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КАФЕДРА ФАРМАКОЛОГИИ

# ФАРМАКОЛОГИЯ

# PHARMACOLOGY

Практикум для специальности «Лечебное дело»

*10-е издание*



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## INTRODUCTION

This study guide is elaborated in accordance with the requirements of the Programme in Pharmacology for students of General Medicine faculties of medical universities and composed for the student's individual work. The guide contains three parts: General Prescription, General Pharmacology and Special Pharmacology.

The part General Prescription contains the rules of making a prescription and writing out a prescription of some medicinal forms. Pharmacology course begins with this section.

General Pharmacology studies the principles of medicinal substances actions on human and animal organisms at different levels (molecular, cellular, systemic) — pharmacodynamics as well as general regularities of absorption, distribution, biotransformation and excretion of medicinal substances — pharmacokinetics. This part of the guide contains practical tasks consolidating the knowledge of pharmacokinetic quantitative regularities and drugs dosage principles.

Each topic of the practical lesson of the part Special Pharmacology is dedicated to the study of a special group of drugs and contains a modern classification of drugs in which the major ones for practical medicine are pointed out and the list of questions for individual study for practical class is provided. All the drugs, included into this guide have an international non-patent name (INN).

The appendices to the guide contain rules of making a prescription and writing out a prescription of some medicinal forms, brief reference information on the basic drugs from various pharmacological groups and examples of writing out prescriptions for various medicinal forms.

After completing the course in Pharmacology the student is **must know**:

- legislative, economic, organizational and deontological aspects of drugs application;
- rules of elaboration and implementation of new drugs into clinical medicine;
- basics of pharmacokinetics and pharmacodynamics of drugs;
- medical nomenclature of drugs;
- mechanisms of action of drugs at the molecular, cellular and systemic levels that ensure their clinical efficacy;
- pharmacological characteristics and basics of clinical application of drugs, their major side effects and contraindications;
- toxic syndromes resulting from drugs overdosage and poisoning, therapy principles of drugs poisoning, antidotes;
- problems of drug allergy, prevention and treatment;
- peculiarities and risks of drugs use in children, elderly population, pregnant and nursing women;
- main mechanisms and principles of drugs interaction.

**To know how:**

- to make efficient use of drugs according to their pharmacological characteristics and clinical indications;
- to make calculation of an individual dosing regimen on the basis of pharmacokinetic parameters of the drug and the patient's individual characteristics;
- to alter the dosing regimen in diseases changing clearance and distribution of drugs in the body;
- to forecast pharmacotherapeutic complications and define ways of their minimization;
- to write out prescriptions for administration of drugs in different medicinal forms.

The authors consider that the study guide will be of help not only in the study of Pharmacology, but also as a source of information in the whole spectrum of modern drugs of different indications and rules of writing out prescriptions in the future study of clinical medicine.

### **CRITERIA FOR EVALUATION KNOWLEDGE OF STUDENTS ON THE DISCIPLINE «PHARMACOLOGY» IN ACCORDANCE WITH A 10 POINT SCALE**

The main criteria for assessment of student learning are:

1. Degree of mastering of the material on the pharmacology curriculum.
2. Degree of development of practical skills in the syllabus of the pharmacology.
3. Degree professional literacy in the design of training documentation (prescriptions for drugs).
4. Depth understanding of the nature and urgency of the issues discussed.
5. Structure of verbal response.

#### **10 points — ten:**

- systematic, deep and full knowledge of all sections of the curriculum in pharmacology, as well as on the major issues that go beyond its limits;
- correct use of professional terminology in pharmacology (including Latin), stylistically competent and logically correct statement answering questions;
- impeccable possession practical skills provided curriculum for pharmacology, ability to use them effectively in the formulation and solution of professional problems;
- demonstrated ability to independently solve complex problems and unusual situations in the curriculum;
- full and profound assimilation of basic and additional literature, the recommended curriculum for pharmacology;
- the ability to navigate in the theories, concepts and directions for the development of pharmacology, giving them a critical assessment;
- creative independent work on laboratory sessions and seminars on the pharmacology, active participation in group discussions of educational material, high level of performance of educational tasks, professionally competent registration of training documentation.

#### **9 points — nine:**

- systematic, deep and full knowledge of all sections of the curriculum in pharmacology;
- correct use of professional terminology (including Latin), stylistically competent and logically correct statement in answering questions;
- fluency conceptual apparatus pharmacology, ability to use it effectively in the formulation and solution of professional problems;
- the ability to solve independently and creatively complex problems and unusual situations in the curriculum in pharmacology;
- a deep understanding of the basic theories and concepts of pharmacology;
- complete assimilation of basic and additional literature, the recommended curriculum for pharmacology;
- independent work on laboratory studies and seminars, creative participation in group discussions of educational material, high level of performance of educational tasks, professionally competent registration training documentation.

**8 points — eight:**

- systematic, deep and full knowledge of the pharmacology of a study program;
- correct use of professional terminology (including Latin), stylistically competent and logically correct statement in answering questions;
- possession of the conceptual apparatus of pharmacology, the ability to use it in the formulation and solution of professional problems;
- ability to solve independently complex problems within the curriculum in pharmacology;
- ability to navigate the basic theories and concepts of pharmacology;
- mastering the basic and additional literature recommended by curriculum for pharmacology;
- active independent work on laboratory studies and seminars, regular participation in group discussions of educational material, high level of performance of educational tasks, competent registration training documentation.

**7 points — seven:**

- systematic, deep and full knowledge of the pharmacology within a study program;
- correct use of professional terminology (including Latin), stylistically and logically correct statement in answering the questions, the ability to make reasonable conclusions;
- possession of the conceptual apparatus of pharmacology, the ability to use it in the formulation and solution of professional problems;
- ability to navigate the basic theories and concepts of pharmacology;
- assimilation of the basic and additional literature recommended by curriculum for pharmacology;
- independent work on laboratory studies and seminars, participate in group discussions of educational material, high level of performance and design of learning tasks in training documentation.

**6 points — six:**

- sufficiently complete and systematic knowledge in a study program in pharmacology;
- correct use of professional terminology (including Latin), stylistically competent and logically correct statement in answering the questions, the ability to make reasonable conclusions;
- possession of the conceptual apparatus of pharmacology, the ability to use it in everyday work;
- ability to navigate the basic theories and concepts of pharmacology;
- mastering the basic literature recommended curriculum for pharmacology;
- active independent work on laboratory studies and seminars, periodic participation in group discussions of educational material, high level of performance and design of learning tasks in training documentation.

**5 points — five:**

- sufficiently complete knowledge of a study program in pharmacology;
- correct use of professional terminology (including Latin), logically correct statement answering the questions, the ability to make reasonable conclusions;
- possession of basic conceptual apparatus pharmacology, ability to decide the standard (typical) tasks within the curriculum in pharmacology;
- mastering the basic literature recommended by curriculum for pharmacology;

- independent work on laboratory studies and seminars, participate in group discussions of educational material, an acceptable level of the performance of educational tasks, the entire layout of the training documentation.

**4 points — four:**

- sufficient knowledge of a study program in pharmacology;
- correct use of professional terminology (including Latin), logically correct statement in answering the questions, the ability to draw conclusions without significant errors;
- possession of basic conceptual apparatus pharmacology, ability to use it in solving standard (typical) tasks;
- mastering the basic literature recommended by curriculum;
- work under the guidance of a teacher at the laboratory classes and seminars, an acceptable level of the performance and design learning tasks in training documentation.

**3 points — three (poor):**

- lack of knowledge of the material of the curriculum in pharmacology;
- lack of knowledge or incorrect use of professional terminology, presentation of answers with significant logical errors;
- poor command of the conceptual apparatus of Pharmacology, incompetence in solving standard (typical) tasks;
- fragmentary understanding of basic literature recommended by curriculum for pharmacology;
- passivity on laboratory sessions and seminars, poor execution of learning tasks and design in training documentation.

