	↓ M_3-ChR (of the bronchi, nose)
Pirenzepine	<A	8 hours**	+	-	±	↓ M_1-ChR (of the stomach)
Tropicamide	<A	3-4 hours•	-	+	-	↓ M_3-ChR (of the 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) →	***Indications***
Dilation of arterial vessels and the BP decrease (the **postload** on the myocardium decreases), improvement of the blood circulation and microcirculation in the vessels of the extremities	Hypertension, the HC reduction, artificial (controlled) hypotension in the surgery of the vessels that is the most dangerous by vast bleedings, surgery of heart and in neurosurgery
Dilation of the venous vessels, decrease of **preload** to the myocardium and the pressure in the pulmonary circulation	Endarteritis, Raynaud's disease, the pulmonary and brain edema
Blockade of the cardiovascular reflexes both pathological (for example, in shock, infarction) and compensatory ones	In surgery for decreasing the risk of the shock development risk
Decrease of the gastric juice secretion, motility and peristalsis of GIT organs	Ulcer of the stomach and duodenum, spastic colitis
Stimulation of the uterine contractions and tone	Labour induction (Pachicarpine hydroiodide)
Side effects →	***Contraindications***
Tachycardia, orthostatic collapse, atony of intestine and urinary bladder, IOP increase, dry mouth, dizziness (vertigo), general weakness	Myocardial infarction at the acute stage, marked hypotension, atony of the stomach and the intestine, glaucoma, pregnancy, atherosclerosis, thrombosis

The pharmacological "face" of Ganglionic blockers

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

Classification of medicines

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.

The pharmacological "face" of muscle relaxants

Medicines	Action		It causes		BP
	Strength	Duration	Bronchospasm	Pseudo-allergy	
Suxamethonium iodide	+	+	-	-	-
Diplacine dichloride	++	++	-	+	↑
Tubocurarine chloride	+++	+++	+	+	↓
Pipecuronium bromide	++++	+++	+	+	↓

The list of medicines

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

Apnoea is the absence of respiratory movements. Cachexia is the emaciation of the organism. Polarization (the state of rest) → depolarization (transmission of a nervous impulse) → 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 3rd and 4th 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

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

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

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.

Classification of medicines

α_1- adrenomimetics, α_2- adrenomimetics*	**β_1- adrenomimetics *, β_2- adrenomimetics, β_1+β_2- adrenomimetics ****	**α_1, α_2, β_1, β_2- adrenomimetics**
Norepinephrine	Dobutamine	Epinephrine

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

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)	→ ***Indications***
Stimulation of **α_1-AR**: the vasoconstrictive effect, the BP increase. "Centralization of the blood circulation" – the vasoconstriction of the skin, subcutaneous tissue, mucous membranes, organs of the abdominal cavity (α_1-AR), but (because of the stimulation of β_2-AR) dilation of vessels (improvement of the blood circulation) of heart, brain, lungs, skeletal muscles	Shock, collapse, hypotension, conjunctivitis, prolongation of the local anesthetics effect
Stimulation of **α_2-AR**: the hypotensive effect	Essential hypertension (EH), hypertensive crisis
Stimulation of **β_1-AR**: the cardio-stimulating effect (the positive inotropic and chronotropic effects), the increase of the oxygen consumption by myocardium	Heart stoppage, cardiogenic shock, bradyarrhythmia
Stimulation of **β_2-AR**: the broncholytic effect	BA, chronic asthmatic bronchitis
Stimulation of **β_2-AR**: the tocolytic effect (decrease of the uterine tone and contractions	Threatened preterm labour
Stimulation of β_2- and β_3-AR: the enhancement of glycogenolysis and lipolysis	Hypoglycemic coma

Side effects	→ ***Contraindications***
Tachycardia, hyperglycemia, hypertension (excluding Clonidine)	Coronarosclerosis, diabetes mellitus, EH (excluding 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.

The pharmacological "face" of adrenergic agonists

Medicines	**Adrenoreceptors**				**Duration of action**
	α_1	**α_2**	**β_1**	**β_2**	
Epinephrine	+++	-	++++	+++	+
Ephedrine	+	-	+++	++	+++
Norepinephrine	++++	-	+	+	+
Tetrizoline	+++	-	-	-	++
Clonidine	-	+++	-	-	++
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, Adrenaline hydrotartrate)	Sol. for inj.0.1%
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.

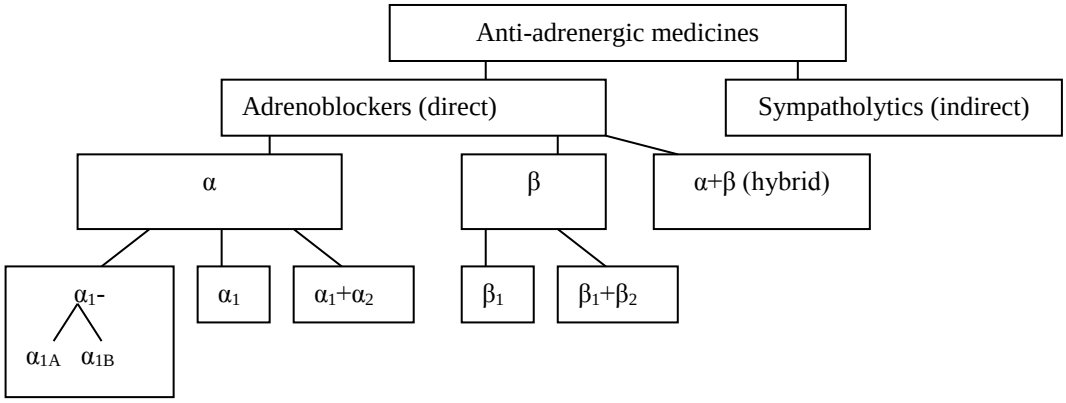

Fig. 2. The classification of anti-adrenergic medicines.

α-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

α-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) → ***Indications***	
Blockade of the α_{1B}-AR in vessels decreases the sympathetic influence on vessels. As a result the vasodilating and hypotensive effects occur	EH, endarteritis, bedsores, pheochromocytoma
Blockade of α_{1A}-AR decreases the tone of the smooth muscles of the urethra prostatic part and the urinary bladder cervix	Benign hyperplasia of the prostate (BHP) (adenoma)
Blockade of α_2-AR improves the blood supply of small pelvis organs and increases potency	Psychogenic impotency, male climacterium
Side effects → ***Contraindications***	
Orthostatic collapse, hypotension	Hypotension, sclerosis of the coronary and brain vessels

The pharmacological "face" of α-adrenoblockers

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

Dihydroergotamine	±	6	Migraine
Nicergoline	+	6	Spasmolytic effect; migraine, disorders of the cerebral blood circulation
Prazosine	++	8	Adenoma, ↑ 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	$\beta_1+\beta_2$-adrenoblockers
Metoprolol Betaxolol Talinolol Bisoprolol Atenolol	Propranolol Oxprenolol Sotalol

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)	→	***Indications***
The β_1-AR blockade in the myocardium: the **antianginal** effect– decrease of the heart rate and contractility resulting in the decrease of oxygen consumption by myocardium		Ischemic heart disease (angina pectoris)
The β_1-AR blockade of the heart's conductive system – the **antiarrhythmic** effect		Tachyarrhythmia
The β_1-AR blockade of the heart (decrease of the heart function) and kidneys (the renin-angiotensin system activity decrease) – the **hypotensive (antihypertensive)** effect		Hypertension
Side effects	→	***Contraindications***
Bradycardia, bronchospasm, angiospasm, hypotension		Bradycardia, BA, peripheral blood circulation disorders, hypotension

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 "face" of β-adrenoblockers

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 →	***Indications***
Hypotensive effect	EH
Side effects →	***Contraindications***
Enhancement of the parasympathetic innervation (hypersecretion in the GIT, bronchospasm)	Peptic ulcer, BA

The pharmacological "face" of sympatholytics

Medicines	Max ↓ 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 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 of medicines

Medicines 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.

The pharmacological "face" of general anesthetics

Medicines	Activity	Going out from narcosis*	Myorelaxation	Stimulation stage	Narcosis managing	Other effects
Ftorotan	+++ +	++	++	±	+++	↓ of BP, breathing; bradycardia
Enfluran	+++	+++	+++	+	++	↓ of BP, breathing
Nitric oxide	+	++++	-	+++	+++	A component of the combined narcosis
Ether for narcosis	++	+	++	+++	++	↓ of BP, irritates mucous membranes
Propanidide	+++ +	++	++	-	-	Laryngospasm, thrombosis, irritation. A short-term narcosis
Thiopental	+++ +	+++	+++	-	-	Convulsions, laryngospasm
Sodium oxybutyrate	+		++	±	-	Sedative, hypnotic, anti-hypoxic effects
Ketamine	+	+++	-	-	-	BP↑, hallucinations, convulsions

* - 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.

Classification of medicines

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

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) → ***Indications***	
Analgesic	Strong and very strong pain caused by traumas (excluding the craniocerebral trauma, hemorrhagic stroke), myocardial infarction, massive burns, shock, malignant tumours, acute inflammatory processes (peritonitis, cholecystitis), colics; insomnia caused by the excessive pain; prevention of the traumatic shock; premedication

Antitussive (anti-cough)	Cough in pneumothorax, lung bleeding; operations on the 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 respiratory centre	Acute pulmonary edema (small doses of morphine cause the rate decrease and the depth increase of breath movements and it leads to the breath relief)
Stimulation of the vagus nerve (parasympathetic innervation prevails: the increase of the smooth muscles tone, etc.)	Radiography of the GIT
Stimulation of the oculomotor nerve (myosis)	Diagnostic importance when intoxicated by morphine and other opioids
Side effects	***→ Contraindications***
Drug dependence (physical, psychological), addiction, abstinence	Chronic pain (excluding cancer diseases)
Inhibition of the respiratory centre	Pregnancy, labour, lactation, craniocerebral trauma, hemorrhagic stroke, children under 2 years old, patients over 60 years old

The pharmacological "face" of narcotic analgesics

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

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
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

Glossary

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.

Classification of medicines

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

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

The pharmacological "face" of non-narcotic analgesics

Medicines	**Analgesic effect**	**Antipyretic effect**	**Anti-inflammatory effect**	**Other peculiarities/effects**
Sodium methamizole	++ (reference)	+	±	
Paracetamol	+	++		A narrow interval of the therapeutic action
Ketorolac	+++	±		
Tempalgin	+++			Tranquilizing
Baralgetas	+++			Spasmolytic
Spasmalgon	++		±	Spasmolytic
Sedalgin Pentalgin	+++			It contains ASA, 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, Tempalgin, Citramone	Tabl.
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 (COG_1) and cyclooxygenase-2 (COG_2). **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).

Classification of medicines

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

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)	→	***Indications***
Anti-inflammatory	Inflammatory diseases of the connective tissue (collagenoses): rheumatism, systemic lupus erythematosus, etc.; arthrites, arthroses, osteochondrosis, radiculitis	
Analgesic	Acute and chronic 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	→	***Contraindications***
Ulcerogenic effect, dyspepsia		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 ≥ Acetylsalicylic acid ≥ 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

Glossary

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 nervous system. **Systemic lupus erythematosus** is the chronic systemic inflammatory autoimmune disease of the connective tissue and vessels. **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).

Classification of medicines

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

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-, H_1-histamine receptors and serotonin-$5HT_2$-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 H_1-histamine receptors blockade.

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

Pharmacodynamics (effects) → ***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 → ***Contraindications***	
Neuroleptic syndrome, drug-induced parkinsonism, dyspepsia	Depression, 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.

The list of medicines

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

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.

Classification of medicines

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

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)	→	***Indications***
Anxiolytic		Neuroses, mild psychoses
Hypnotic		Insomnia (especially caused by negative emotions)
Sedative		Neurogenic diseases
Anticonvulsant		Convulsions (epilepsy)
Potentiating		Premedication
Side effects	→	***Contraindications***
Drowsiness, weakness, disorders of attention and locomotion, tolerance, addiction		Activities that require rapid psychomotor reactions, long-term courses of treatment, 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.

The pharmacological "face" of tranquilizers

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

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

The list of medicines

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

Glossary

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 plant origin	**Bromides* and combined 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 (effects)	**→**	***Indications***
Sedative	Mild form of neuroses, increased irritability, neurogenic diseases (hypertention, peptic ulcer, angina pectoris)	
Potentiating	Intensification of effects of CNS depressants	
Side effects	**→**	***Contraindications***
Decrease of the mental and physical activity, feeling of fatigue, drowsiness		Activities that require rapid psychomotor 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.

The pharmacological "face" of sedative medicines

Medicines	**Effects**		**Composition/other effects**
	Sedative	*Spasmolytic*	
Sodium bromide	+++		Anticonvulsant
Motherwort herb tincture	+	±	

Medicines containing valerian:			
Valerian extract	+	+	Spasmolytic
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.

Classification of medicines

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

Phenobarbital*	Zolpidem* Bromisoval **	(cyclobarbital+diazepam)

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.

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

The pharmacological "face" of hypnotic medicines

Medicines	**Sleep duration**	**Effective in disorder of**		**Disorder of the sleep phases**	**Syndrome**		**Accumulation**	**Dependence/ tolerance**
		falling asleep	*sleep duration*		*After action*	*With-drawal*		
Phenobarbital	8-10	+	+	+++	+++	+++	++	++/+
Cyclobarbital	4	+		+++	++	+++	+	++/+
Nitrazepam	6-8	+	+	++	++	++	±	+/+
Zolpidem	6	+	+	+	±			+/-
Zopiclone	8	+	+	±	±			±
Bromisoval	5-7	+		±	++	+	+	+/+
Reladorm	8	+	+	+	++	+++	+	++/+

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.

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

Glossary

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.

Classification of medicines

Benzodiazepines	**Valproates**	**Barbiturates**
Diazepam Clonazepam	Valproic acid	Benzobarbital Phenobarbital
Succinimides	**Iminostilbens**	**Others**
Ethosuccimide	Carbamazepine	Tolperizone

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.