**2 points — two (poorly):**

- fragmentary knowledge of the material in the curriculum in pharmacology;
- lack of knowledge or incorrect use of professional terminology, sufficient errors in answering the questions, lack of skills to solve standard (typical) tasks;
- fragmentary understanding of basic literature recommended by curriculum for pharmacology;
- passivity on laboratory sessions and seminars, poor execution of learning tasks and design in training documentation.

**1 point (poor):**

- lack of knowledge of the curriculum in pharmacology;
- refuse to answer.

# GENERAL PRESCRIPTION

## LESSON 1. INTRODUCTION. PRESCRIPTION. SOLID MEDICINAL FORMS

**Objective:** To study the structure of the prescription, learn the rules and get practical skills in writing out solid medicinal forms in prescription.

To carry out practical tasks on prescriptions it is recommended to use Appendix 1.

### Key questions:

1. Pharmacology as a science and the basis of therapy. Main development milestones of modern pharmacology. Sections of Pharmacology.
2. The concept of medicinal substance, medicinal agent (medicinal drug, drug), medicinal form.
3. The concept of the pharmacological action and types of the action of drugs.
4. The sources of obtaining drugs.
5. International and national pharmacopeia, its content and purpose.
6. Pharmacy. Rules of drug storage and dispensing.
7. Prescription and its structure. Prescription forms. General rules for writing out a prescription. State regulation of writing out and dispensing drugs.
8. Name of medicinal products (international non-proprietary name — INN, trade name).
9. Peculiarities of writing out narcotic, poisonous and potent substances in prescription.
10. Drugs under control. Drugs prohibited for prescribing.
11. Solid medicinal forms: tablets, dragee (pills), powders, capsules. Their characteristics, advantages and disadvantages. Rules of prescribing.

### Write out prescriptions for:

1. 20 tablets of Sertraline 0.1 g. 1 tablet orally once a day.
2. 20 coated tablets of Ticlopidine 0.25 g. 1 tablet orally once a day during or immediately after a meal.
3. 10 chewable tablets of Montelukast 0.0005 g. For the children 6–15 years old, 1 chewable tablet once a day in the evening.
4. 10 tablets of Nystatin 100 000 IU. For intravaginal use 1 tablet 4 times a day.
5. 20 tablets of Verapamil retard 240 mg each. Take 1 tablet orally once a day.
6. 10 tablets of «Co-trimoxazolum». Combined drug. 1 tablet orally 2 times a day.
7. 50 capsules of Zidovudine 0.25 g. 1 capsule orally 6 times a day.
8. 20 dragees of Chlorpromazine 0.25 g. 1 dragee orally 1 time a day.
9. 5 powders of Codeine 0.015 g. 1 powder orally twice a day.
10. 10 powders of Didanosine 0.25 g in sachets to prepare solution for internal use. Accept inside twice a day one sachet powder after dissolution in a glass of boiled water.
11. Powder of Azithromycin 0.46 g in the bottle to prepare suspension 100 mg / 5 ml. Dissolve the contents of the bottle in boiled water. Take orally 5 ml once a day 1 hour before meals or 2 hours after a meal, for 3 days.
12. 50 mg of Alteplase powder in the bottle. Dissolve the content of the bottle in 50 ml of saline. First 15 ml introduce intravenously streamly, then intravenous drip.
13. 5 sachets containing 100 mg of Nimesulide granules. Take 100 mg orally (1 sachet) 2 times a day after dissolving the granules in half a glass of water.
14. 50 caramels of Dequalinium chloride 0.015 g. Take one caramel every 4 hours (kept in the mouth to complete resorption).



DOCTOR'S PRESCRIPTION		The date of prescription «__» _____ 20__	
		The doctor's prescription is valid from «__» _____ 20__	
Full name of the patient _____			
Date of Birth _____			
Full name of the doctor _____			
Rp:			
Rp:			
Rp:			
		Signature of the doctor Doctor's personal stamp	
This prescription is valid for 30 days, 60 days (cross out the unnecessary)			

DOCTOR'S PRESCRIPTION		The date of prescription «__» _____ 20__	
		The doctor's prescription is valid from «__» _____ 20__	
Full name of the patient _____			
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Full name of the patient _____			
Date of Birth _____			
Full name of the doctor _____			
Rp:			
Rp:			
Rp:			
Signature of the doctor Doctor's personal stamp			
This prescription is valid for 30 days, 60 days (cross out the unnecessary)			

## LESSON 2. LIQUID MEDICINAL FORMS

**Objective:** To learn the rules and get practical skills in writing out liquid medicinal forms in prescription.

### Key questions:

1. General characteristics and rules of writing out liquid medicinal forms. Dosage.
2. Solutions for external and internal use. Solvents. Officinal solutions. Suspensions.
3. Liquid medicinal forms made from plant medicinal material: infusions, broths, teas, galenic (tinctures, extracts) and neogalenic drugs, mucus, emulsions, liniments.
4. Mixtures.

### Write out prescriptions for:

1. 25 ml of a 0.05 % solution of Chlorhexidinum. To rinse the oral cavity 3 times a day.
2. 10 ml eye drops 0.3 % solution of Gentamycin. By 1 drop into both eyes 3 times a day.
3. 10 ml 0.0009 % oil solution of Alfalcidol. By 3 drops orally once a day in the morning.
4. 10 ml of 2 % alcoholic solution of Mentholum in a vial. Rub into the affected joint area 2 times a day.
5. 180 ml solution of Potassium iodide, for the patient to get 0.45 g of potassium iodide per one dose. 1 table spoonful orally 3 times a day.
6. 50 ml 0.08 % syrup of Ondansetron. Orally 2.5 ml once a day.
7. 240 ml 1 % suspension of Nevirapine. Orally 20 ml once a day.
8. 200 ml emulsion from 30 ml Oleum Ricini. Orally for 3 doses.
9. 200 ml of decoction from 20 g of the root of the Polygala (Radices Polygalae). Apply orally 1 tablespoon 4 times a day.
10. 25 ml tincture of Echinopanacis. 35 drops orally 2–3 times before meals.
11. 15 ml of Adonisidum. 15 drops orally 2–3 times a day.
12. The mixture containing 180.0 ml infusion from 0.45 g herba Thermopsidis and 0.2 g Codeini phosphas. 1 table spoonful orally 3 times a day.
13. 100 ml mixture containing 2.0 g of Chloralum hydratum and equal amounts of Amylum and distilled water. For 2 enemas.
14. 50 ml of 70 % Spiritus aethylicus. For processing of the surgical field.

DOCTOR'S PRESCRIPTION		The date of prescription «___» _____ 20___	
		The doctor's prescription is valid from «___» _____ 20___	
Full name of the patient _____			
Date of Birth _____			
Full name of the doctor _____			
Rp:			
Rp:			
Rp:			
Signature of the doctor Doctor's personal stamp			
This prescription is valid for 30 days, 60 days (cross out the unnecessary)			

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Date of Birth _____			
Full name of the doctor _____			
Rp:			
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Rp:			
Signature of the doctor Doctor's personal stamp			
This prescription is valid for 30 days, 60 days (cross out the unnecessary)			

DOCTOR'S PRESCRIPTION		The date of prescription «___» _____ 20___	
		The doctor's prescription is valid from «___» _____ 20___	
Full name of the patient _____			
Date of Birth _____			
Full name of the doctor _____			
Rp:			
Rp:			
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Signature of the doctor Doctor's personal stamp			
This prescription is valid for 30 days, 60 days (cross out the unnecessary)			

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This prescription is valid for 30 days, 60 days (cross out the unnecessary)			

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Full name of the doctor _____			
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Full name of the doctor _____			
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This prescription is valid for 30 days, 60 days (cross out the unnecessary)			

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Full name of the doctor _____			
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This prescription is valid for 30 days, 60 days (cross out the unnecessary)			

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		The doctor's prescription is valid from «___» _____ 20___	
Full name of the patient _____			
Date of Birth _____			
Full name of the doctor _____			
Rp:			
Rp:			
Rp:			
Signature of the doctor Doctor's personal stamp			
This prescription is valid for 30 days, 60 days (cross out the unnecessary)			

### LESSON 3. MEDICINAL FORMS FOR INJECTIONS. SOFT MEDICINAL FORMS

**Objective:** To learn the rules and get practical skills in writing out prescription for soft medicinal forms and medicinal forms for injections.