Pharmacodynamics (effects)	***→ Indications***
Anticonvulsant effect	Convulsions of different origin (epilepsy, craniocerebral traumas, tumours of the CNS, meningitis)
Side effects	***→ Contraindications***
CNS inhibition, mental confusion, drowsiness, depression, tolerance	Activities that require attention; depression

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).

The pharmacological "face" of anticonvulsants

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

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

The list of medicines

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

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	Dophaminergic 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 (effects) → ***Indications***	
Antiparkinsonian effect	Parkinson`s disease, syndrome of parkinsonism
Side effects → ***Contraindications***	
Anticholinergic: tachycardia, increase of IOP, paralysis of accommodation, dry mouth	Tachycardia, glaucoma
Dophaminergic: hypotension, arrhythmia, development of psychoses	Disorders of the cardiac activity, psychoses
Antiglutamatergic: convulsions, hypotension	Epilepsy, hypotension

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

The pharmacological "face" of antiparkinsonian medicines

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

The list of 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 (effects) →	***Indications***
Analeptic: the stimulation of the respiratory and vasomotor centres	Asphyxia, shock, collapse, reflex stoppage of 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 →	*Contraindications*
Stimulation of the CNS, insomnia, hypertension, convulsions	Psychoses, insomnia, essential hypertension, predisposition to convulsions

The pharmacological "face" of analeptics

Medicines	**Stimulation**		**Effects**		**Other effects**
	RC*/**	**VMC**	**"Awaken-ing"**	**Convulsant**	
Caffeine	+/-	+	+	++	As analeptic it is weaker than bemegride and nicethamide
Bemegride	++++/-	++	++++	++++	It is effective in intoxications with OA and barbiturates
Nicethamide	++/++	+++	+	++	Antipellagric
Sulphocam-phocaine	++/+	++	++	++	It is stronger than camphor, can 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, it means that cytisine and carbonic acid do not act
Carbonic acid	++++/++				

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

The list of medicines

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 benzoate	Amphetamine sulphate	Mesocarb Feprosidnine hydrochloride

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 (effects)	***Indications***
Psychostimulating: increase of mental (cognitive functions) and physical activity	To increase mental and physical activity of healthy people in the extreme conditions
"Awakening", analeptic	Poisoning by general anesthetics, narcotic analgesics and hypnotic medicines
Elimination of drowsiness	Pathologic drowsiness
Thymoleptic (improvement of depressed mood in patients)	Psychic depression (neuroses, depression, alcoholism)
Side effects	***Contraindications***
Insomnia, increased excitability and irritability, hypertension, tachycardia	Insomnia, increased excitement, essential hypertension, atherosclerosis, diseases of the cardiovascular system

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

The pharmacological "face" of psychomotor stimulants

Medicines	**↑BP**	**Thymoleptic**	**Other peculiarities**
Caffeine sodium benzoate	++		It is not prescribed to children under 2 years old. It potentiates the effect of OA; stimulates the gastric juice secretion; has the cardiostimulating and anti-aggregant effect, causes "centralization" of the blood circulation
Amphetamine sulphate	+++	+++	It is a powerful stimulant of the CNS ("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

Feprosidnine hydrochloride	+	+	Moderate antidepressant and cholinolytic 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

Glossary

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.

Classification of medicines

The Ist generation (non-selective ones)		
Irreversible-acting MAO inhibitors	*Inhibitors of the monoamines re-uptake*	*Inhibitors of the receptor action, plant origin ones**
Nialamide	Amitriptyline Imipramine Doxepine	Mianserine Hypericine*
The IInd generation (selective ones)		
Reversible-acting MAO inhibitors	*Inhibitors of the serotonin re-uptake*	
Pyrazidol	Paroxetine Fluoxetine Sertraline	
The IIIrd generation (medicines with a "double" action)		
Venlafaxin		Milnaciprane

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

The pharmacological "face" of antidepressants

Medicines	**Effects**					**Other effects/peculiarities**
	thymoleptic	*psychostimulating*	*sedative*	*cholinolytic*	*anxiolytic*	
Amitriptyline	+++		+++	+++	++	Antihistaminic, analgesic, decrease of libido
Imipramine	+++	++		+++	+	
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

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

The list of medicines

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

Glossary

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.

Pharmacodynamics (effects) →	***Indications***
Nootropic effect (improvement of memory, speech, learning; increase of the brain's resistance to hypoxia and intoxication, decrease of dizziness, headache, drowsiness, apathy)	Craniocerebral traumas, stroke, mental retardation in children, senile dementia, disorders of memory, attention, speech; atherosclerosis, encephalopathy
Side effects →	***Contraindications***
Insomnia, irritability, nausea	Disorders of sleep, neurosis, pregnancy

The pharmacological "face" of nootropic medicines

Medicines	**Effects**		**Other peculiarities**
	psycho-stimu-lating	*sedative*	
Pyracetam	+		The reference medicine. The stressprotective, adaptogenic effects. It increases the effect of anti-anginal medicines
Pyritynol	++	+	Antidepressant, anti-asthenic
Calcium gopantenate	+	+	Anticonvulsant, analgesic; it has a low toxicity, 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 plant origin		**Medicines of animal and synthetic* origin**
Ginseng root tincture	Schizandra tincture	Pantocrine
Aralia tincture	Leuzea extract	Citrullin*
Eleutherococcus extract	Toniphyt	

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

NB! To avoid the disturbance of sleep adaptogens should not be administered in the evening.

The pharmacological "face" of adaptogens

Medicines	**Peculiarities**
Ginseng root tincture	↓ 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 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

Glossary

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 compensatory mechanism is exhausted and cardiac insufficiency comes into the decompensation 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. Cyanosis is caused by 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.

Classification of medicines

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

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 Ca^{2+}-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.

The pharmacological "face" of CGs

Medicines	**Route of administration**				**Accu-mulation**	Absorption in the GIT
	intravenously		**perorally**			
	Start (min)	Duration (days)	Start (hours)	Duration (days)		
Digoxin	15-40	5-6	1.5-3	5-6	+	+
Digitoxin			2-4	14-21	++	+
Lantoside	10-30	5-7	1-2	5-7	±	+
Strophanthine G	5-10	2-3				
Corglycon	5-10	3-4				
Adoniside			15-40	3-4		+

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.

Neurohormonal factors of the vascular tone regulation

Vasoconstrictors	**Vasodilators**
constrict vessels	*dilate vessels*
Adrenaline Noradrenaline Angiotensin II Vasopressin (ADH) Dophamine	Nitrogen monoxide (NO) Acetylcholine Histamine Bradykinin

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.

Classification of medicines

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

Medicines decreasing the activity of the nervous system sympathetic part

Classification of medicines

Agonists of central α_2-adreno- and imidazoline* receptors	**Sympatholytics* and ganglionic blockers**	**β-adrenoblockers (cardioselective* and non-cardioselective)**	**α_1- and α + β *-adrenoblockers**
Clonidine hydrochloride Methyldopha Moxonidine*	Reserpine* Hexamethonium benzosulphonate	Atenolol* Bisoprolol* Propranolol	Prazosine Doxazosine Labethalol*

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

The list of medicines

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 vasodilating medicines

Classification of medicines

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

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 Ca^{2+} 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 (effects) →	***Indications***
Hypotensive effect (all medicines decrease BP and TPVR, dilate arteries)	Hypertension and hypertensive crisis
Decrease of post-load and/or pre-load to the heart	Hypertension in combination with angina pectoris (calcium antagonists). Chronic HF (inhibitors of ACE, antagonists of angiotensin II receptors)
Spasmolytic effect (myotropic spasmolytics)	Spasms of the smooth muscles of the internal organs
Moderate immune-stimulating effect	Decrease of immunity (Bendazol)

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

The pharmacological "face" of hypotensive medicines

Medicines	**Application in hypertension**		**Effect in hypertensive crisis**		**Effect to the heart load**
	medium	*severe*	*start, min*	*duration, h*	
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	+				

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 TPVR (decrease of the heart **post-load**). The decrease of pre- and 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 Ca^{2+} 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.

Antianginal 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.

Classification of medicines

Medicines decreasing oxygen consumption by myocardium and increasing oxygen delivery to the myocardium		**Medicines decreasing oxygen consumption by myocardium**
Nitrovasodilators (organic nitrates)	*Calcium canals blockers (phenylalkylamines*,benzothi-azepines**, dihydropyridines), different medicines●*	*β-adrenoblockers (β_1, β_1+ β_2*)*
Glycerol trinitrate Isosorbide dinitrate	Nifedipine Amiodaron● Amlodipine Verapamil* Dilthiazem**	Atenolol Metoprolol Bisoprolol Propranolol*

Medicines increasing the oxygen delivery to the myocardium (coronarolytics)	**Medicines improving the metabolism in myocardium**
Carbocromen Dipyridamol Menthol in bromisovalerianate	Trimethasidine 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).

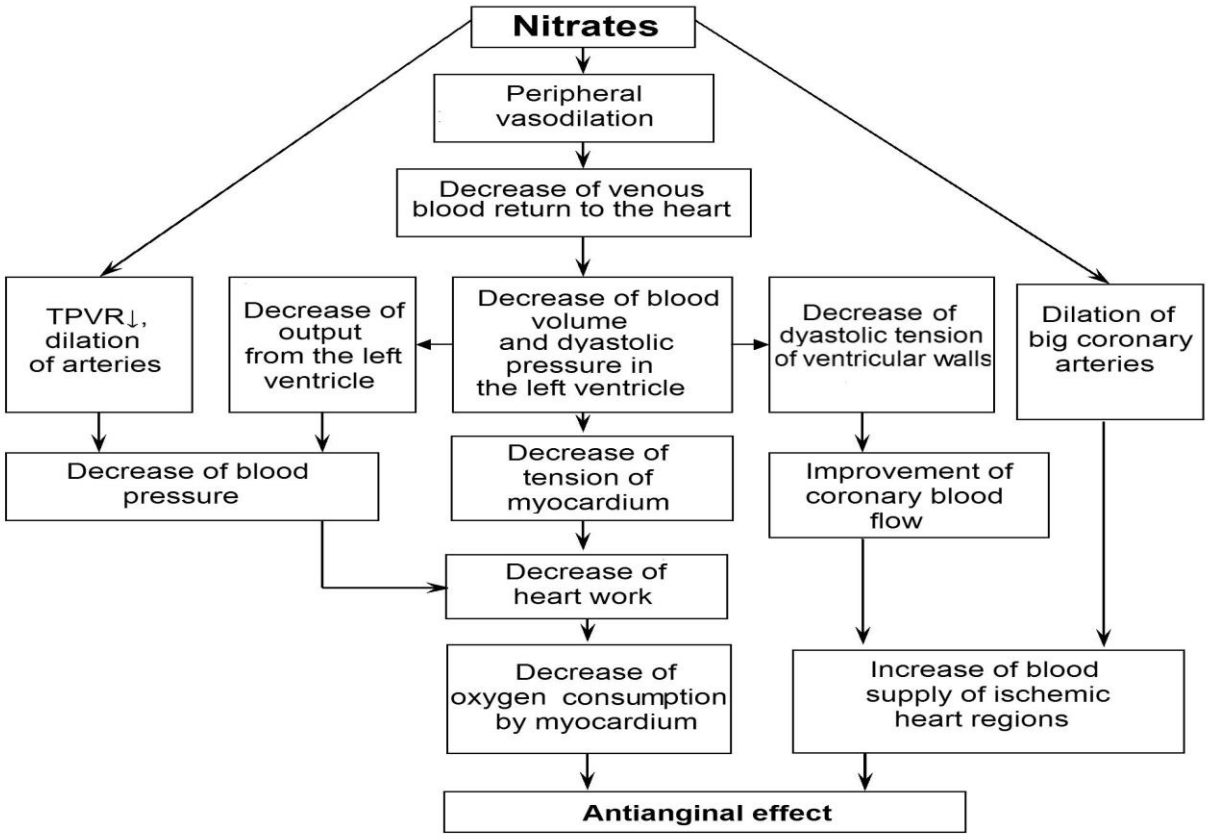

Fig. 3. The mechanism of the anti-anginal effect development by nitrates.

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 **β-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.

The pharmacological "face" of nitrovasodilators

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

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

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

Group	Medicines	$T_{1/2}$, h	Effect		
			hypotensive	*anti-anginal*	*anti-arrhythmic*
A	Nifedipine (I)	4	+++	+++	+
	Amlodipine (III)	35-50	++	+++	+
	Verapamil (I)	6	++	+++	++
B	Atenolol	6-9	+++	+++	+++
	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, Trinitrolong, Nitroointment, Nitroderm)	Tabl. 0.00025
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

Glossary

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.

Classification of medicines

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

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

The pharmacological "face" of hypolipidemic medicines

Medicines	**Alternative of choice**		**Primary HL**	**Severe HL**	**↓ChS absorption**	**↓ChS synthesis**
	I	**II**				
Lovastatin	+		+	+		+
Simvastatin	+		+	+		+
Phenofibrate	+	+	+			+
Cyprofibrate	+	+	+			+
Cholestiramine	+		+		+	

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

The 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

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

Glossary

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^+, Ca^{2+}, Mg^{2+} 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

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

The mechanism of action

Membrane-stabilizing medicines prevent Na^+, K^+, Ca^{2+} 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.

Pharmacodynamics (effects) →	***Indications***
Anti-arrhythmic (all medicines), local anesthetic (Lidocaine)	Atrioventricular tachyarrhythmia, ventricular extrasystolia; local anesthesia (Lidocaine)
Anti-anginal, antihypertensive (β-adreno-blockers, calcium antagonists) (fig. 4)	Angina pectoris, hypertension
Side effects →	***Contraindications***
Neurotoxicity, increase of the cardiac insufficiency symptoms, the BP decrease	Chronic cardiac, renal and hepatic insufficiency

The pharmacological "face" of anti-arrhythmic medicines

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

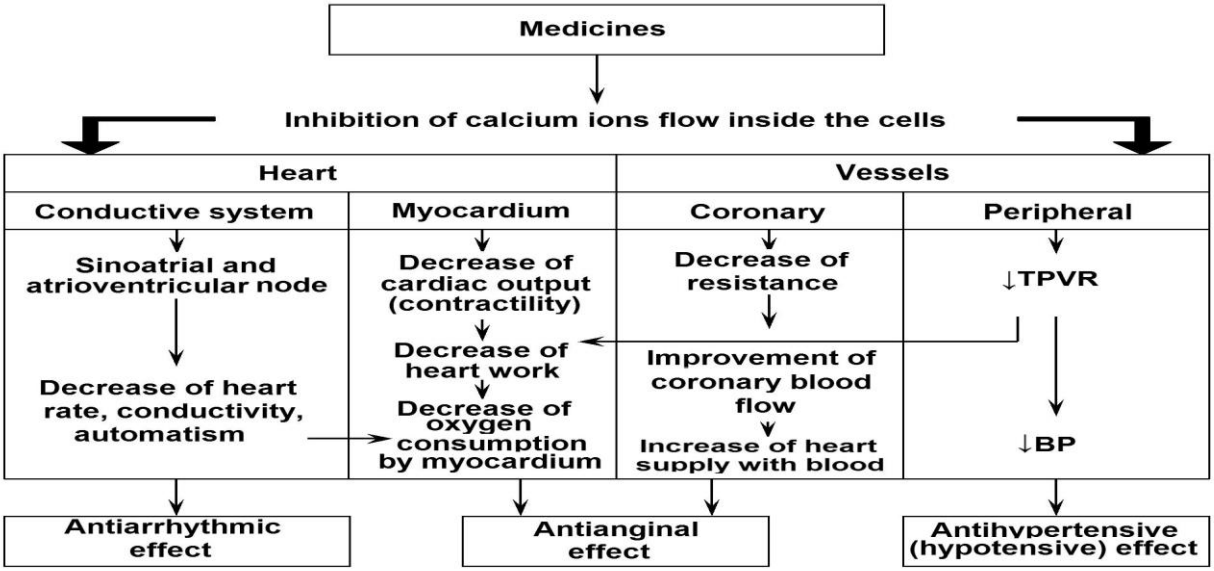

Fig. 4. Effects of calcium canals blockers on the cardiovascular system

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 (Asparkam, Panangin)	Tabl. 0.35
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%

Glossary

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.

Classification of medicines

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

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

The pharmacological "face" of medicines affecting appetite

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 stimulants)	Indirect-acting adrenomimetic; very 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 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

Glossary

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: *central- and reflex*-acting*	**Anti-emetic medicines** *(M-cholinoblockers*, H_1-histaminoblockers**, 5-HT_3-serotoninoblockers***, D_2-dophaminoblockers)*
Apomorphine h/chl. Ipecacuanha root syrup *	Scopolamine h/chl.* Diphenhydramine** Tropisetron*** Metoclopramide Haloperidol

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-HT_3-receptors of the emetic centre trigger zone; M-ChR and H_1-histamine receptors in the CNS.

Pharmacodynamics (effects)	***→ 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	***→ Contraindications***
BP decrease, extrapyramidal disorders	Extrapyramidal disorders (D_2-dophaminoblockers), diseases of the heart and the CNS

The pharmacological "face" of anti-emetic medicines

Medicines	**Used in**		
	motion sickness	*Chemo-, radiation therapy of tumours*	*toxicosis*
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%

Glossary

Extrapyramidal disorders see neuroleptics (antipsychotics).

ANTI-ULCER MEDICINES

Classification of medicines

Antisecretory medicines			**Antacid and covering medicines (monocomponent and combined*)**
Inhibitors of H^+/K^+-ATPase	*H_2-histamine receptors blockers*	*M_1-cholino-blockers*	
Omeprazole	Famotidine	Pirenzepine	Aluminium phosphate Almagel* Maalox*
Gastroprotectors	**Antihelicobacter medicines**		**Medicines of plant origin**
Bismuth subcitrate Misoprostol	Metronidazole Bismuth-containing medicines		Gastrophyt 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 H_2-histamine receptors** inhibit the secretion of the hydrochloric acid in the stomach by competing inhibition of the histamine interaction with H_2-histamine receptors of stomach cells. **M_1-cholinoblockers** block M_1-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.

Pharmacodynamics (effects) →	***Indications***
Anti-ulcer effect	Peptic (stomach and duodenal) ulcer, hyperacidic gastritis (all, except Plantaglucide). Hypoacidic gastritis, peptic ulcer with normal or decreased acidity (Plantaglucide, Gastrophyt)
Side effects →	***Contraindications***
Dyspepsia, headache, dizziness	Hepatic, renal functional disorders; pregnancy

The pharmacological "face" of anti-ulcer medicines

Medicines	**↓ of HCl/pepsin**	**↑of secretion****	**↓ H. pylori**	**Other effects/peculiarities**
Aluminium phosphate	+*	+	-	It is effective in intoxications
Almagel	*/+	+	-	Adsorbent, covering, choleretic, laxative effects
Maalox	*/+	+	-	Covering effect
Bismuth subcitrate	-	+	++	Antiseptic, astringent effect
Omeprazole	++++/+	-	+	Cytoprotective
Pirenzepine	++/+	-	-	Spasmolytic effect
Famotidine	+++/+	-	-	The IIIrd 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

Glossary

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.

Classification of medicines

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

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.

Pharmacodynamics (effects) →	***Indications***
Hepatoprotective, antitoxic, antioxidant, membrane-stabilizing, anti-inflammatory	Hepatitis, hepatic cirrhosis, chronic cholecystitis, dyskinesia of the biliary tract and the gall bladder
Side effects →	***Contraindications***
Dyspepsia, discomfort in the epigastric area	Acute hepatitis, hepatic coma, chronic renal insufficiency

The pharmacological "face" of hepatoprotectors

Medicines	Effects				Other effects/peculiarities
	a/i	a/o	m/s	ch/r	
Antral	+	+	+	+	Analgesic, immunostimulating
Lioliv	+	+	+	+	
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

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

Glossary

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.

Classification of medicines

Medicines stimulating intestinal chemoreceptors	**Medicines stimulating intestinal mechanoreceptors**
Plant origin*:** Glaxena Regulax Ramnus cathartica bark Castor oil ***Synthetic: Sodium picosulphate	***Medicines swelling in the intestine:*** Laminaria saccharina ***Salt laxatives:*** Magnesium sulphate
Medicines making intestinal contents soft	
Vaseline oil	

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.

Pharmacodynamics (effects)	→	***Indications***
Laxative effect	Constipation, preparation to operations, instrumental examination of the GIT; food poisonings; regulation of stool in hemorrhoid and proctitis	
Side effects	→	***Contraindications***
Increase of the GIT motility and peristalsis (colic-like pain). Disorder of drug and food absorption from the GIT		Intestinal obstruction, spastic colitis. Simultaneous intake with medicines that are absorbed 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.).

The pharmacological "face" of laxative medicines

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

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-nesine)	Pwd. 50.0
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.

Classification of medicines

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

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

The pharmacological "face" of enzymatic medicines

Medicines	**Composition**	**Effect**			
		↑ 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-forte	Pancreatine, bile components, aminoacids, HCl	+	+	-	-

The list 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

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%); medium-acting 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.

Diuretics acting on

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

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 $NaHCO_3$ (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^-, Ca^{2+}, Mg^{2+} 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 diuresis. **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^-, H_2O 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 (effects) →	***Indications***
The main effect of diuretics is diuretic	Pulmonary edema, edemas in diseases of heart, vessels, kidneys and liver
Loop, thiazide and **thiazide-like diuretics** have the hypotensive effect	The complex therapy of hypertension, hypertensive crisis
Spironolactone decreases the cardiac post-load, **loop diuretics** decrease the pre-load on the heart	Edema in heart failure
Osmotic and **loop diuretics, carboanhydrase inhibitors** cause the dehydrative effect, decreasing the IOP and ICP	Brain edema, glaucoma
Acetazolamide has the anti-epileptic effect	Epilepsy (petit-mal)
Medicines of the **plant origin** have also the hypoazotemic (Lespenephril, Nephrophyt), anti-inflammatory, antimicrobial, spasmolytic, choleretic effects; some of them excrete urinary concrements (Cowberry leaf, Nephrophyt)	Prevention of edemas in cardio vascular, renal and hepatic diseases
Side effects →	***Contraindications***
Hypokalemia (carboanhydrase inhibitors, thiazide, loop diuretics); **hyperkalemia** (potassium-sparing); **hyposodemia, hypomagnemia** (loop diuretics, potassium-sparing, thiazide diuretics); **hypercalcemia** (thiazide and thiazide-like); hypochloremic **alkalosis** (loop, thiazide and thiazide-like diuretics); hyperchloremic metabolic **acidosis** (carboanhydrase inhibitors, potassium-sparing); **hyperglycemia, hyperuricemia** (loop, thiazide and thiazid-like, potassium-sparing diuretics)	Acidosis, uremia, hepatic cirrhosis, renal diseases, Addison's disease (carboanhydrase inhibitors); hypomagnemia, hypokalemia, hyposodemia, dehydration, severe forms of diabetes (loop, thiazide diuretics)

The pharmacological"face" of diuretics

Medicines	**Effect**			**Cause**	
	strength	*start*	*duration (h)*	*acidosis*	*alkalosis*
Furosemide	++++	5 min i/v; 30-40 min per os	4-8		+

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.

Classification of medicines

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

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 (effects) →	***Indications***
Antigouty effect	Gout, hyperuricemia
Side effects	***→ Contraindications***
Dyspepsia, hyperthermia, eosinophilia, leukopenia	Peptic ulcer, diseases of blood, liver, 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 synthesized in thrombocytes, stimulates vasoconstriction 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)

Classification of medicines

Direct-acting anticoagulants		**Indirect-acting anticoagulants**
Resorptive-acting ones	**Local-acting ones**	Acenocumarol Fenindion
Heparin** Calcium nadroparin*	Heparin ointment	

- – low molecular heparins; ** – high molecular heparins

Fibrinolytics	**Antiaggregants**
Fibrinolysine Urokinase Streptokinase	Dipyridamol Ticlopidine 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) → ***Indications***	
Direct-acting anticoagulants	
Anticoagulant (inhibition of blood coagulation at all phases)	Myocardial infarction, direct blood transfusion, surgery on the heart or vessels. Prophylaxis and treatment of embolism and vascular thrombosis
Fibrinolysis activation, improvement of blood rheological properties	Prophylaxis of thrombosis after coronary vessels shunting and prosthetics of the heart valves
Antiaggregant (inhibition of adhesion and aggregation of thrombocytes and erythrocytes, normalization of the blood rheological properties, improvement of microcirculation of the brain, myocardium, retina, etc.)	Thrombophlebitis, trophic ulcers of the shin, hemorrhoids, subcutaneous hematomas, hypercoagulation syndrome
Hypolipidemic (decrease of the lipid level in blood)	Prophylaxis and treatment of atherosclerosis
Coronarodilating (improvement of blood stream in the myocardium)	Myocardial infarction, stable angina of 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 filaments and recent (up to 3 days) thrombi)	Venous and arterial thrombosis, acute myocardial infarction, pulmonary embolism

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

The pharmacological "face" of anticoagulants and antiaggregants

Medicines	**Route of administration**	**Onset of effect**	**Duration of 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.

The pharmacological "face" of fibrinolytics

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

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

Glossary

Hematoma is a limited accumulation of blood 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 medicines

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

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)	→	***Indications***
Hemostatic effect: stoppage or decrease of bleedings		**Inhibitors of fibrinolysis**: bleedings caused by the increased fibrinolysis, thrombocytopenia, including ones caused by peptic and duodenal ulcer, postnatal bleedings
		Hemostatics: bleedings in surgery, obstetrics, traumatology caused by deficiency of blood 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	→	***Contraindications***
Increase of blood coagulation		Predisposition to thrombosis, thromboembolism

The pharmacological "face" of medicines increasing the blood coagulation

Medicines	**The route of administration**	**Other effects / peculiarities**
Aminocapronic acid	per os, i/v	Anti-inflammatory, anti-allergic
Fibrinogen	i/v, locally	It is a component of the blood coagulation system
Calcium chloride	per os, i/v	
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

Glossary

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.

Classification of medicines

Erythropoiesis stimulants			**Erythropoiesis inhibitors**
Iron-containing medicines for enteral and parenteral administration	*Vitamins*	*Erythropoietins*	
Iron fumarate Jectofer Ferroplex Iron sulphate Iron saccharate Iron chloride Iron hydroxide polymaltose complex	B_{12}, B_6, B_2, C, Bc, E	Human erythropoietins (α, β, ώ)	Sodium phosphate solution labeled by phosphorus-32

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 tissues oxygenation	Prevention and treatment of iron deficiency (hypochromic) anaemias
Side effects →	***Contraindications***
Ulceration of the GIT, constipation, diarrhea, pain in the epigastric area, intestinal colics	Diseases of the GIT, anaemias that are not connected with the deficiency of iron in 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.

Pharmacodynamics (effects) →	***Indications***
Stimulation of erythropoiesis	Anaemias (especially hyperchromic)
Side effects	***→ 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, ώ** 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.

Pharmacodynamics (effects) →	***Indications***
Increase of erythrocytes and reticulocytes number, the amount of hemoglobin	Anaemias caused by the chronic renal insufficiency, HIV- infection, after usage of cytostatics, in preterm born infants, hypo- and aplastic anaemias
Side effects	***→ Contraindications***
Increase of BP	Hypertension

The pharmacological "face" of iron-containing medicines

Medicines	**The route of administration**	**The frequency of administration**	**Composition**
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 polymaltose complex	i/m	individually	Iron (III) hydroxide polymaltose complex
Ferroplex	per os	3 times a day	Iron (II) sulphate, ascorbic acid

II, III – the iron valency.