**Key questions:**

1. The base for preparation of soft medicinal forms.
2. Ointments, pastes. Rules of prescribing them.
3. Dosed soft medicinal forms — suppositories. Types of suppositories. Rules of prescribing them.
4. Basic medicinal forms for injections.
5. General characteristics and requirements to medicinal forms for injections.
6. Rules of writing out injection forms manufactured at the plant and made at the pharmacy.

**Write out prescriptions for:**

1. 20.0 g 1 % ointment of Dequalinium chloride. Assign to handle the corners of the mouth and lips (for fungal infections).
2. 30.0 g 3 % ointment of Tetracycline. Apply to the affected skin area 2 times a day.
3. 5.0 g 1 % eye ointment of Pilocarpine. Apply in the conjunctival sac every 4 hours.
4. 30.0 g (30 000 IU/1.0 g) ointment of Amphoterecin B. Apply a thin layer to the affected skin area 1–2 times a day.
5. 30.0 g 2.5 % liniment of Griseofulvin. Apply a thin layer to the affected skin area at a daily dose of not more than 30 g.
6. 25.0 g of a 25 % Zinci oxydum paste. Apply to the affected area of the skin 2 times a day.
7. 10.0 g paste based on vaseline and lanoline (equally) containing 5 % Benzocaine. Apply to the affected skin area.
8. 50.0 g of 5 % Ibuprofenum cream. Apply to the affected area of the skin 3 times a day.
9. 50.0 g of 1 % gel of Indometacinum. Rub into the skin in the affected area 2 times a day.
10. 12 rectal suppositories containing 0.1 g Tramadol. 1 suppository into the rectum 2 times a day.
11. 20 vaginal suppositories containing 0.5 g Metronidazolum. 1 suppository into the vagina at bedtime.
12. 20 rectal suppositories of Ultraproct. Combined drug. 1 suppository into the rectum 2 times a day.
13. 10 ampules containing 10 ml 1 % solution of Ciprofloxacinum. 10 ml intravenously 2 times a day.
14. 10 ampules containing 1 ml 2.5 % solution of Progesterone in oil. 1 ml intramuscularly once a day.
15. 5 bottles containing 5 ml of a 3 % solution of Emoxipinum. Intravenously 5 ml, 2 times a day.
16. 10 ampules containing 0.1 g Doxycycline. The content of the ampule to be dissolved in 100 ml of isotonic solution NaCl 1 mg/ml. Intravenously drip-feed.
17. 10 vials containing 0.5 g of Cefotaxim powder. Dissolve the contents of the vial in 5 ml of water for injection. Inject slowly intravenously 0.5 g 2 times a day.
18. 6 bottles containing 1 200 000 IU Benzylpenicillin-Benzatin. The content of the bottle to be dissolved in 2–3 ml water for injections. 1 200 000 IU intramuscularly once per 2 weeks.

19. 5 vials containing 100 ml of a 5 % solution of Acidum aminocapronicum. The contents of the vial administered by slow intravenous drip to stop the bleeding.
20. 200 ml sterile 0.5 % solution of Procaine in physiological sodium chloride solution for surgical cabinet.
21. 6 ampoules containing 1 ml (5 IU) of Oxytocinum. The contents of the ampoule are administered intramuscularly to stimulate labor.
22. 10 ampoules containing 2 ml of a solution of Tramadol (50 mg/ml). Introduce intravenously in 20 ml of isotonic sodium chloride solution.
23. 15 ml of a metered aerosol containing 300 doses of Ipratropium bromide. In one dose — 20 mcg of ipratropium bromide. Inhalation of 2–4 breaths (2–4 doses of aerosol) 3 times a day.
24. 15 ml of «Berodual» aerosol. Inhalation 1–2 doses of aerosol 3 times a day.
25. 10 ml sublingual spray containing 200 doses of Nitroglycerinum. One dose contains 0.4 mg of nitroglycerin. When an attack of angina pectoris, spraying in a sitting position under the tongue for 1–2 doses (mouth must be closed immediately after each dose). No more than 3 doses within 15 minutes! Spray should not be inhaled!

DOCTOR'S PRESCRIPTION		The date of prescription «__» _____ 20__ The doctor's prescription is valid from «__» _____ 20__	
Full name of the patient		_____	
Date of Birth		_____	
Full name of the doctor		_____	
Rp:			
Rp:			
Rp:			
Signature of the doctor Doctor's personal stamp			
This prescription is valid for 30 days, 60 days (cross out the unnecessary)			

DOCTOR'S PRESCRIPTION		The date of prescription «__» _____ 20__ The doctor's prescription is valid from «__» _____ 20__	
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# GENERAL PHARMACOLOGY

## LESSON 4. PHARMACOKINETICS OF DRUGS. PART I

**Objective:** Grasp basic concepts and terms of pharmacokinetics, methods of administration of drugs into the body, mechanisms of their transport through the cellular and tissue barriers to absorption, distribution and excretion from the body, to examine the main quantitative parameters of pharmacokinetics (bioavailability, volume of distribution, clearance, elimination constant, semi-elimination period) used for rational dosing of drugs.

### Key questions:

1. Pharmacokinetics, its definition and role in rational pharmacotherapy.
2. Routes of drug administration into the body:
  - a) enteral (oral, sublingual, transbuccal, rectal, via probe);
  - b) parenteral (subcutaneous, intramuscular, intravenous, intraatrial, subarachnoidal, intraosseous, intracavitary, inhalation, transdermal, etc.);
  - c) local (topical) application of drugs.Comparative characteristics of different routes of administration, their advantages and disadvantages.
3. Drug transfer in the body as the main process that ensures their absorption, delivery to the tissues, the pharmacological effect and excretion.
  - 3.1. Aqueous diffusion through epithelial barriers. Its dependency of barrier structure, physic and chemical properties of the substance, binding with the ligands of the plasma and tissues. Filtration transfer of agents in the capillaries, mechanisms, localization.
  - 3.2. Medicinal substance diffusion through lipid barriers (cell membranes, blood-brain barrier, placenta), conditions and limitations of the transfer.
    - a) The dependence of diffusion in the lipid phase from the physico-chemical properties (molecular weight, distribution coefficient oil/water, the transfer distance and area), Fick's diffusion equation.
    - b) Influence of ionic character of substance on transfer efficiency through lipid barriers in the processes of absorption, distribution and excretion of drugs; Henderson-Hasselbach's ionization equation, transfer control of substances with variable ionization.
  - 3.3. The transmembrane transport of substances with transporters, the main transporters of ionic and nonionic organic molecules and their role in the processes of absorption, distribution and excretion of drugs.
  - 3.4. Microvesicular transport.
4. Major constituents of pharmacokinetics: bioavailability, distribution, clearance.
  - 4.1. Bioavailability of drugs: definition, calculation, determinants, dependence from the dosage form and route of administration. Features of the bioavailability of medications produced in dosage forms with modified release of the active substance (sustained continuous — prolonged, delayed — enteric dosage forms, intermittent / pulsating, accelerated).
  - 4.2. Presystem elimination (including presystem metabolism) of drugs: essence, clinical significance, effect on bioavailability. The concept of “prodrugs.” The concept of bioequivalence of drugs, the analysis of bioequivalence and the quality of generic drugs.

#### 4.3. Drug distribution in the body.

- a) Major distribution compartments and ligands in plasma and tissues, distribution determinants.
- b) Volume of distribution (Vd), dimensions, quantitation.
- c) Volume of distribution variants of medicinal substances, quantitative ratio between anatomical divisions and body dimensions.
- d) Clinical significans of Vd.

#### 4.4. Main ways and mechanisms of drug elimination.

- a) Kinetics of elimination of 1st order (linear kinetic): mathematical essence, a graphic description in normal and log-normal coordinates, characteristic parameters (Kel, Cl,  $T_{1/2}$ ).
- ❖ Clearance (Cl) — concept, dimensions, definition. General clearance and its constituents. Expression via Vd,  $T_{1/2}$ , Kel parameters. Clinical significans of Cl.
  - Renal clearance of drugs and its components (filtration, secretion, reabsorption). Dependence on physical and chemical properties of drugs (unpolar, polar, ionogenic substances), bindind with blood ligands, hemodynamics and functional condition of kidneys, urine pH. Renal clearance management of substances with variable ionization (weak acids and bases).
  - Hepatic clearance of drugs (mechanisms, determinants, restrictions). General strategy of biotransformation of xenogenous substances.  
Non-synthetic reactions of xenobyotics biotransformation (I phase): oxidation, reduction, hydrolysis.  
Synthetic reactions of xenobyotics biotransformation (II phase): conjugation with endogenous substrates (glucuronic acid, sulfuric acid, glycine, glutathione, etc.).
  - Excretion with bile and enterohepatic circulation of a drug.
  - Other routes of elimination of drugs (skin, mucous membranes, lungs, intestine).
- ❖ Elimination rate constant (Kel) — concept, dimensions, calculation options.
- ❖ Excretion half-life ( $T_{1/2}$ ) — concept, dimensions and calculation options via Kel, Vd, Cl paramenters. Clinical significans of  $T_{1/2}$ .
- b) Non-linear pharmacokinetic.
  - ❖ Kinetics of elimination of the 0-th order, a graphic description. Examples of drugs with non-linear (saturating) kinetics of elimination.

#### 4.5. Pharmacokinetic models of distribution and elimination of drugs, their clinical significans.

- a) One-compartment model, graphic and mathematical description in normal and log-normal coordinates.
- b) Multi-compartment model; graphic and mathematical description of two-compartment model in normal and log-normal coordinates.
- c) Clinical significance of pharmacokinetic models.

#### Tasks for individual study

Calculate absorbability in the stomach (pH = 2) and in the intestine (pH = 7.3)

1. weak acids: Ibuprofen (pKa = 4.4), chromoglycic acid (pKa = 2), furosemide (pKa = 3.9);
2. weak bases: chlorpromazine (pKa = 9.3), diphenhydramine (pKa = 9), ephedrine (pKa = 10.6).

Compare the results and make conclusions.

Given:  
 $\text{pH}_{\text{stom}} = 2$   
 $\text{pH}_{\text{intes}} = 7.3$   
 $\text{pK}_a =$

Solution:

Given:  
 $\text{pH}_{\text{stom}} = 2$   
 $\text{pH}_{\text{intes}} = 7.3$   
 $\text{pK}_a =$

Solution:

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Given:  
 $\text{pH}_{\text{stom}} = 2$   
 $\text{pH}_{\text{intes}} = 7.3$   
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Solution:

## LESSON 5. PHARMACOKINETICS OF DRUGS. PART II

**Objective:** To learn the practical applications of pharmacokinetics, methods of approximate calculation of the main dosing regimes of drugs based on standard and individual (for the patient) pharmacokinetic parameters.

### Key questions:

1. Dosing regimens of drugs, their components and the clinical significance.
2. A single (bolus) administration of drugs.
  - a) Kinetics of drug concentration in blood during various ways of single administration.
  - b) The concept of the effective threshold concentration of drug in the blood plasma. Relation between drug concentration in plasma and time of onset, duration and strength of its action.
  - c) The concept of the therapeutic index, therapeutic window and therapeutic range of drug concentration in blood.
3. Kinetics of drug concentration in blood during its continuous administration (infusional).
  - a) Kinetics of drug concentration in blood during continuous administration.
  - b) The concept of steady-state concentration ( $C_{ss}$ ) of drugs, kinetics of growth of the concentration to the  $C_{ss}$  level, reaching  $C_{ss}$  time depending on the infusion rate and the half-life of the substance. Approximate calculation of  $C_{ss}$  in continuous introduction of substances with constant speed attainment time.
  - c) Kinetics of drug plasma concentration when during infusion its rate of administration or clearance is changed.
  - d) Approximate calculation of infusion rate, ensuring the achievement of effective drug concentration in blood plasma.
4. Discrete dosing regimen of drugs with linear pharmacokinetics.
  - a) Kinetics of drug concentration in blood during discrete dosing regimen.
  - b) Kinetics and time of achievement of the  $C_{ss}$  level depending on the half-life, single dose and drug delivery interval.
  - c) Kinetics of drug concentration in blood when discrete dosing regimen is changed (dose, interval or skipping doses).
  - d) Calculation of  $C_{ss}$  and limits of its fluctuations ( $C_{ss}^{max}$ ,  $C_{ss}^{min}$ ).
  - e) Approximate calculation of effective therapeutic dose during discrete dosing regimen.
5. Load (initial, introductory) dose. Therapeutical aim. Conditions and limitations of load dose application. Approximate calculation.
6. Drug dosing regimen correction during individual pharmacokinetics violations: bioavailability, distribution, clearance.
  - a) Dosing regimen correction when bioavailability of drugs is changes (selection of medicinal form, prescription of drugs taking into account mode and features of nutrition, combined application of other medications).
  - b) Dosing regimen correction when  $V_d$  of drugs is changes (during body overweight, a liquid sequestration (edemas), pregnancy, in childhood and advanced age).
  - c) Pharmacotherapy correction when changes clearance of drugs (liver and kidneys diseases):
    - general approaches;
    - correction under the control of the total clearance of drugs;
    - correction under the control of residual renal function;
    - correction under the control of liver function;
    - correction under control of drug concentration in blood plasma.

### Tasks for individual study

1. How much drug “A” (produced in 2 ml ampoules of a 5.0 % solution) must be administered to a patient weighing 78 kg in order to quickly (within a few minutes) achieve a therapeutic plasma concentration  $C_{ther} = 1.8 \text{ mcg/ml}$ ? Justify the chosen route of administration and dosage regimen. Present graphically the dynamics of changes in the concentration of the drug in the blood plasma at a given dosing regimen. Reference data:  $V_d = 2.8 \text{ l/kg}$ .

2. To relief an attack of paroxysmal tachycardia of the patient who weighs 80 kg 4 ml of 0.1 % solution of drug “P” was intravenously injected. As the attack was not relieved the injection of the same dose was repeated in 5 minutes and the attack was relieved. Why the first drug dose did not relieve the attack? Present a diagram of the change in the concentration of the drug in the blood plasma at this dosage regimen. Reference data:  $V_d = 4.3 \text{ l/kg}$ ; therapeutic concentration range = 15–90 ng/ml.

3. For the treatment of acute cholecystitis a patient weighing 80 kg has to take drug “D” in capsules. Calculate an individual dosing regimen. Present a diagram of the change in the concentration of the drug in the blood plasma at this dosage regimen. Reference data:  $F = 93 \%$ ;  $Cl = 0.4 \text{ ml/min} \times \text{kg}$ ;  $V_d = 0.75 \text{ l/kg}$ ; effective concentration = 3 mcg/ml; toxic concentration > 12 mcg/ml.

4. A patient weighing 75 kg with a diagnosis of “hypertension” a month ago was prescribed the drug “C” in tablets of 0.075 mg 3 times a day. The patient showed a reduction in renal excretory function by 50 %. Find out whether the administration of the specified drug will be accompanied by drowsiness and dry mouth if the concentration, at which these side effects appear, is 1 ng/ml? Present a diagram of the change in the concentration of the drug in the blood plasma at this dosage regimen. Reference data:  $F = 95 \%$ ; renal excretion = 60 %;  $V_d = 2.1 \text{ l/kg}$ ;  $T_{1/2} = 12 \text{ hours}$ .

5. In reference books and manuals recommended infusion rate of the drug “Z” is 58 mg/h, however, examination of the patient to whom this drug was prescribed revealed a decrease in its excretory function of the kidneys by 67 %. Correct the rate of drug administration for this patient, taking into account residual renal function. Reference data:  $Cl = 4.4 \text{ ml/min} \times \text{kg}$ ; renal excretion = 72 %.