The list of medicines

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

Erythropoiesis inhibitors

The mechanism of action

Medicines suppress the erythrocytic part of the bone marrow.

Pharmacodynamics (effects) →	***Indications***
Decrease of the erythrocytes amount in blood	Erythremia
Side effects	***→ Contraindications***
Anaemia	Erythropenia, HIV-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

Leukopoiesis stimulants including colony-stimulating factors (CSF)	**Leukopoiesis inhibitors**
Lenograstim Methyl-oxymethyluracil Molgramostim Sodium nucleospermate Ethyl-carboxyphenyl-thiazolidine-acetate	Busulfan Mercaptopurine

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

The pharmacological "face" of leukopoiesis stimulants

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

Sodium nucleo-spermate	Increases the production of neutrophiles, lymphocytes	Stimulates the metabolic processes	The mixture of polyhydrates of Na salts of DNA and RNA derivatives obtained from the sturgeon milts

The list of medicines

INN, (Trade name)	Medicinal form, dosage
Leukopoiesis stimulants	
Ethyl-carboxyphenyl-thiazolidine-acetate (Leukogen)	Tabl. 0.002
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

Glossary

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.

Classification of medicines

Medicines stimulating expectoration	Mucolytics	Anti-tussive medicines	Surfactants
Reflex- and resorptive*-acting ones	**Monocomponent and combined***	**Central- (narcotic and non-narcotic*), peripheral**-acting ones**	
Althaea* root Glycyrrhiza root Mentoclar Plantain leaf Inula* root Bronchophyt	Ambroxol Acetylcysteine Bromhexin Althemix	Codeine phosphate Dimenoxadol hydrochloride Glaucin hydrochloride Acetylaminonitropropoxy benzen**	Colphosceryl palmitate Poractant alpha

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.

Surfactants make up endogenous surfactant deficiency.

Pharmacodynamics (effects)	→	***Indications***
Expectorant (all expectorants); mucolytic (mucolytics)		Inflammatory diseases of the respiratory tract (acute and chronic tracheitis, bronchitis and pneumonia)
Anti-tussive (all anti-tussive medicines)		Long-lasting dry non-productive cough
Surfactant-like (surfactants)		Respiratory distress-syndrome (surfactants, Bromhexin, Ambroxol)
Side effects	→	***Contraindications***
Dyspepsia, hypotension (expectorants, mucolytics, anti-tussive medicines)		The first trimester of pregnancy
Pulmonary bleedings especially in newborns with the marked signs of the unripe lungs (surfactants)		Pulmonary bleedings

The pharmacological "face" of expectorants and mucolytics

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
Acetylaminonitropropoxybenzen	Disinfectant, local anesthetic effects. In otolaryngology it is 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 chloride (B_1)		Folic acid (B_c)	
Riboflavin (B_2)		Ascorbic acid (C)	
Pantothenic acid (B_5)		Nicotinic acid (PP)	
Pyridoxine hydrochloride (B_6)		Rutin (P)	
Cyanocobalamine (B_{12})		Pyridoxalphosphate	
Pangamic acid (B_{15})		Lipoic acid	
Fat-soluble vitamins and their water-soluble analogues*			
Retinol (A)		Tocoferol acetate (E)	
Ergocalciferol (D)		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) → 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 hypoxia	Acute hypoxia
Enhancement of the plasticity processes and energy formation	Unhealed wounds, burns, hypotrophy, frostbites
Normalization of vision	Conjunctivites, ceratites
Enhancement of the erythropoietin synthesis	Anaemias, radiation sickness, leukemia
Pantothenic acid (Vitamin B_5)	
Improvement of the nerve impulse conductivity	Neuritis
Participation in the metabolism of proteins, fats, carbohydrates in oxidation-reduction processes	Diabetes mellitus, eczema, dermatites, trophic ulcers, hepatites, atony of the intestine and 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 (Vitamin B_{12}) (anti-anaemic, hemopoietic)	
Hemopoietic Anti-anaemic	Hyperchromic anaemia, radiation sickness, leukemia
Activation of the liver function	Fatty degeneration of the liver
Activation of the nervous system function	Diseases of the CNS and peripheral nervous system
Regulation of carbohydrate and lipid metabolism	Dystrophy in children
Pangamic acid (Vitamin B_{15})	
Improvement of lipid metabolism	Atherosclerosis
Increase of the creatine phosphate level in muscles	Dystrophic damage of the myocardium, ischemic heart disease
Increase of the glycogen content in muscles and liver	Hepatitis
Antihypoxic	Hypoxia

Folic acid (Vitamin B_c)	
Stimulation of hemopoiesis	Anaemia, radiation sickness, leukemia
Improvement of trophism and regeneration of tissues	Tropical sprue
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 blood coagulation	Prophylaxis and treatment of scorbutus, 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 metabolism. Lipotropic, detoxication	Complex therapy of liver diseases (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

Glossary

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.

Fat-soluble vitamins

Pharmacodynamics (effects) → ***Indications***	
Retinol (Vitamin A) (antixerophthalmic)	
Regulation of the organism's growth and development	Complex therapy of rickets, hypotrophies, 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 and immunity	ARVI, chronic bronchopulmonary diseases
Ergocalciferol (Vitamin D) (antirachitic)	
Participation in phosphorus and calcium metabolism regulation	Rickets, osteoporosis, consolidation of bones, hypocalcemia, spasmophilia
Tocoferol (Vitamin E) (antisterile)	
Regulation of the reproductive organs function	Menstrual cycle disorders, sterility, 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 coagulation)	Hemorrhagic diathesis, hemolytic disease of newborns, hepatitis, bleedings

Side effects → *Contraindications*	
Vitamin A	
Teratogenicity	The first trimester of pregnancy
Vitamin D	
Calcification of soft tissues, vascular walls, heart valves	Heart diseases, hypercalcemia, pulmonary tuberculosis, hepatic and renal diseases, peptic ulcer
Vitamin 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.

Classification of medicines

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

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.

Pharmacodynamics (effects) →	***Indications***
Antihypoxic	Hypoxia (but it is not used 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.

Pharmacodynamics (effects) →	***Indications***
The energy source **(Isotonic solution - 5%)**	The medicines dilution, as the blood substitute
Hypertensive **(Hypertonic solution – 10-40%)**	It is a component of the antishock liquid. Increase of the BP in collapse and shock
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 (effects) →	***Indications***
Vasodilating, antihypoxic, anabolic, anti-arrhythmic, anti-aggregant	Obliterating endarteritis, thrombophlebitis, venous insufficiency, IHD, tachyarrhythmia

Inosine

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

Pharmacodynamics (effects) →	*Indications*
Antihypoxic, anti-arrhythmic, anabolic	IHD, cardiomyopathies, arrhythmias, cachexia, hepatic cirrhosis, radiation-induced leukopenia

Trimethasidine

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

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

Pharmacodynamics (effects) →	*Indications*
Cytoprotective, antihypoxic	IHD, hypoxia, dysfunction of the cerebral and peripheral blood circulation, respiratory insufficiency

Rumalon

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

Pharmacodynamics (effects) →	*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) →	***Indications***
Chondroprotective	Osteoarthrosis, osteochondrosis
Cardioprotective	Prevention of the cardiotoxic effect of medicines
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 (effects) →	***Indications***
Anti-inflammatory, reparative (accelerate the tissue regeneration)	Gastro-intestinal, eye diseases, wounds

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.

Pharmacodynamics (effects) →	***Indications***
The influence on the vascular permeability, microcirculation, the BP, the rate of the blood flow. Locally irritative (except Apilak), anti-inflammatory effect	**Apisarthron** (bee poison medicine) is an ointment that is used in rheumatism, myalgia, sciatica and sport traumas. **Apilak** (a dry substance of the bee **"**milk") is used for treatment of hypotrophism and anorexia in babies and infants. **Propolis** (a bee 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 necessary for supporting the body growth and nitric balance in the organism	Lipid dystrophy with the insufficient amount of methionine or toxic damage of the liver
Glutaminic acid promotes the ammonium dehydration	Psychoses, mental deficiency, encephalitis
Cystein is a replaceable acid that is synthesized with the help of methionine	Cataract (because the cysteine content is disordered)
Cerebrolysine is a complex of neuropeptides from the swine brain. It has the neuroprotector properties, decreases the neurotoxic effect of the stimulatory aminoacids (glutamate)	Brain traumas, ischemic stroke, children mental deficiency, senile dementia
Hydrolysine solution. It is obtained in the acid hydrolysis of the cattle blood proteins when adding glucose, it has a detoxication property and it is a source of proteins	It is a medicine for parenteral nutrition in protein defficiency

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

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)	***→ Indications***
Cerebrolecitin is esters of glycerin, phosphoric and fatty acids (it is obtained from the cattle's brain tissue)	Poor bone fracture healing, rickets, diseases of the nervous system, anaemia, glaucoma
Medicines containing iodine (**iodides)** are necessary for the normal functioning of the organism, the synthesis of thyroxin (the thyroid hormone) that stimulates metabolism. The molecular iodine has the antimicrobial effect; it has the "resolving" effect in atherosclerosis and syphilis; the expectorant effect	Endemic goiter, hyperthyroidism. Operation field preparation in surgery and obstetrics, for washing of wounds. Skin diseases, inflammatory diseases of the respiratory tract (as expectorants). Syphilis, atherosclerosis. **5% iodine alcoholic solution, complex iodine solution** are used. **Potassium iodide** is an effective mucolytic
Medicines containing sodium (the main intracellular cation) provide the constancy of the osmotic pressure, ionic balance of the organism's internal medium, acid-alkaline balance	**Sodium chloride isotonic solution (0.9%)** is a blood substituent. **Hypertonic solution** is used for treatment wounds, ulcers, abscesses (it promotes pus removal, causes antimicrobial effect). **Sodium hydrocarbonate** is an antacid
Medicines containing potassium (the main intracellular cation) participate in the transmission of the nerve impulses, increase diuresis moderately	Hypokalemia, arrhythmia, overdosage of cardiac glycosides, as a diuretic
Medicines containing calcium provide the endurance of the skeleton and teeth, take part in regulation of the cellular membrane penetration for sodium and potassium (thicken the membranes), stimulate the heart work (potassium antagonists), participate in blood coagulation	Hypocalcemia, osteoporosis, bone fractures; allergic and inflammatory diseases; for increase of blood coagulation, the medicines are the components of blood substituents. Of these medicines **calcium chloride** (it is introduced intravenously only) and **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) →	***Indications***
Regeneration of the normal blood circulation, decrease of intoxication	Treatment and prevention of shock, acute 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 →	***Contraindications***
Glutaminic acid - vomiting, diarrhea, fissures on lips, excitation. With a prolonged application the decrease of the hemoglobin content and leukopenia can be observed	Fever, diseases of the liver, kidneys, GIT, blood-forming organs; the increased excitability of the CNS
Inosine - itch, redness of the skin, with a prolonged application – exacerbation of gout	Gout
Adenosine monophosphate - headache, tachycardia, diuresis increase; in intravenous administration – nausea, redness of the face	Acute myocardium infarction
Liquid Aloe extract injections are painful. A feeling of burning can appear while irrigating the wound with **Kalanchoe juice**	**Liquid Aloe extract for injections** – severe diseases of the cardiovascular system and kidneys, pregnancy
Trimethasidine - nausea, pain in the epigastrium, skin itch	**Trimethasidine** – pregnancy, lactation
Solcoseryl in the form of gel can cause burning of the skin	Individual intolerance
Actovegin - lacrimation (while using eye gel)	It is undesirable to use this medicine in the period of lactation
Cytochrome C shivering with the increase of the body temperature (with a rapid introduction)	Individual intolerance

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

The list of medicines

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.

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).

Classification of medicines

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

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

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

Medicines of the hypophysis anterior lobe

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

Medicine of the hypophysis posterior lobe (oxytocin)

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

Hypophysal hormones secretion inhibitors

Pharmacodynamics (effects) →	*Indications*
Danazol inhibits secretion of the hypophysal gonadotropins (FSH and LH), causes atrophy of the endometrium	Endometriosis, benign mammary gland tumours, gynecomastia
Bromocryptin inhibits the secretion of the hypophysal STH and LTH	Menstrual cycle disorders accompanied by hyperprolactinemia and acromegalia
Side effects	***→ Contraindications***
Danazol – alopecia, dysmenorrhea, edema, increase of the ICP	Tumours of the reproductive system, 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 beta-cells 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.

Classification of medicines

<table>
<tr><th colspan="3">Human insulins and their analogues*</th></tr>
<tr><td>Short-acting</td><td>Medium-acting</td><td>Long-acting</td></tr>
<tr><td>Insulin lispro*
Human insulin
Insulin aspart*</td><td>Human insulin</td><td>Human insulin
Insulin glargin</td></tr>
<tr><th colspan="3">Insulins of animal origin</th></tr>
<tr><td colspan="3">Short-, medium- and long-acting ones</td></tr>
<tr><td colspan="3">Porcine insulin</td></tr>
<tr><th colspan="3">Combination of short- and medium-acting insulins</th></tr>
<tr><td colspan="2">Human ones</td><td>Animal ones</td></tr>
<tr><td colspan="2">Human insulin</td><td>Porcine insulin</td></tr>
</table>

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

The pharmacological "face" of insulins

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

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

Classification of medicines

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

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

The pharmacological "face" of peroral hypoglycemic agents

Medicines	**Generation**	**Hypoglycemic effect**	**$T_{1/2}$, h**	**Action, h**	
				start	*duration*
Tolbutamide	I	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 list of medicines

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

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 HORMONE 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.