6. The drug “M” was started for young and elderly patients at a rate of 0.1 mg/min $\times$ kg. It is known that an elderly patient suffers from chronic renal failure with a decrease in renal function by 50 %. After what time will  $C_{ss}$  be achieved in an elderly patient and what will be  $C_{ss}$ , if  $C_{ss} = 1.0 \text{ mcg/ml}$  became in a young patient after 5 hours, and elimination of the drug by the kidneys is 60 %?

7. The doctor prescribed the drug “K” in a dose of 25 mg 3 times a day to a patient weighing 74 kg. Three days later, the patient again went to the doctor with complaints about the lack of effect of the prescribed drug. The doctor decided to double the dose of the drug. Did the doctor do the right thing? Justify the answer with calculations and present graphically the changes in the concentration of the drug in the patient's plasma. Reference data:  $F = 52 \%$ ;  $V_d = 2.9 \text{ l/kg}$ ;  $Cl = 8.9 \text{ ml/min} \times \text{kg}$ ; the minimum effective concentration of the drug is 0.01  $\mu\text{g/ml}$ ; toxic concentration — 0.11  $\mu\text{g/ml}$ .

8. For the treatment of epilepsy, a patient weighing 70 kg was prescribed the drug “E” in tablets. A preliminary examination of the patient revealed a 40 % decrease in liver excretory function. Calculate the individual dosage regimen of the drug. Present graphically the dynamics of changes in the concentration of the drug in the blood plasma at a given dosing regimen. Reference data:  $F = 70 \%$ ; renal excretion — 1 %;  $Cl = 1.3 \text{ ml/min} \times \text{kg}$ ;  $V_d = 1.0 \text{ l/kg}$ ;  $T_{1/2} = 12 \text{ hours}$ ; minimum effective concentration — 1  $\mu\text{g/ml}$ ; toxic concentration — 10  $\mu\text{g/ml}$ .

9. Suggest the optimal discrete dosage regimen for the drug “K” produced in 325 mg tablets ( $F = 80 \%$ ) for a patient weighing 65 kg, who suffers from renal failure with a 50 % decrease in excretory function of the kidneys. Present graphically the dynamics of changes in the concentration of the drug in the blood plasma at a given dosing regimen. Reference data: renal excretion ~ 70 %;  $Cl = 1.4 \text{ ml/min} \times \text{kg}$ ;  $V_d = 1.4 \text{ l/kg}$ ; therapeutic range of concentrations = 2–15  $\mu\text{g/ml}$ .

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## LESSON 6. PHARMACODYNAMICS OF DRUGS

**Objective:** To study the main terms, concepts and quantitative laws of pharmacodynamics, to be able to use them for the explanation of the principles and mechanisms of action of drugs, evaluation of their pharmacological activity, efficacy and safety. To master main approaches to quantitative assessment of pharmacological effects.

### Key questions:

1. Pharmacodynamics, its content and objectives.
2. The concept of pharmacotherapy: etiotropic, pathogenetic, symptomatic, replaceable.
3. The concept of therapeutic, side and toxic effects of drugs.
4. Molecular nature of the action of drugs. Physico-chemical and chemico-biological mechanisms of pharmacological effect.
5. The concept of receptors in pharmacology.
  - a) Molecular nature of receptors as a targets of primary pharmacological action of drugs.
  - b) Basic types of chemical signaling transmission in receptors of living systems and their importance in the drug action.
  - c) Specificity, selectivity and nonspecificity of drugs effect from the positions of receptors conception.

6. Quantitative laws of the pharmacological effect. The graphic description of the typical dependence of the effect and the concentration (dose) of drugs in normal and log-normal coordinates.
7. Clark-Ariens model, describing interaction between ligand and receptor, showing quantitative dose-response pattern. Model parameters ( $K_d$ , intrinsic activity), determining affinity of interaction of medicines with the receptor, maximum value of effect.
8. Terms and concepts of quantitative pharmacology: effect, efficiency, activity of drugs. Parameters of quantitative evaluation, their clinical applications.
9. The concept of agonism and antagonism in pharmacology.
  - a) Full and partial agonists, particularly their ligand-receptor interactions, effects of the interaction of full and partial agonists, clinical applications.
  - b) Drug interactions that lead to increased effect (addiction, potentiation, synergy).
  - c) Drug interactions which lead to a weakening effect: antagonism (pharmacological, physiological, chemical).
  - d) Pharmacological antagonists: competitive, non-competitive (allosteric). Changes in the activity and efficacy of agonists at a competitive and non-competitive antagonism. The clinical significance of these differences.
  - e) The physiological and chemical antagonism.
10. Quantitative assessment of pharmacological effect. Gradual and quantum (alternative) assessment of the effects, their use in experimental and clinical practice.
11. Drug safety assessment in experimental and clinical practice: concept of therapeutic index (TI), therapeutic range (TR), standard safety margins (SSM),  $ED_{50}$ ,  $EC_{50}$ ,  $LD_{50}$ , minimal toxic dose.
12. Types of drug dosing, which use in pharmacotherapy: minimum (threshold), average, maximum (single, daily); load (initial), course dose; their clinical significans. Toxic and lethal doses.
13. Changes in the action of drugs at repeated and prolonged administration.
  - a) The concept of cumulation of drugs (physical and functional). Their analysis from positions of pharmacokinetics and pharmacodynamics.
  - b) Changes in the body's sensitivity to drugs in the process of pharmacotherapy: tolerance and tachyphylaxis, sensitization and desensitization, idiosyncrasy. Drug allergy (hypersensitivity).
  - c) Drug dependence (physical, mental).
14. Patient factors that affect at variability of the action of drugs (functional state of the organism, body weight, edema, obesity, age, sex, race, genetic variability of target receptors and biotransformation mechanisms of drugs, smoking, alcohol).
15. Influence of drugs on prenatal fetal development (embryotoxicity, fetotoxicity, teratogenicity).
16. Mutagenic and cancerogenic effects of drugs.

## LESSON 7. FINAL LESSON ON GENERAL PHARMACOLOGY AND GENERAL PRESCRIPTION

### Objective:

1. To reinforce skills of writing out prescriptions and discharging of drugs in various medicinal forms.
2. To consolidate knowledge of the main terms, concepts and patterns of pharmacodynamics and pharmacokinetics.
3. To reinforce skills of calculation of an individual dosing regimen of drugs and quantitative assessment of pharmacological effect.

**For the lesson** the rules of writing out of the prescription and discharging of drugs in various medicinal forms (lessons No. 1–3); material on a pharmacodynamics and pharmacokinetics (lessons No. 4–6) should be repeated.

### Questions for individual study:

1. Pharmacology as a science. Parts of modern pharmacology.
2. Advantage and risk of drug prescription. Bases for drugs use.
3. Give a definition of concepts: medicinal substance, medicinal agent, drug, medicinal form.
4. State regulation of writing out and dispensing drugs.
5. Prescription and its structure.
6. Medicinal forms, characteristics, application.
7. Requisites to medicinal forms for injections.
8. Rules of prescription of solid, liquid, soft medicinal forms, medicinal forms for injections.
9. Rules of prescription of poisonous, narcotic and potent drugs.
10. Drugs under control: narcotic drugs, psychotropic substances with anabolic activity, etc.
11. Drugs prohibited for prescribing.
12. The concept of original and generic drugs.
13. Main concepts of pharmacology: pharmacological activity, pharmacological action, pharmacological effect of medicinal agents.
14. The concepts of pharmacokinetics and pharmacodynamics.
15. The factors providing therapeutic effect of drugs — pharmacodynamic action, placebo effects.
16. Routes of drug administration into the body. Resorptive, systemic and local action of drugs.
17. Drug transfer through biological barriers: main mechanisms and determinants.
18. Drug transfer through water spaces of biological barriers. Mechanisms, determinants and restrictions.
19. Drug transfer in the system of interstitial tissue / blood channel. Mechanisms, determinants and transfer restrictions.
20. Drug transfer through lipid barriers. Mechanisms and transfer determinants. Fick's diffusion equation.
21. Mechanisms of drug transfer through epithelial barriers: mucous membrane of stomach, intestine, oral cavity and other mucous membranes.
22. Features of drug transfer through hematoencephalic barrier and placenta.
23. Active transport of drugs. Transmembrane transporters and their role in the bioavailability and elimination of drugs.
24. Transfer through biological barriers of substances with variable ionization. Henderson–Hasselbach's equation, principles of management of ionogenic substances transfer.

25. Influence of ionization on the absorption and elimination of drugs, possibilities of correction of drug transfer based on ionization control.
26. The binding of drugs with plasma macromolecular ligands. Its impact on pharmacological effect, transfer and elimination of drugs.
27. Concentration of drug in blood plasma — the main parameter to control pharmacological effect. To substantiate the indicated postulate. Identify problems to be solved on the basis thereof.
28. Presystemic elimination and bioavailability of drugs: essence, determinants, dependence on medicinal form and patient factor. Bioequivalence of medicines and its evaluation.
29. Drug distribution in the body. Distribution compartments, molecular ligands of drugs. Distribution determinants. The role of blood flow.
30. Volume of distribution: essence, dimension, quantitative expression, determinants.
31. The concept of the pharmacokinetic models of distribution and elimination of drugs (single chamber, dual chamber, multi-chamber), represented in graphical form the kinetics of elimination of drugs, typical for these models.
32. The concept of linear and non-linear pharmacokinetics, and their role in pharmacotherapy.
33. Exponential kinetics of elimination of drugs (1st order), its essence, graphical representation in normal and log-normal coordinates (for the single-chamber model), characteristic parameters.
34. Elimination of the zero-order kinetics, a graphic representation, examples of drugs with such elimination kinetics.
35. Elimination rate constant: essence, dimension, connection with other pharmacokinetic parameters.
36. Excretion half-life: essence, dimension, connection with other pharmacokinetic parameters.
37. Clearance as pharmacokinetic parameter: essence, dimension, connection with other parameters.
38. Dose. Types of doses. Units of drug dosage.
39. Routes of drug administration into the body: enteral, parenteral. Advantages and disadvantages. Selection of routes depending on therapy purposes.
40. Modes of administration of drugs used in pharmacotherapy. Their components.
41. Kinetics of substance concentration in blood plasma at its introduction into blood channel at the constant rate. Essence of steady-state concentration of drug ( $C_{ss}$ ). Achievement time of  $C_{ss}$ .  $C_{ss}$  dependence from the rate of administration, clearance, half-life, volume of distribution.
42. Calculation of  $C_{ss}$  reached during continuous administration of a drug to the system blood flow at constant rate, management of the  $C_{ss}$  level.
43. Kinetics of substance concentration in blood during discrete administration of drugs in a body.  $C_{ss}$  average, maximum and minimum.
44. Calculation of  $C_{ss}$  in blood plasma reached during discrete dosing regimen.
45. Approximate calculation of drug concentration limits of fluctuations in blood plasma at steady-state phase during discrete administration of drugs.
46. Management of the  $C_{ss}$  level and scope of fluctuations of medicinal substance concentration in blood plasma by change of a dose and a dosing interval.
47. Therapeutic and toxic ranges (intervals) of drug concentration in blood. The concept of an adequate regimen of administration of discrete doses.
48. Load (initial) dose, therapeutic sense. Calculation of a load dose. Conditions and restrictions of using load doses in pharmacotherapy.

49. Maintenance doses, therapeutic sense. Approximate calculation of an optimum dosing regimen at systematic administration of drugs.
50. Renal clearance of drugs, mechanisms, qualitative characteristics.
51. The factors influencing on renal clearance of drugs. Dependence of renal clearance on physical and chemical properties of medicinal substances, renal haemodynamics, tubular epithelium.
52. Management of renal clearance of medicinal substances with variable ionization.
53. Hepatic clearance of drugs, determinants and restrictions. Enterohepatic circulation of drugs, consequences.
54. Factors changing the drugs clearance.
55. Correction of drug therapy at liver and kidneys diseases. General approaches.
56. Correction of the dosing regimen of drugs under control of residual renal function (based on creatinine clearance).
57. Correction of drug therapy at liver damages and other pathological conditions influencing on the clearance of drugs.
58. Biotransformation of drugs, phases, its biological sense. Influence of biotransformation on pharmacological activity and rate of elimination of drugs.
59. Metabolic drug interactions. The diseases influencing on biotransformation of drugs.
60. Routes and mechanisms of elimination of drugs. Possibilities of management of elimination processes of drugs.
61. Physical-chemical and chemical-biological mechanisms of action of medicinal substances.
62. The concept of receptors in pharmacology: molecular nature of receptors, signal mechanisms of action of drugs. Types of the transmembrane signaling and the secondary intermediaries participating in the realization of action of drugs.
63. Specificity and selectivity of action of drugs. Therapeutic, side and toxic effects of drugs, their nature from positions of the concept of receptors.
64. Quantitative patterns of pharmacological effect. Clark-Ariens model and its consequences. General view of the concentration — effect dependence in normal and log-normal (half-logarithmic) coordinates.
65. The concepts of quantitative pharmacology: effect, efficiency, activity of drugs. Parameters of their quantitative evaluation.
66. Pharmacological agonists (full, partial), criteria of their differences, effects of interaction.
67. The concept of types of antagonism of drugs: pharmacological, physiological, chemical (pharmaceutical).
68. Pharmacological antagonism: competitive, noncompetitive. Character of activity and efficiency changes of drugs depending on type of pharmacological antagonism.
69. The concept of additivity, synergy and potentiation at interaction of drugs.
70. Gradual and alternative (quantum) quantitative assessment of pharmacological effect: essence, clinical use.
71. Change of drug action at continuous administration (tolerance and tachyphylaxis, sensitization and desensitisation, hypersensitivity).
72. Individual variability of drug action, its reasons and rational strategy of pharmacotherapy. Idiosyncrasy.
73. Assessment of safety of drugs. Therapeutic index and standard safety margins.
74. Teratogenic, embryotoxic, fetotoxic, mutagenic, cancerogenic actions of drugs.
75. Drug incompatibility.

## SPECIAL PHARMACOLOGY

Course of special pharmacology is constructed on system principle, comprising communication of teaching of Pharmacology with clinical disciplines. Drugs consolidated in groups of drugs that affect the different functional systems of the body, pathological conditions, or used for the treatment of infectious diseases and tumors.

While considering the questions of special pharmacology *the AIM* of every practical class is:

### For the groups of medicinal drugs:

- classification of drugs, including several representatives (at least 1–2) of each pharmacological group or subgroup;
- main action determining pharmacotherapeutical significance of drugs of the given group;
- main use in medicine.

### For the main drugs of the group:

- the place in the classification;
- pharmacodynamics — mechanisms of molecular and systemic action, general pharmacological effects;
- pharmacokinetics — absorption, distribution, elimination, routes of administration;
- main side and toxic effects;
- clinical application, contraindications;
- comparative estimation of a drug among other drugs of the given group.

To carry out practical tasks on prescriptions it is recommended to use Appendix 2 as well as reference literature on drugs (see Literature to study).

## DRUGS AFFECTING PERIPHERAL NERVOUS SYSTEM

### LESSON 8. CHOLINOMIMETIC AND ANTICHOLINESTERASE DRUGS

#### Key questions:

1. General scheme of structure, neurotransmitters and receptors of peripheral (somatic and vegetative) nervous system.
2. Cholinergic signal transmission.
  - 2.1. The structure of cholinergic synapses and mechanism of nerve impulses transmission. Mechanism of acetylcholine release and its regulation.
  - 2.2. Stages of transmission of nerve impulses in cholinergic synapses and pharmacological approaches to management of cholinergic mediation:
    - subtypes of muscarinic cholinoreceptors ( $M_1$ - $M_5$ ), it's localization, secondary mediators in realization of their stimulating and inhibitory effects;
    - effects of physiologic and pharmacologic stimulation of  $M_1$ -,  $M_2$ - и  $M_3$ -cholinoreceptors in various organs and tissues;
    - subtypes of nicotinic cholinoreceptors ( $N_m$ ,  $N_n$ ): localization and stimulation effects;
    - presynaptic and extrasynaptic cholinoreceptors, effects of their stimulation.
3. Classification of cholinomimetic (cholinergic) drugs.