Classification of medicines

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

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

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) →	***Indications***
Thyreostatic (decrease of the thyroid gland hormones synthesis), decrease of the basal metabolism	Hyperthyroidism, thyreotoxicosis, diffusion toxic goiter
Side effects	***→ Contraindications***
Spreading and increasing of vascularisation of the thyroid gland (a strumogenic effect). Leukopenia, agranulocytosis	Hypothyroidism, nodular goiter, inhibition of blood cells formation (leukopenia, 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)	→ ***Indications***
Parathyroidine	
It promotes calcium release from bones and increase of its amount in blood, intensifies the calcium absorption by the intestinal mucous membrane, its reabsorption in renal tubules; retains reabsorption of phosphates	Prophylaxis of tetany in hypo-parathyroidism, diseases caused by disorder of the phosphorus-calcium exchange (spasmophilia, hypo-calcemic convulsions, etc.)

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

The list of medicines

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-acting ones	***Local-acting ones***		
	for inhalation	***for external and intranasal use***	***combined medicines***
Hydrocortisone Dexamethasone Mazipredone Triamcinolone	Budesonide Dexamethasone Triamcinolone Flunisolide	Hydrocortisone Budesonide Dexamethasone Triamcinolone Fluocinolone acetonide	Aurobin Trimistine

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.

Pharmacodynamics (effects) →	*Indications*
Regulation of water-salt metabolism: increase of the blood pressure, retention of Na^+, H_2O and elimination of K^+	Primary and secondary insufficiency of adrenal cortex (hypocorticism, Addison's disease)
Normalization of the tone and improvement of the skeletal muscles activity	Myasthenia
Side effects **→**	***Contraindications***
Edema, increase of BP, hypokalemia, increase of intraocular and intracranial pressure	Hypertension, heart failure, treatment with loop and thiazide diuretics, glaucoma

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) →	*Indications*
Protein metabolism: increase of the protein disintegration, inhibition of their synthesis **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. Anti-inflammatory, immunosuppressive, anti-allergic, antishock, antitoxic effects	**Substitution therapy** of chronic and acute adrenal insufficiency (hypocorticism, Addison's disease) Collagenoses, glomerulonephritis, acute pancreatitis, organ transplantation, severe allergic reactions, shock
Side effects **→**	***Contraindications***
Water retention, ↑BP, "steroid" diabetes, ulcer, psychosis; muscle weakness, gastric bleedings, osteoporosis, increased blood coagulability, body weight increase	Severe hypertension, diabetes mellitus, peptic ulcer, osteoporosis, psychic dysfunctions, predisposition to thrombo-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.

The pharmacological "face" of glucocorticoids

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

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, Synaflan, Flucinar)	Gel 0.025%
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

Classification of medicines

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

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)	→	***Indications***
Estrogenic effect: - stimulation of development of the sexual organs and the secondary female sexual characters; - proliferation of the endometrium during the first part of the menstrual cycle; - increase of the uterine contractility and tone		The insufficient function of ovaries (amenorrhea, dysmenorrhea, climacterium, sterility), hypoplasia of the genitals and underdevelopment of the secondary sexual characters Labour induction
Side effects	→	***Contraindications***
Cystic degeneration of ovaries, carcinoma of the uterus and the mammary gland, uterine bleedings, edema, hypertension		Tumours of uterus and ovaries, cystic mastopathies, uterine bleedings, severe forms of hypertension, pregnancy, lactation

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 (effects) →	***Indications***
Gestagenic effect: - stimulation of the endometrium's secretory phase in the second part of the menstrual cycle; - preparation of the endometrium to implantation of the impregnated ovum; - inhibition of the hypophysis gonadotropic function (in high doses); - decrease of the uterine contractility	Endocrine forms of infertility, dysfunction of the menstrual cycle, habitual abortions, threatened preterm labour, peroral contraception
Side effects	***→ Contraindications***
Increase of BP, acne, hirsutism, libido changes, body weight increase	Hypertension, uterine bleedings, hormone-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) →	***Indications***
Androgenic effect: - stimulation of development of the genitals and the secondary male sexual characters; - providing the reproductive function; - regulation of spermatogenesis, potency, libido after puberty of the organism Moderate **anabolic** effect	Infertility, infantilism, impotency, pathological male climacterium, malignant tumours of the mammary gland and ovaries in women (up to 60 years old)

Side effects →	*Contraindications*
Edema, BP increase, prostate hyperplasia, hypercalcemia, spermatogenesis dysfunction, musculinisation (in women), hepatotoxicity	Hypertension, prostate cancer, hypercalcemia, renal and hepatic insufficiency, pregnancy, for men over 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 (effects) →	*Indications*
Anabolic effect (stimulation of the protein synthesis, retention of nitrogen, calcium, phosphorus in the body) Moderate **androgenic** effect	Cachexia, hypotrophy; radiation and glucocorticoid therapy, burns, myocardial infarction, osteoporosis, traumas
Side effects →	*Contraindications*
Hepatotoxicity, cancerogenic effect, edema, BP increase, hypercalcemia, hyperglycemia, hyperlipidemia	Liver and kidney diseases, prostate cancer, hypertension, hypercalcemia, epilepsy, pregnancy, lactation, for children

The pharmacological "face" of anabolic steroids

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	Mifepristone	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) →	***Indications***
Anti-estrogens	
Ovulation stimulation, inhibition of estrogen-dependent tumours	Anovulatory sterility, breast cancer, endometriosis, dysfunctional uterine bleedings
Antigestagens	
Antigestagenic (in particular, uterotonic) effect	Interruption of pregnancy at early stages (medical abortion)
Anti-androgens	
Anti-androgenic (decrease of potency, decrease of spermatogenesis, inhibition of androgen-dependent tumours growth) effect	Androgenization in women, preterm puberty in boys, non-operative prostate carcinoma
Side effects →	***Contraindications***
Anti-estrogens	
Thromboses, hypercalcemia, edema, ovarian hyperstimulation syndrome, metrorrhagia	Thromboembolic states, hypercalcemia, uterine bleedings, pregnancy
Antigestagens	
Dizziness, weakness, fever, dyspepsia, metrorrhagia	Bleeding, pregnancy
Anti-androgens	
Changes in body weight and libido, depression, gynecomastia, spermatogenesis disorder, edema, thromboses, hepatotoxicity	Spermatogenesis disorder, pregnancy, edema, thromboses, liver function 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 list of medicines

INN, (Trade name)	Medicinal form, dosage
Clomiphencitrate (Clomiphene)	Tabl. 0.05
Cyproterone (Androcur)	Tabl. 0.01
Mifepristone (Penkrofton)	Tabl. 0.2

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.

Classification of medicines

Combined (estrogen-gestagen)			**Microdoses of gestagens (mini-pills)**
monophasic	*biphasic*	*tri-phasic*	
Ovidon Logest	Antiovin	Tri-regol Triquilar	Linestrenol
Postcoital		**Vaginal contraceptives (spermicides)**	
Levonorgestrel		Benzalkonium chloride	

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) →	***Indications***
Contraceptive (for all medicines), **anti-ovulatory** (for hormonal medicines); **spermicidal** (for spermicides) effect	Contraception
Side effects →	***Contraindications***
Estrogen-dependent complications include thromboses, increase of the blood pressure, edema, headache, nausea, vomiting, chloasma. **Gestagens** cause fatiguability, depression, body weight increase, libido decrease, painfulness of mammary glands, intermenstrual bleedings	Thromboembolism, hypertension, ischemic heart disease, diabetes mellitus in a severe form, hormone-dependent tumours, epilepsy, neuroses, psychoses, pregnancy and lactation, progressive diseases of liver and kidneys, diseases of the brain vessels, marked hyperlipidemia
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.

The pharmacological "face" of contraceptives

Medicines	**The peculiarities of contraception For women:**	**Other indications**
Ovidon	With the phenotype of the estrogen character	Dysfunctions of the menstrual cycle
Logest	Over 35 years old, after abortion, with hyperandrogenisation	Dysfunctions of the menstrual cycle + juvenile uterine bleedings
Antiovin	With the phenotype of the gestagen character	Dysfunctions of the menstrual cycle
Tri-regol	Young women, adolescents	
Triquilar		
Levonorgestrel	In lactation, irregular sexual life (high doses); concomitant diabetes mellitus, hypertension, obesity (mini-pills)	
Benzalkonium chloride	Any age, in irregular sexual life	Prevention of some sexually transmitted diseases, endometriosis

The list of medicines

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

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	Uterolytics (tocolytics)
Oxytocin Dinoprost Estron Ergotal Pachycarpine hydroiodide	Fenoterol Salbutamol Progesterone

Uterotonics

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.

Pharmacodynamics (effects) →	***Indications***
Uterotonic effect	Labour induction, hypotonic uterine bleedings
Side effects	***→ 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 (effects) →	***Indications***
Tocolytic effect	Threatened preterm labour
Side effects	***→ Contraindications***
β_2-adrenomimetics – tachycardia, blood pressure decrease, hyperglycemia	Arrhythmias, hypotension, diabetes mellitus
Gestagens – hypertension, thromboses	Hypertension, predisposition to thrombosis

The pharmacological "face" of medicines affecting the myometrium

Medicines	**UTEROTONICS**				
	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		**Other effects**		
Fenoterol	β_2-adrenomimetics		Broncholytic		
Salbutamol					
Progesterone	gestagens		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

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 metals**	**Acids**
Chloramine B Chlorhexidine Povidone-iodine	Hydrogen peroxide Potassium permanganate	Sodium tetraborate	Mercury dichloride Silver nitrate	Salicylic acid Benzoic acid
Phenols	**Dyes**	**Nitrofurans**	**Derivatives of 8-oxyquinoline**	**Aldehydes and alcohols**
Phenol Tricresol	Brilliant green Methylene blue	Nitrofural Furadonine	Nitroxoline	Formaldehyde Hexamethylen-tetramine Ethanol

Tars and resins	**Antibacterial medicines of natural origin**	**Detergents**
Ichthammol Medical ozokerite	Novoimanine Chlorophyllipt Ectericide	Ethonium Decamethoxine Miramistine

The mechanism of action

They cause the protein coagulation in microbes, alter the permeability of their cell wall, inhibit the enzymatic activity.

Pharmacodynamics (effects) → ***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

The list of medicines

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%

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**.

Classification of antibiotics by the mechanism and type of action

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

• 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.

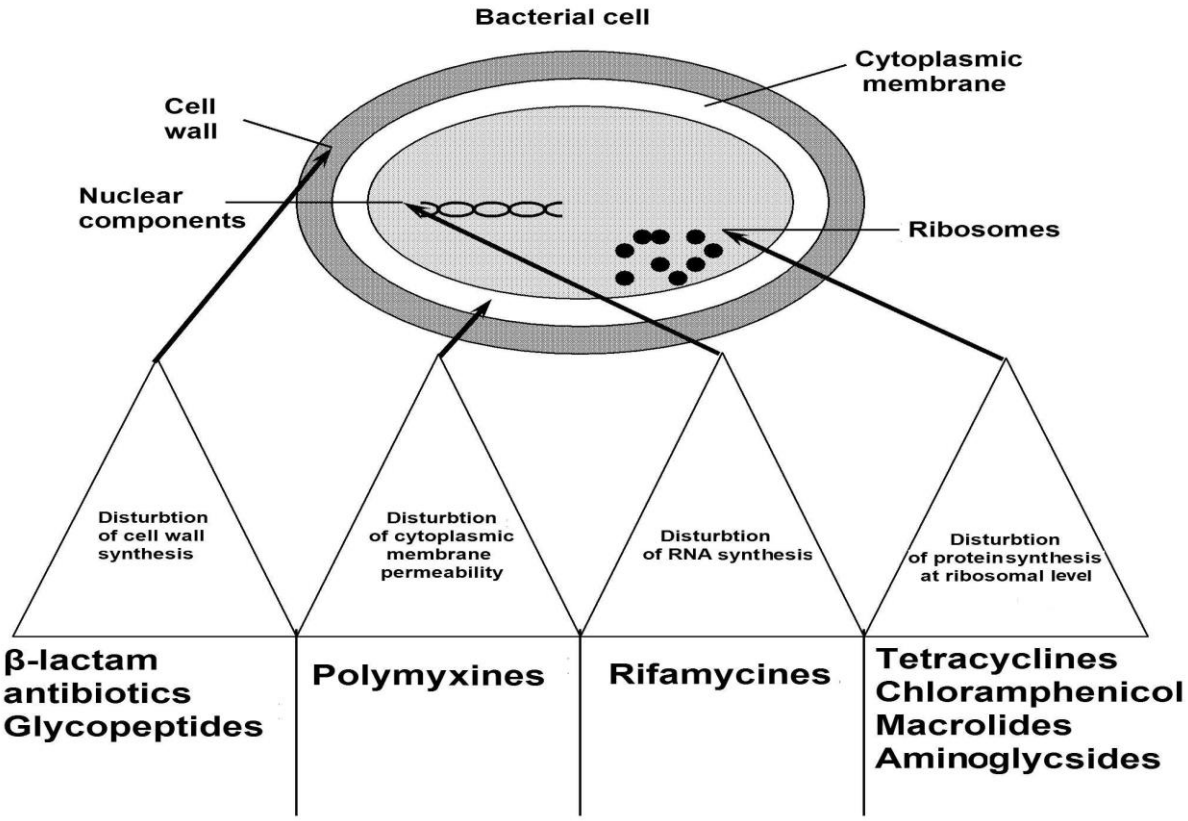

Fig. 5. The main mechanisms of the antibiotics antimicrobial action

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.