#### 4. Cholinomimetics of direct action (choline ethers and natural alkaloids).

##### 4.1. Muscarinic agonists — M-cholinomimetics (pilocarpine, cevimeline, bethanechol, aceclidine, muscarine):

- pharmacological effects: influence on the eye (eye pupil width, intraocular pressure, accommodation), smooth muscles of internal organs, secretion of exocrine glands, heart, vessels, bronchi, GIT (motility and sphincters), urinary bladder;
- clinical application, side effects, contraindications;
- effects of overdosing and poisoning of cholinomimetics; antidote therapy.

##### 4.2. Nicotinic agonists — N-cholinomimetics (nicotine, varenicline, cytisine):

- nicotine pharmacology and toxicology, nicotine and its dangers;
- use of nicotinic agonists for the treatment of nicotine dependence (varenicline (Chantix), cytisine (Tabex), nicotine (Nicorette)).

##### 4.3. M, N-cholinomimetics of direct action (acetylcholine chloride, carbachol), effects, use in medicine.

#### 5. Cholinomimetics of indirect action.

##### 5.1. Anticholinesterase drugs, mechanism of action, pharmacological effects, use in medicine:

- reversible cholinesterase inhibitors: physostigmine, neostigmine, pyridostigmine bromide, galantamine, donepezil;
- irreversible cholinesterase inhibitors (organophosphorous compounds): paraoxon, sarin; insecticides, chemical war gases;
- acute poisoning with anticholinesterase drugs and antidote therapy (atropine — the first choice drug, cholinesterase reactivators — trimedoxime bromide).

##### 5.2. Stimulants of endogenous acetylcholine release (metoclopramide, domperidone, itopride). Mechanism of action, use as gastrointestinal motility stimulants.

#### **As a result, you should be able to:**

- Identify the location and types of cholinergic receptors, effects of their stimulation in various organs and systems (central nervous system, autonomic ganglia, eyes, heart, blood vessels, bronchi, intestines, urinary organs, skeletal muscle, exocrine glands).
- Describe the secondary transmitters, involved in realization of acetylcholine effects.
- Describe the pharmacological effects of cholinomimetics and indicate their main clinical use.
- Describe the pharmacodynamic differences between cholinomimetics of direct and indirect action.
- Describe the symptoms of intoxication with cholinomimetics (muscarine, insecticides) and specific antidotes.

**Write out the following drugs:** pilocarpine (eye ointment, eye covers), pyridostigmine bromide (solution), galantamine (tablets).



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## LESSON 9. CHOLINERGIC ANTAGONIST (ANTICHOLINERGIC) DRUGS

### Key questions:

1. M-cholinergic antagonist (M-anticholinergic drug). General characteristics, mechanism of action, main pharmacological effects.
  - 1.1. Classification:
    - 1.1.1. Natural/plant alkaloids (belladonna, henbane, datura) — atropine, hyoscine hydrobromide, hyoscyamine.
    - 1.1.2. Synthetic and semisynthetic muscarinic antagonists:
      - a) tertiary amines — homatropine, tropicamide, cyclopentolate, dicycloverine, pirenzepine, darifenacine, tolterodine, trihexyphenidyl;
      - b) quadratiary amines — hyoscine butylbromide, ipratropium bromide, propantheline bromide.
  - 1.2. Pharmacological effects of M-cholinergic antagonists: influence on eye, cardiac function, smooth muscles of internal organs, exocrine glands, central nervous system.
  - 1.3. Clinical use of M-cholinergic antagonists as midriatics, spasmolytics, antiarrhythmics, antisecretory agents and premedication in anesthesia.
  - 1.4. Side effects and toxicity of M-cholinergic antagonists, antidote therapy.

2. Nicotinic antagonists (N-cholinergic blockers).
  - 2.1. Ganglionic blockers: trimethaphan, pharmacological effects, clinical application.
  - 2.2. Muscle relaxant drugs (curare-type, peripheral muscle relaxants).
    - 2.2.1. Non-depolarizing type of action: atracurium, pipecuronium bromide, pancuronium bromide, rocuronium.
    - 2.2.2. Depolarizing type of action: suxamethonium chloride.
    - 2.2.3. Comparative characteristics of muscle relaxants (mechanism of action, effects, clinical application).
  - 2.3. Application of acetylcholinesterase inhibitors (neostigmine, pyridostigmine) as curariform antagonists in surgery.
  - 2.4. Complications from muscle relaxants. Application of dantrolene for relief of malignant hyperthermia.
3. M, N-cholinergic antagonists (atropine), pharmacological effects, use in medicine.
4. Drugs, blocking acetylcholine release (botulinum A toxin), pharmacological action, use in medicine.

**As a result, you should be able to:**

- Describe effect of atropine on the main organs and systems (central nervous system, eyes, heart, blood vessels, bronchi, gastrointestinal tract, urogenital organs, exocrine gland, and skeletal muscles).
- Identify symptoms of overdose and poisoning with atropine, therapy.
- Specify clinical indications and contraindications for muscarinic antagonists.
- Describe effects of ganglionic blockers.
- Name at least one antimuscarinic agent, which is used for the following purposes: mydriasis and cycloplegic, the treatment of Parkinson's disease, bronchial asthma, spasms of urinary bladder, spastic gastrointestinal conditions, treatment of poisoning with muscarine-contained mushrooms and anticholinesterase insecticides.
- Describe mechanism of action and clinical application of acetylcholinesterase reactivators.
- Name basic non-depolarizing muscle relaxants and a single depolarizing; compare their effects, pharmacokinetics and application.
- Indicate method to eliminate non-depolarizing block.

**Write out the following drugs:** atropine (eye ointment, solution), ipratropium bromide (aerosol), pirenzepine (tablets, solution), hyoscine hydrobromide (coated tablets, suppositories), tolterodine (tablets), trihexyphenidyl (tablets).

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## LESSON 10. ADRENERGIC DRUGS

### Key questions:

#### 1. Adrenergic mediation.

1.1. Stages of transmission of nerve impulses in adrenergic synapses and approaches to pharmacological management activity of the sympathetic nervous system (at the level of the synthesis, release, interaction with receptors, neurotransmitters reuptake and degradation).

#### 1.2. Adrenergic receptors heterogeneity:

- $\alpha_1$ - and  $\alpha_2$ -adrenoreceptors — localization, effects of physiologic and pharmacological stimulation;
- $\beta_1$ -,  $\beta_2$ - and  $\beta_3$ -adrenoreceptors — localization, effects of physiologic and pharmacological stimulation;
- extrasynaptic adrenoreceptors, their biological significance.

#### 2. Adrenergic agonists (direct acting adrenomimetic drugs, adrenomimetics): classification, features of pharmacodynamics and pharmacokinetics, medical use as cardiovascular, anti-shock, bronchodilators, tocolytic, ophthalmic drugs and decongestants.

##### 2.1. Catecholamines (adrenomimetics of mixed action and non-selective adrenergic agonists):

- epinephrine (adrenalin) —  $\alpha_1$ ,  $\alpha_2$ ,  $\beta_1$ ,  $\beta_2$ ,  $\beta_3$ -agonist;
- norepinephrine (noradrenalin) —  $\alpha_1$ ,  $\alpha_2$ ,  $\beta_1$ ,  $\beta_3$ -agonist;
- dopamine —  $D_1$ ,  $\beta_1$ ,  $\alpha_1$ -agonist;
- dobutamine —  $\beta_1 > \beta_2 \gg \alpha_1$ -agonist;
- isoprenaline —  $\beta_1$ ,  $\beta_2$ ,  $\beta_3$ -agonist;

##### 2.2. Alpha-adrenomimetics:

- phenylephrine —  $\alpha_1$ -agonist;
- clonidine —  $\alpha_2$ -agonist;
- naphazoline, xylometazoline, oxymetazoline —  $\alpha_1$ ,  $\alpha_2$ -agonists (decongestants).