Classification of medicines

Natural			
Short-acting			*Depo-medicines*
Sodium and potassium salts of benzylpenicillin			Bicillin-5
Semi-synthetic			
Antistaphylococcal	*Aminopenicillins*	*Antipseudomonal*	*Combined*
• Oxacillin ▪ Cloxacillin	▪ Ampicillin ▪ Amoxicillin	Carbenicillin Azlocillin	▪ Amoxiclav (Amoxicillin+ clavulanic acid) ▪ Helicocin (Amoxicillin+ Metronidazole)

• -resistant to β-lactamases, ▪ -acid resistant

Pharmacodynamics (effects) → ***Indications***	
Antibacterial effect. **The type** of action is bactericidal. **The spectrum** of action is moderate (natural penicillins) and broad (semi-synthetic penicillins), including G^+ and G^- cocci, G^+ bacilli, anaerobes, spirochetes	Rheumatism, syphilis, angina, pneumonia, meningitis, abscess, otitis, diphtheria, gas gangrene, peptic ulcer, anthrax
Side effects → ***Contraindications***	
Neurotoxicity (tremor, convulsions, hallucinations), bleeding	Epilepsy (especially in endolumbal administration). High doses during pregnancy 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 β-lactamases, 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 (Penicillin)	Pwd. for inj. 1000000 U
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).

Classification of medicines

The Ist generation	**The IInd generation**	**The IIIrd generation**	**The IVth generation**
Cephazolin ▪ Cephalexin	Cefuroxime ▪ Cephaclor	Cephtriaxone ▪ Cephixim	Cephepim Cephpirom

▪ 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 cephalosporins	**Effectiveness against**	
	Gram-positive bacteria	**Gram-negative bacteria**
The first	+++	+/-
The second	++	+
The third	+	+++
The fourth	++	+++

Pharmacodynamics (effects)	***→ Indications***
Antibacterial effect. **The type** of action is bactericidal. **The spectrum** of action is broad	Infections of respiratory tract, skin and soft tissues, bones and joints, urinary tract, heart; prevention of infections after surgery. Meningitis and blue pus (pseudomonal) infection –cephalosporins of the III-IV generations
Side effects	***→ Contraindications***
Bleeding, hemato-, nephro-, neuro-, hepatotoxicity	Porphyria, epilepsy, severe disorders of kidneys and 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 • Meropenem*	• Aztreonam

• – 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) → ***Indications***	
Antibacterial effect. **The type** of action is bactericidal. **The spectrum** of action is extremely broad covering the majority of aerobic and anaerobic G^+ and G^- bacteria. Chlamydia, mycoplasmas, tuberculous and leprosy mycobacteria, pseudomonads (except blue pus bacillus) have a natural resistance to carbapenems	Severe hospital infections caused by a multi-resistant strains of microorganisms; infections of bones and joints, skin and soft tissues, abdominal cavity, female reproductive organs, urinary tract; bacterial endocarditis (imipenem), pneumonia, septicemia, meningitis (meropenem)
Side effects → ***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) → ***Indications***	
Antibacterial effect. **The type** of action is bactericidal. **The spectrum** of action is narrow (G^- aerobes, gonococci, meningococci, Salmonellas, Shigellas, Klebsiellas, Proteus, E. coli and blue pus bacilli)	Severe infections of different location caused by gram-negative flora that is resistant to the 3rd generation of cephalosporins, to the 2nd and 3rd generations of aminoglycosides, and antipseudomonal penicillins
Side effects → ***Contraindications***	
Bleeding, hepatotoxicity	Bleeding, dysfunctions of the liver and kidneys. They should be used carefully in pregnancy and lactation

The list of medicines

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.

Classification of medicines

Natural	Semi-synthetic
Tetracycline	Methacycline Doxycycline

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) →	***Indications***
Antibacterial effect. **The type** of action is bacteriostatic. The **spectrum** of action is broad (including G^+ and G^- cocci, bacilli, intracellular pathogens, anaerobes).	Infections of respiratory tract, biliary tract, abdominal and intestinal infections, syphilis, Helicobacter pylori eradication
Side effects →	***Contraindications***
Dysbiosis, dyspepsia, decrease of the body weight, hepato-, hemato-, nephro-, neurotoxicity, muto- and teratogenecity, photodermatitis, growth disorder of bones and teeth	Severe diseases of the liver and kidneys, pregnancy, lactation, myasthenia, age 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%

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.

Classification of medicines

Macrolides and azalides*			
The Ist generation	*The IInd generation*	*The IIIrd generation*	*Combinations of macrolides with tetracylines and other* medicines*
Erythromycine	Roxythromycine Clarythromycine	Azythromycine*	Oletetrin Zynerit*

A group of azalides is close to macrolides group, they are sometimes considered as the IIIrd 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) → ***Indications***	
Antibacterial effect. **The type** of action is bacteriostatic. **The spectrum** of action is broad (including G^+, G^-cocci, intracellular microorganisms)	Infections of respiratory, urinary, biliary tract; reproductive system; diphtheria, syphilis, skin infections
Side effects → ***Contraindications***	
Seldom: hepatotoxicity, photo-dermatitis, arrhythmias	Dysfunctions of the liver, kidneys, heart

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 Ist and IInd generation*	*The IIIrd generation*
Streptomycine Neomycine Gentamycine* Canamycine	Amycacine Tobramycine

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 IInd and the IIIrd 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) → ***Indications***	
Antibacterial effect. **The type** of action is bactericidal. **The spectrum** of action is broad (including aerobes, G$^-$ microflora: E. coli, Proteus, Salmonellas, Klebsiella, Enterobacter, Shigellas). Medicines of the IInd and the IIIrd generations affect blue pus bacillus	Hospital infections; sepsis, peritonitis, endocarditis, pneumonia, infections of small pelvis organs (pyelonephritis, urosepsis), osteomyelitis, meningitis of the unclear etiology
Side effects → ***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

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 (effects) → ***Indications***	
Antibacterial effect. **The type** of action is bactericidal. **The spectrum** of action is broad (including G^+ aerobic and anaerobic microorganisms: strepto-cocci, pneumococci, enterococci)	Severe hospital infections caused by resistant strains of staphylococci; enterococci, streptococci resistant to penicillins; sepsis, pneumonia, meningitis, endocarditis, infections of the skin and soft tissues, bones and joints, pseudomembranous colitis
Side effects → ***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

Classification of medicines

Lincosamides	**Fusidines**	**Chloramphenicols**	**Rifamycines**
Lincomycine hydrochloride	Fusidic acid	Chloramphenicol Levosin Levomecol	Rifampicine

Phosphomycines	**Polymyxines**	**Oxazolidinones* and others**
Phosphomycine	Polymyxine B sulphate	Linezolide * Fusafungin Gramicidine

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.

Lincosamides

Pharmacodynamics (effects) → ***Indications***	
Antibacterial effect. **The type** of action is bactericidal and bacteriostatic. **The spectrum** of action is broad (including G^+ microorganisms, anaerobes)	Reserve antibiotics in treatment severe staphylococcal, streptococcal, anaerobic infections
Side effects → ***Contraindications***	
Dyspepsia, pseudomembranous colitis. Hepatotoxicity. Leukopenia, neutropenia, thrombocytopenia	Colitis. Liver diseases. Leukopenia, neutropenia, thrombocytopenia

Chloramphenicols

Pharmacodynamics (effects) → ***Indications***	
Antibacterial effect. **The type** of action is bacteriostatic. **The spectrum** of action is broad (including G^+ microorganisms, anaerobes)	Infections of the GIT, meningitis, gas gangrene, plague, rickettsioses, typhoid, abdominal and pelvis infections
Side effects → ***Contraindications***	
Accumulation in the bone marrow. Inhibition of blood formation	Pregnancy, lactation, children under 10, anaemias, leukopenia, HIV-infection

Fusidines

Pharmacodynamics (effects) → ***Indications***	
Antibacterial effect. **The type** of action is bacteriostatic. **The spectrum** of action is narrow (staphylococci, anaerobes)	Staphylococcal infections when staphylococci are resistant to other antibiotics and if there is allergy to β-lactams
Side effects → ***Contraindications***	
Dyspepsia	Diseases of the GIT

Oxazolidinones

Pharmacodynamics (effects) → ***Indications***	
Antibacterial effect. **The type** of action is bacteriostatic. **The spectrum** of action is broad (including G^+ aerobes, anaerobes, resistant to other antiobiotics)	Pneumonia, endocarditis, severe infections caused by enterococci
Side effects → ***Contraindications***	
Anaemia, thrombophlebitis	Pregnancy, lactation
Increase of bilirubin level	Liver diseases

Polymyxines

Pharmacodynamics (effects) → *Indications*	
Antibacterial effect. **The type** of action is bactericidal. **The spectrum** of action is narrow (G^- bacteria, including Salmonellas, cholera vibrion, blue pus bacillus)	Severe G^- infections caused by multi-resistant hospital strains of microorganisms
Side effects → ***Contraindications***	
Nephrotoxicity	Hepatic insufficiency
Neurotoxicity	Myasthenia, pregnancy, children under 12, administration of muscle relaxants

NB! Polymyxines are used only by vital indications because of their toxicity.

Rifamycines

Pharmacodynamics (effects) → *Indications*	
Antibacterial effect. **The type** of action is bactericidal. **The spectrum** of action is broad (including G^- microorganisms, chlamydia, tuberculous mycobacteria)	Tuberculosis, leprosy, pneumonia, infections of urinary and biliary tract, osteomyelitis, meningitis
Side effects → ***Contraindications***	
Hepato-, hematotoxicity	Liver diseases. Pregnancy, age under 1 year old

Phosphomycines

Pharmacodynamics (effects) → *Indications*	
Antibacterial effect. **The type** of action is bactericidal. **The spectrum** of action is broad (including G^- microorganisms)	Acute non-complicated infections of urinary and biliary tract, sepsis, meningitis
Side effects → ***Contraindications***	
Dyspepsia	Children under 5

Gramicidine

Pharmacodynamics (effects) → *Indications*	
Antibacterial effect. **The type** of action is bactericidal. **The spectrum** of action is moderate (including G^- microorganisms)	Purulent inflammatory processes of the skin and mucous membranes
Side effects → ***Contraindications***	
Contact dermatitis	Dermatitis

Fusafungin

Pharmacodynamics (effects) → *Indications*	
Antibacterial effect. **The type** of action is bacteriostatic.	Infections of the upper respiratory tract

The spectrum of action is broad (including G^+ and G^- microorganisms, anaerobes)	
Side effects → ***Contraindications***	
Nasopharynx irritation, laryngo-, bronchospasm	Children under 2.5 years old, laryngospasm

Comparison of the pharmacological "face" of antibiotics of different groups

Medicines	**Spect-rum**	**Type of action**	**Resistance**	**Toxi-city**	**Peculiarities of action**
Lincosamides	B	Bs, bc	slowly	++	Accumulation in bones and joints
Polymyxine B sulphate	N (G^-)	Bc	-//-	++++	It is not absorbed from the GIT
Gramicidine	M	Bc	no	+++	Only local admi-nistration
Chloramphenicol	B	Bs	-//-	++++	GIT infections. Reserve **A**!
Fusidines	N	Bs	rapidly	++	Reserve **A**! 90% of bioavailability
Rifamycine	B	Bc	rapidly	++	Microsomal enzymes inductor. It is effective in TB
Phosphomycines	B $G^+<G^-$	Bc	slowly	++	Infections of urinary tract
Oxazolidinones	B $G^-<G^+$	Bs	slowly	++	Severe infections
Fusafungin	B	Bs	no	+	Anti-inflammatory effect

A – antibiotic; B – broad, N – narrow, M – moderate; bc – bactericidal, bs – bacteriostatic; TB – tuberculosis

The list of medicines

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 Ist generation	**The IInd generation**	**The IIIrd generation**
Norfloxacine Ofloxacine Cyprofloxacine	Levofloxacine Sparfloxacine	Moxifloxacine

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) → ***Indications***	
Antibacterial effect. **The type** of action is bactericidal. **The spectrum** of action is super broad (including G^+ and G^- aerobic and anaerobic microorganisms, chlamydia, mycoplasmas, legionellas, mycobacteria)	Infections of urinary and respiratory tract, bones and joints, skin, soft tissues; intestinal infections, sepsis; gonorrhea, meningitis, chlamydiasis, tuberculosis
Side effects → ***Contraindications***	
Chondrotoxicity	Persons under 18

Comparison of the pharmacological "face" of antibiotics (A) and fluoroquinolones

Antibiotics group	Spectrum	Type of action	Toxicity	PAE	ICA	Resistance	Other peculiarities/ indications
P	M*/B	bc	+	-		q	For peptic ulcer. A cross allergy with **CS**
CS	B	bc	++	+**			A cross allergy with **P**. A high resistance to β-lactamases
C	SB	bc	+++	+		s	A high resistance to β-lactamases
M	N	bc	+++	+			
T	B	bs	+++	-	+	q	It is used for peptic ulcer
ML	B	bs	+	-	+		For peptic ulcer. The prolonged action
GP	B	bc	+++	+		n	They are used for pseudomembranous colitis
AG	B	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.

The list of medicines

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

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-aminosalicylic acid derivatives*	*Antibiotics and isonicotinic acid thioamide derivatives**
Isoniazide Phthivazide Para-aminosalicylic acid (PASA)*	Rifampicine Streptomycine sulphate 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) → Indications	
Tuberculostatic or tuberculocidal effect	Tuberculosis of various forms and location
Side effects → Contraindications	
Dyspepsia, CNS disorders	Peptic ulcer, acute gastritis, erosive-ulcerous colitis; CNS diseases

Pharmacological "face" of antituberculous medicines

Medicine	**Type of action**		**Spectrum of action**		**Activity**	**Toxicity**
	Ts	*Tc*	*Broad*	*Narrow*		
Isoniazide	+	+		+	s	+++
Phthivazide	+			+	<s	+++
PASA	+			+	<s	++
Rifampicine*	+	+	+		=s	++
Ethionamide*	+			+	<s	+
Streptomycine	+	+	+		<s	+++
Capreomycine	+			+	<s	++

Ethambutol	+			+	<s	++
Florimycine	+		+		<s	++
Cycloserine	+		+		<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

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.

Classification of medicines

MONOCOMPONENT		
1. Resorptive-acting (absorbed in the intestine)		
Short-acting	**Long-acting**	**Super long-acting**
Sulphanylamide Sulphathiazole	Sulphadimethoxine	Sulphamethoxipyrazine
2. Acting in the intestine (poorly absorbed from the GIT)	*3. Derivatives of sulphonamides and 5-aminosalicylic acid*	*4. For external use*
Phthalylsulphathiazole	Salazosulphapyridine	Sulphacetamide Silver sulphathiazole Maphenide
COMBINED		
1. Resorptive-acting (Sulphonamide+Trimethoprim)	*2. For external use*	
Co-trimoxazole	Algimaf Streptonitol	

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 dihydrofolate-reductase 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).

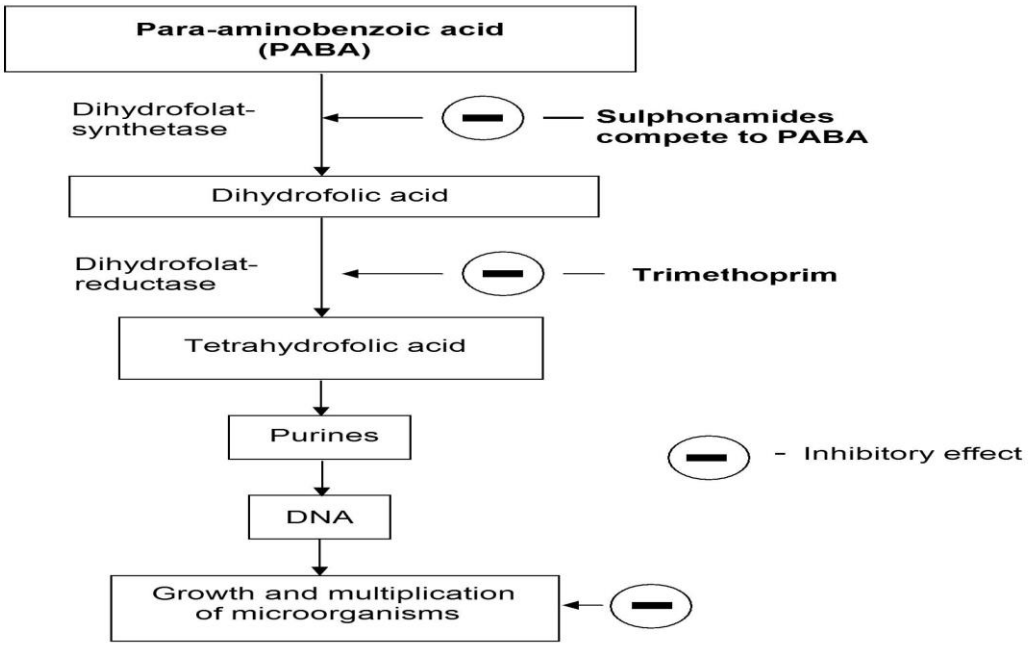

Fig. 6. The mechanism of the sulphonamide action

Pharmacodynamics (effects) →	***Indications***
The antibacterial effect. **The type** of action is bacteriostatic or bactericidal. The broad **spectrum** of action: microorganisms that synthesize the folic acid – staphylococci, streptococci, pneumococci, gonococci, meningococci, causative agents of intestinal infections (Salmonellas, Cholera vibrion, E.coli), chlamydias, protozoa (malarial plasmodium, toxoplasms)	Infectious diseases: quinsy, bronchitis, pneumonia, intestinal infections, cystitis, urethritis, prostatitis, cholecystitis, meningitis, otitis, wound infection, malaria

Side effects → *Contraindications*	
Crystaluria, agranulocytosis, leukopenia; teratogenicity	Renal insufficiency, blood formation 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).

The pharmacological "face" of sulphonamides

Medicines	**Action**		**Absorption in the GIT**	**Bs/Bc**	**Dose, g/day**
	duration	*strength*			
Sulphanylamide	s	r	+++	+/-	3-6
Sulphathiazole	s		+++	+/-	3-4
Phthalylsulphathiazole	s		+	+/-	6
Sulphadimethoxine	l	≥r	+	+/-	1
Salazosulphapyridine	l		+	+/-	2
Sulphacetamide	sl		+++	+/-	
Silver sulphathiazole	sl	>r		+/+	
Co-trimoxazole	sl	>r		+/+	
Maphenide **	sl			+/-	
Algimaf**(C)	sl			+/-	
Streptonitol (C)		>r		+/-	

S – short (to 8 h), l – 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.

The list of medicines

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

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 acting on schizogony (schizontocides, schizontotropic)		***Medicines acting on sporogony (gamontocides, gamontotropic)***	***Combined medicines***
Affecting the tissue cycle (in the liver) (histoschizontocides)	*Affecting the erythrocytic cycle (in erythrocytes) (hematoschizontocides*)		
Pyrimethamine Proquanyl h/chl. Quinocide Fansidar	Pyrimethamine Proquanyl h/chl. Chloroquine Mefloquine Fansidar	Pyrimethamine Proquanyl h/chl. Quinocide Mefloquine	Fansidar (Pyrimethamine + sulphadoxine)

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 (effects)	→	***Indications***
Antimalarial effect		Treatment and prevention of malaria

Side effects	→ *Contraindications*
Hepato- and nephrotoxicity	Diseases of the liver and kidneys
Teratogenicity	Pregnancy (especially the 1st 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.

The pharmacological "face" of **antimalarial medicines**

Medicines	**Resis-tance deve-lopment**	**Acti-vity**	**The rate of the effect's deve-lopment**	**Accu-mula-tion**	**Other indications**	
					Protozoal infections	*Non-infectious diseases*
Pyrimethamine	rapidly	>Q*	+	+	Toxo-plasmosis	
Proquanyl	rapidly		++	no		
Quinocide		>Q				
Chloroquine	slow	>Q	++	++		**RA, SLE, TA**
Mefloquine			+	++		

*****-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

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.

Classification of medicines

Antibiotics				**Bismuth-containing medicines**
Penicillins	*Cephalosporins*	*Macrolides and azalides**	*Tetracyclines*	
Benzylpenicillin sodium and potassium salts	Cephaloridine	Erythromycine Azythromycine	Tetracycline	Biyoquinol

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) →	***Indications***
Antibacterial (antispirochetal) effect	Syphilis (all forms and stages)
Side effects →	***Contraindications***
Bismuth-containing medicines: salivation, "bismuth border" on the gums, stomatitis, colitis, nephrotoxicity, leukopenia, pain in the site of injection	Dysfunctions of the liver, kidneys, blood formation organs; pregnancy, lactation

The pharmacological "face" of antisyphilitic medicines

Medicines	**Type of action**		**Peculia-rities of action**	**Toxi-city**	**Route of admini-stration**	**Other peculiarities**
	Bc	Bs				
Benzylpenicillin	+		All stages of syphilis	+	p/e	AB of the medium spectrum
Cephaloridine	+			+	p/e	AB of the broad spectrum
Azythromycine	+	+	I, II stages of syphilis	+	p/o	AB of the broad spectrum
Tetracycline		+		+++	p/o	AB of the broad spectrum
Biyoquinol			All stages of syphilis	++	p/e	Anti-inflammatory effect, used in non-syphilitic diseases of the CNS

p/e- parenteral, **p/o** – peroral, **AB –** antibiotic.

The list 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

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.

Classification of medicines

Medicines used in intestinal nematodoses (*-broad spectrum ones)	Medicines used in intestinal cestodoses and trematodoses*	Medicines used in extraintestinal helminthiases
Mebendazole* Albendazole* Pyrantel Levamisole Prasiquantel* Tansy flowers	Aminoacrichine Prasiquantel Mebendazole Ethylene tetrachloride*	Prasiquantel Mebendazole Albendazole

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) → Indications	
Antihelminthic effect	Helminthiases (according to spectrum of action)

Side effects → 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.

Pharmacological "face" of antihelminthic medicines

Medicines	**Indications**				
	Ascaria-sis	Entero-biasis	Cesto-doses	Trichocepha-liasis	Ancylo-stomiasis
Albendazole	+	+	+	+	+
Aminoacrichine			+		
Levamisole*	+				
Mebendazole	+	+	+	+	+
Pyrantel	+	+			+
Prasiquantel			+		

* - 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

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 Natamycine	Nystatin Griseofulvin*		
Antifungal medicines of synthetic origin			
Azoles (imidazole and triazole derivatives)*	*N-methylnaphthalene derivatives, pyrimidines**	*Undecylenic acid derivatives*	*Combined medicines*
Clotrimazole Ketoconazole Miconazole Fluconazole* Itraconazole*	Terbinafine Flucytosine*	Zincundan	Clion D Pimafucort

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) → Indications	
Antifungal effect. **Type** of action: fungicidal and/or fungistatic	Systemic and local mycoses
Side effects → Contraindications	
Dyspepsia, teratogenicity (associated with resorptive effect)	GIT diseases, pregnancy

Amphoterycine B, itraconazole, fluconazole, ketoconazole have broad spectrum of antifungal activity.

Pharmacological "face" of antifungal medicines

Medicines	**Effects**			**Mycoses**		**Absorption in GIT**
	fc	**fs**	**antimicrobial**	**local**	**systemic**	
Amphoterycine	+			+	+	+
Nystatin	+			+	+	±
Natamycine	+			+		
Griseofulvin		+		+		
Clotrimazole	+	+	+	+		
Ketoconazole	+	+	+	+	+	+
Miconazole	+	+	+	+		
Fluconazole	+	+	+	+	+	+
Itraconazole	+	+	+	+	+	+
Terbinafine		+	+	+		
Flucytosine		+	+	+		
Zincundan		+	+	+		
Clion D	+	+	+	+		

fc – fungicidal effect, **fs** – fungistatic effect.

The list of medicines

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

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.

Classification of medicines

Anomalous nucleosides	**Adamantane and other groups* derivatives**	**Pyrophosphate analogues**
Acyclovir Ribavirine Gancyclovir Famcyclovir	Remantadine Amantadine Oxolin*	Sodium foscarnet
Interferons and immunoglobulins*	**Interferon synthesis inducers (interferonogens)**	**HIV- proteinase and reverse transcriptase inhibitors***
Interferon-(α-1, α-2B, β-1B) Normal human immunoglobulin*	Cycloferon Amixin Inosine pranobex	Saquinavir Nelfinavir Didanosine* Zidovudine*

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) → Indications	
Antiviral effect (all drugs). Immune-stimulating effect (interferons, immunoglobulins, interferon synthesis inducers)	ARVI, herpes, influenza A, B; encephalomyelitis, cytomegaloviral infections, viral pneumonias, chickenpox, conjunctivitis, viral hepatitis (A, B, C), chlamydiasis
Antiretroviral effect (antiviral effect against HIV-infection)	HIV-infection
Side effects → Contraindications	
Nephro- and hepatotoxicity, teratogenicity, CNS disorders (tremor, hallucinations, convulsions)	Renal and hepatic failure, pregnancy and lactation, epilepsy

Pharmacological "face" of antiviral medicines

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		A						
Amantadine		A						
Foscarnet	+		+					
Ribavirine	+	A, B						
Gancyclovir		A, B, P	+					
Famcyclovir	+							
Oxolin	+	A						
Interferon-α-2B		A, B		B, C, Δ	+	+	+	
Immunoglo-bulin	+			A				

Cycloferon	+	A, B, P	+	A, B, C, Δ	+	+	+	+
Amixin	+	A, B, P	+	A, B, C		+		
Inosine	+		+	B, C		+		
Saquinavir								+
Nelfinavir								+
Didanosine								+
Zidovudine								+

P – para-influenza, **Δ** – delta.

The list of medicines

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, Retrovir)	Tabl., caps. 0.1, 0.25

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

<table>
<tr><td colspan="5">1. Alkylating compounds</td></tr>
<tr><td>Derivatives of chlorethylamine</td><td colspan="2">Derivatives of ethylenimine</td><td>Derivatives of sulphonic acid</td><td>Derivatives of nitrosourea, hydroxyurea</td></tr>
<tr><td>Chlorethylaminouracil
Cyclophosphamide</td><td colspan="2">Thiophosphamide
Phosphemide</td><td>Busulphan</td><td>Nimustine
Hydroxycarba-mide</td></tr>
<tr><td colspan="3">Metal-organic compounds</td><td colspan="2">Other alkylating compounds</td></tr>
<tr><td colspan="3">Cisplatin</td><td colspan="2">Dacarbazine</td></tr>
<tr><td colspan="5">2. Antimetabolites</td></tr>
<tr><td>Antagonists of the folic acid</td><td colspan="3">Antagonists of the purine bases</td><td>Antagonists of pyrimidine</td></tr>
<tr><td>Methotrexate</td><td colspan="3">Mercaptopurine</td><td>Fluorouracil</td></tr>
<tr><td colspan="5">3. Cytostatics of the plant origin</td></tr>
<tr><td>Alkaloids of Vinca rosea (vinca alkaloids)</td><td colspan="3">Alkaloids of Podophyllum (podophyllotoxins)</td><td>Alkaloids of Colchicum speciosum</td></tr>
<tr><td>Vincristine</td><td colspan="3">Podophylline</td><td>Colchamine</td></tr>
<tr><td colspan="5">Terpenoids of Taxus tree (taxozides)</td></tr>
<tr><td colspan="5">Paclitaxel</td></tr>
<tr><td colspan="5">4. Hormonal and antihormonal medicines</td></tr>
<tr><td>Gestagens</td><td>Estrogens</td><td>Antiestrogens</td><td>Androgens</td><td>Antiandrogens</td></tr>
<tr><td>Megestrol</td><td>Ethynylestradiol</td><td>Tamoxyphen</td><td>Testosterone propionate</td><td>Ciproterone acetate</td></tr>
<tr><td colspan="3">Analogues of gonadoliberin</td><td colspan="2">Inhibitors of adrenal cortex hormones biosynthesis</td></tr>
<tr><td colspan="3">Gozerelin</td><td colspan="2">Aminoglutetimide</td></tr>
<tr><td colspan="3">5. Antitumour antibiotics</td><td colspan="2">6. Inhibitors of topoisomerase I, aromatase*</td></tr>
<tr><td>Actinomycines</td><td>Anthra-cyclines</td><td>Phleomycines</td><td rowspan="2">Topothecan</td><td rowspan="2">Anastrozol *</td></tr>
<tr><td>Dactinomycine</td><td>Doxorubicine</td><td>Bleomycine</td></tr>
<tr><td colspan="3">7. Cytokins</td><td colspan="2">8. Enzymes</td></tr>
<tr><td colspan="3">Aldesleukin</td><td colspan="2">L-asparaginase</td></tr>
<tr><td colspan="5">9. Recombinant monoclonal antibodies</td></tr>
<tr><td colspan="5">Trastusumab</td></tr>
</table>

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) →	***Indications***
Antitumour medicines have cytostatic, cytotoxic and immune-suppressive effects (all, except hormonal and antihormonal ones). **Hormonal and antihormonal medicines** retard the division of hormone-dependent tumour cells and promote their differentiation, have androgenic (androgens), antiandrogenic (antiandrogens, estrogens), estrogenic (estrogens), antiestrogenic (gestagens, antiestrogens, inhibitors of the adrenal glands hormones biosynthesis) effects; inhibit hormone synthesizing function of testes and ovaries - cause the pharmacological castration (analogues of gonadoliberin); cause the pharmacological andrenalectomy (aminoglutetimide)	Tumours of different location
Side effects	***→ Contraindications***
Inhibition of the blood formation, immune suppression, dyspepsia; mutagenicity, teratogenicity	Inhibition of the hemopoiesis, immune deficiency, peptic ulcer (with caution); pregnancy, lactation

The pharmacological "face" of antitumour medicines (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,

	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, erythremia*	30, 7*

Numbers 1-31 are the numbers of medicines in classification.

The pharmacological "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 list of medicines

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%

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 preceedes 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.

Pharmacological description

Medicines	Group	Origin/ composition	Pharmacological «face»
Thymalin Tactivin	**Endogenous polypeptides**	Polypeptide fractions from the cattle's thymus	They normalize T-lymphocytes and their ratio with B- lymphocytes, cellular immunity reactions; increase the activity of natural killers, intensify phagocytosis and production of lymphokins. They are used in burns, trophic ulcers, inhibition of hemopoiesis, immunity, in radiation and chemotherapy
Myelopid		Cell culture of bone marrow of calves, pigs	It stimulates proliferation and the functional activity of T- and B-killers. It is used in secondary immune deficiency states (the humoral immunity), for prevention of complications after operations and traumas
Immunofan		Synthetic hexopeptide	It stimulates interleukin-2 formation, 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 medicines**	Imidazole derivative (see "Antihelmintic medicines")	It regulates differentiation of T-lymphocytes, promotes the synthesis of immunoglobulins
Polyoxydonium		Synthetic polymer	Immune-stimulating, detoxication effects
Bronchomunal	**Microbial medicines and their analogues**	Bacteria lyophylic lysate	It stimulates the humoral and cellular immunity, increases the amount and activity of lymphocytes and 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

Prodigiosan		Complex from microorganisms *B. prodigiosum*	It increases non-specific and specific resistance of an organism (activates B-lymphocytes, interferons, lysocim, complement). It is used in chronic inflammations, poor healing of wounds, radiation therapy
Interferon α, β*, α-2a, β-1b*	**Interferons**	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	**Interferon 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 polyribonucleic complex	It affects viruses of a simple herpes (herpes conjunctivitis, keratitis, iridocyclitis, etc.)
Cycloferon		Low-molecular compound	Antiviral (see "Antiviral medicines"), anti-inflammatory, immune-stimulating, antichlamydial, radioprotective effects. It is used in tick-borne encephalitis, herpes, cytomegalovirus and HIV-infections; in collagenoses
Roncoleukin	**Interleukins**	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 interleukin-1	Increases leukopoiesis and immunity. Used in chemo- and radiation therapy of tumours, immune deficiencies
Molgramostim, Filgrastim, Lenograstim	**Colony-stimulating factors**	Recombinant human colony-stimulating factors	See "Leukopoiesis stimulants"

Normal human immunoglobulin	**Human immunoglobulins**	Immunoglobulin G	It is used in immune deficiency states, thrombocytopenic purpura, etc.
Pentaglobin		Immunoglobulin G enriched by immunoglobulins M, A	It is used in severe bacterial infections (sepsis), immune deficiencies
Cytotect		Specific hyperimmune immunoglobulins G against the certain pathogens	It is used in cytomegaloviral infections
Hepatect			It is used in hepatitis B

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.

Classification of medicines

Medicines		
normalizing the flora: *probiotics - monocomponent, polycomponent *, combined ***	**stimulating the normal flora growth:** *prebiotics and symbiotics**	**inhibiting the conditional pathogenic microflora:** *bacteriophages and others**
Lactobacterin Bactisubtil Linex* Bificol* Bifidumbacterin forte*	Potassium permanganate Hilak-forte Lactulose Bifiform*	Staphylococcal and pseudomonal bacteriophages Fluconazole* Natamycine* Ketoconazole*

The mechanism of action

Promote the formation of the acetic, lactic acids in the intestine inhibiting the putrefactive and gas-forming flora	Decrease pH of the large intestine. Contain the components necessary for nutrition and reproduction of bifidobacteria and lactobacteria	Destroy the conditional-pathogenic flora; fungicidal and fungistatic effects against Candida fungi

Pharmacodynamics

Support the balance of the normal microflora; reduce meteorism, normalize digestion and absorption in the intestine; promote the organism's resistance to infection	Stimulate the growth and reproduction of the normal microflora of the intestine, strengthen the peristalsis of the GIT	Antibacterial, antifungal effects

Side effects	→ ***Contraindications***
Seldom – dyspepsia (all); meteorism (Lactulose, Fluconazole); hepatotoxicity (Fluconazole)	Infants before 6 months (Bificol); liver diseases, pregnancy, lactation (Ketoconazole); porphyria (Natamycine); intestinal obstruction

Side effects and contraindications have not been determined for Bactisubtil, Bifidumbacterin forte, Bificol, Bifiform, Potassium permanganate, Lactobacterin and Linex.

The pharmacological "face" of medicines for dysbiosis treatment

Medicines	**Dysbiosis**			**Other indications**		
	Com-pensa-ted	Subcom-pensated	Decom-pensated	Acute intestinal infections	Diarrhea in children	Chronic entero-colitis
All, except Fluconazole[@], Natamycine [@], Ketoconazole [@]	+	+	+	+**	Hilak-forte, Lactobac-terin	+*

* - except bacteriophages inhibiting conditional pathogenic flora; ** - only probiotics; [@] - except dysbiosis it is used in mycoses.

The list of medicines

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	

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: H_1-, H_2-, H_3- and H_4-receptors. Allergic reactions are connected with stimulation of H_1-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 H_1-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.

Classification of medicines

Blockers of H_1-histamine receptors	**Blockers of serotonin* receptors, combined** agents**
Promethazine Clemastine Terfenadine Loratadine Diphenhydramine	Ciproheptadine* Clarinase**

Membrane stabilizers	**Glucocorticosteroids**	**Selective antagonists of leukotriene receptors**
Cromoglycic acid	Prednisolone Triamcinolone acetonide	Zafirlucast

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 (effects) → ***Indications***	
Anti-allergic effect	Allergic reactions (anaphylactic shock, bronchial asthma, dermatitis, angioneurotic edema, etc.)
Side effects → ***Contraindications***	
Inhibition of the CNS (decrease of attention, sedative effect), cardiotoxic effect, hypotension	The activity that requires attention, craniocerebral trauma, hypertension, liver diseases, pregnancy, lactation

The pharmacological "face" of anti-allergic medicines

Medicines	**Recep-tors blockers**	**Effects**			**Duration of action**	**Other effects**
		Spas-mo-lytic	**Seda-tive**	**Anti-inflam-matory**		
Promethazine (I)	H_1+H_2	+	+	+	8-12	Local anesthetic, potentiating, hypnotic
Clemastine (I)	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

I, II –generations of histamine-blockers

The list of medicines

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

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 mechanism of action	Pharmacodynamics	Indications (poisonings)
Activated carbon, Polyphepan	Absorption of a poison	Decrease of the poison absorption in the GIT, its elimination	Food toxical infection, poisoning by orally administered poisons
Dipyroxim, Isonitrosine	Restoration of the cholinesterase activity	Normalization of the cholinergic neurotransmission	Poisoning by irreversible-acting anticholinesterase medicines, FOC
Unithiol	Formation of low toxic water soluble complexes with thiolic poisons	Reduction of the thiolic enzymes activity, binding to thiolic poisons	Poisoning by heavy metals, cardiac glycosides, arsenic
Calcium trisodium	Formation of chelate	Elimination of a poison in form of	Poisoning by metals

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 metabolism	Decrease of formation of highly toxic formaldehyde	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.

The list of medicines

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%

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 table).

Table 6

Group	It is described in the corresponding groups or in table 7*
Hypertensive medicines	Analeptics, psychomotor stimulants, adaptogens, adrenomimetics (α_1, $\alpha + \beta$). Dophamine*, Angiotensinamide*
Gastroprotectors	Antiulcer medicines (bismuth-containing medicines, astringents, covering medicines, cytoprotectors – prostaglandins analogues)
Inhibitors of proteases (anti-enzymatic)	Enzymatic and anti-enzymatic medicines (Aprotinine); medicines increasing blood coagulation (Aminocapronic acid)
Prokinetics	Domperidone*, Methoclopramide*
Anti-aggregants	Medicines decreasing blood coagulation (Aspirin, Dipyridamol, Ticlopidine). Abcyximab*
Cholelitholytic medicines	Hepatoprotectors (Ursodeoxycholic acid). Chenodeoxycholic acid*
Cholagogue (choleretic) medicines	Hepatoprotectors (Flamine). Allochol*, Himechromone*
Normothymics	Anticonvulsants (Carbamazepine, valproates), calcium antagonists (Verapamil, Dilthiazem, etc. – see anti-anginal, hypotensive, anti-arrhythmic medicines). Salts of lithium* (carbonate, gluconate, chloride, etc.)
Antidiarrheal medicines	Inhibitors of hypophysis hormones secretion (Synthetic somatostatin*). Nifuroxaside*, Hilac forte *, Smekta*, Loperamide*
Enzymatic medicines	Pancreatic enzymes; medicines decreasing blood coagulation (fibrinolytics). Hyaluronidase*, Trypsin*, Cytochrome C *, Penicillinase*, Deoxyribonuclease*
Immunotropic: - immunodepressants - immunostimulants	- glucocorticosteroids, antitumour medicines (alkylating medicines, antibiotics, etc.), antibiotics. Thymoglobulin*, Azathioprin*, Daclizumab*, Cyclosporin* - Antihelminthic (Levamisole), antiviral (interferons and their inducers), leukopoiesis stimulants, immunostimulants, hypotensive medicines (bendazole)

Table 7

The pharmacological "face" of medicines

Dophamine	**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 - ↑ TPVR, constricts renal vessels. **It is used** in hypotension, shock of different etiology

Angiotensi-namide	**Hypertensive** (amide of the natural angiotensin II). ↑ TPVR, secretion of adrenaline and aldosterone. **It is used** in shock and related vasomotor collapse
Domperi-done	**Prokinetics** (D_2-dophamine receptors blocker). It intensifies the GIT peristalsis, has anti-emetic effect. **It is used** in dyspepsia with the gastro-enteral reflux, esophagitis; nausea and vomiting of various genesis
Metho-clopramide	**Prokinetics** (blocker of dophamine and serotonin receptors). It 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 fibrinogen to glycoproteins IIb/IIIa in the membrane of thrombocytes, disturbs their aggregation. **It is used** to prevent thromboses
Chenode-oxycholic acid	**Cholelitholytic**. It decreases the synthesis, absorption of cholesterol and formation of cholesterol stones in the gallbladder. **It is used** in 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-mone	**Cholagogue** (synthetic choleretics). It intensifies reflexively bile 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 salts	**Normothymics.** They correct the mood disorders, have antimaniac and antidepressant effects. **They are used** during phasic psychotic mood disorders
Synthetic somatosta-tin	**Antidiarrheal.** It decreases secretion of somatotropin and insulin, production of gastric juice, inhibits the GIT peristalsis. **It is used** in intractable diarrhea, acromegalia, tumours of the gastro-entero-pancreatic system
Nifuroxa-side	**Antidiarrheal** (synthetic antibacterial). **It is used** in bacterial 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
Deoxyribonuclease	**Enzymatic** (proteolytic enzyme). See "Trypsin" + antiviral effect. **It is used** in bedsores, keratitis, conjunctivitis
Hyaluronidase	**Enzymatic medicine**. It increases tissue permeability decreasing viscosity of hyaluronic acid; softens scars, removes contractures in joints, hematomas. **It is used** in hematomas, contractures in joints, rheumatoid arthritis
Cytochrome C	**Enzymatic.** It improves tissue breathing, restores oxidative processes. **It is used** in asphyxia of newborns, chronic pneumonia, HF, IHD, hypoxia
Penicillinase	**Enzymatic**. It inactivates penicillins destroying the β-lactam ring. **It is used** in acute allergy caused by penicillins
Thymoglobulin	**Immunodepressant** (polyclonal antibodies, antithymocytic 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 rubbing, compresses in inflammatory diseases of the locomotor organs
Resorptively:	
Foam-extinguishing	Pulmonary edema (as inhalation)
Antishock	Shock (seldom)
Antidote in poisonings by methanol (inhibition of highly toxic formaldehyde formation)	Poisoning by methanol

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) → the CNS inhibition (hypnotic effect, analgesia) → 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
COMT	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
HF	Heart failure
HIV	Human immunedeficiency virus
ICP	Intracranial pressure
IHD	Ischemic heart disease
INN	International name
i/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
↓	Decrease
↑	Increase