##### 2.3. Beta-2 ( $\beta_2$ ) adrenomimetics:

- salbutamol, salmeterol, fenoterol, hexoprenaline, terbutaline.

##### 2.4. Beta-3 ( $\beta_3$ ) adrenomimetics:

- mirabegron, amibegron, solabegron.

##### 2.5. Dopaminomimetics — dopamine — agonist $D_1 = D_2$ and $\gg \beta_1 \gg \alpha_1$ receptors, dopexamine — a mixed agonist of $\beta_2$ and $D_1$ receptors.

#### 3. Adrenomimetics with indirect action (sympatomimetics): pseudoephedrine (systemic decongestant), ephedrine, amphetamine, cocaine. Mechanism of action, effects, medical use, cautions.

### As a result, you should be able to:

- Identify typical non-selective  $\alpha$  agonist, a selective  $\alpha_2$  agonist, non-selective  $\beta$  agonist, relatively selective agonist  $\beta_1$  (in low doses), selective  $\beta_2$  agonist,  $\alpha_1$ ,  $\alpha_2$ ,  $\beta_1$ ,  $\beta_3$  agonist and  $\alpha_1$ ,  $\alpha_2$ ,  $\beta_1$ ,  $\beta_2$ ,  $\beta_3$  agonist.
- Identify main localization of  $\alpha_1$  and  $\alpha_2$  receptors.
- Identify main localization of  $\beta_1$  and  $\beta_2$  receptors.
- Describe effect on major organs and systems of pure  $\alpha$  agonists, pure  $\beta$  agonists, of mixed  $\alpha$  and  $\beta$  agonists.
- Give examples of indirect agonists, describe their effects.
- Identify main areas of clinical application of adrenergic agonists.

**Write out the following drugs:** dobutamine (solution), clonidine (solution), phenylephrine (solution), dopamine (solution).

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## LESSON 11. ADRENERGIC ANTAGONISTS (ANTIADRENERGIC) DRUGS

### Key questions:

1. Adrenergic antagonists (antiadrenergic drugs, adrenergic blockers).

1.1. Alpha-adrenergic antagonists:

1.1.1. Non-selective adrenergic antagonists: dihydroergotamine, nicergoline, phentolamine.

1.1.2. Selective alpha-adrenergic antagonists:

- $\alpha_1$ -adrenergic antagonists: doxazosin, prazosin, terazosin,
- $\alpha_{1A}$ -adrenergic antagonists: tamsulosin, alfuzosin (selective for urethral sphincter);
- $\alpha_2$ -adrenergic antagonist — yohimbine.

1.1.3. Pharmacological properties of alpha-blockers of selective and non-selective action, clinical use in essential hypertension, hypertensive crises, pheochromocytoma, prostatic hyperplasia, erectile dysfunction, Raynaud's disease.

## 1.2. Beta-adrenergic antagonists:

### 1.2.1. Nonselective $\beta_1$ , $\beta_2$ -adrenergic antagonists:

- $\beta_1$ ,  $\beta_2$ -adrenergic antagonists without intrinsic sympathomimetic activity (ISA): propranolol (the prototype of short-term acting beta-antagonists); nadolol, sotalol (long-term action); timolol.
- $\beta_1$ ,  $\beta_2$ -adrenergic antagonists with ISA, partial adrenergic agonists: pindolol (short-term action), penbutolol (long-term action).

### 1.2.2. Selective $\beta_1$ -adrenergic antagonists (cardioselective):

- $\beta_1$ -adrenergic antagonists without ISA: atenolol, metoprolol (short-term action); betaxolol, bisoprolol (long-term action); esmolol (ultra-short action); nebivolol (with additional NO-dependent vasodilating effect);
- $\beta_1$ -adrenergic antagonists with ISA: acebutolol (short-term action).

### 1.2.3. Selective $\beta_2$ -adrenergic antagonists: butaxamine (use in experimental pharmacology).

### 1.2.4. Mixed-action $\beta$ -, $\alpha$ -adrenergic antagonists (block $\beta_1$ , $\beta_2 \gg \alpha_1$ ): carvedilol, labetalol; urapidil ( $\alpha_1 \gg \beta_1$ , $\beta_2$ ),

### 1.2.5. Beta-adrenergic antagonists with local anesthetic action (additionally inhibit sodium-ion channels): propranolol, acebutolol, metoprolol, pindolol, labetalol.

### 1.2.6. Beta-adrenergic antagonists with higher lipophilicity: propranolol, metoprolol, pindolol, labetalol, carvedilol.

### 1.2.7. Pharmacological characteristics of selective and non-selective beta-blockers, definition of intrinsic sympathomimetic activity (ISA), significance of locally anesthetic (membrane-stabilizing) activity and lipophilicity in action of beta-blockers, features of mixed $\beta$ -, $\alpha_1$ -blockers.

### 1.2.8. Use of beta-blockers in medicine: in various cardiovascular diseases, in ophthalmology for glaucoma, migraine, hyperthyroidism and tremor.

### 1.2.9. Side effects of beta-blockers, their dependence on selectivity, contraindications.

## 1.3. Sympatholytics (blockers of norepinephrine releasing in the sympathetic nerve endings): guanethidine, reserpine, pharmacological effects, medical use.

### **As a result, you should be able to:**

- Describe and compare effects of  $\alpha$ -blockers on blood pressure and heart rate under the action of epinephrine, norepinephrine, phenylephrine.
- Compare pharmacodynamics of propranolol, metoprolol, labetalol, and pindolol.
- To substantiate the clinical significance of cardioselectivity, ISA and the presence of the alpha blocking effect in the action of beta-blockers.
- Compare pharmacokinetics of propranolol, atenolol, esmolol and nadolol.
- Identify the main clinical indications and side effects of typical alpha and beta blockers.
- Name adrenergic blocker used to treat glaucoma.

**Write out the following drugs:** doxazosin (tablets), tamsulosin (capsules), propranolol (solution), nadolol (tablets), atenolol (tablets), bisoprolol (tablets), pindolol (oral solution), carvedilol (tablets).

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## LESSON 12. DRUGS AFFECTING AFFERENT NERVES ENDINGS

### Key questions:

#### 1. Local anesthetics.

##### 1.1. Classification:

##### A. According to clinical application.

Surface anesthetics: lidocaine, tetracaine, benzocaine, cocaine.

Injectable anesthetics:

1. Short-acting with low activity: procaine, chloroprocaine.

2. Average duration of the action, intermediate activity: lidocaine, articaine, mepivacaine, prilocaine, trimecaine.

3. Long-acting high activity: bupivacaine, levobupivacaine, ropivacaine.

4. Fast action: articaine, lidocaine, chloroprocaine.

5. Intermediate action speed: mepivacaine, bupivacaine, ropivacaine, prilocaine.

6. Slow action: procaine, tetracaine.

##### B. According to chemical structure:

Esters (*in INN of the drug one letter "i"*): cocaine, procaine, chloroprocaine, benzocaine, tetracaine;

Amides (*in INN of the drug two letters "i"*): lidocaine, mepivacaine, bupivacaine, prilocaine, articaine, ropivacaine, prilocaine.

#### 1.2. Mechanism of action of local anesthetics. Influence on ionic currents and action potential of nerve fibers and endings.

#### 1.3. The dependence of the rate, duration and potency of the physico-chemical properties of anesthetics (pKa, lipophilicity) sensitivity type, thickness and myelination of nerve fibers, discharge frequency in the nerve fibers, diffusion rate of the anesthetic to the site of administration, presence of vasoconstrictors in solution.

#### 1.4. Application for different types of anesthesia — infiltrative, conductive, surface. Anesthesia of dental hard tissues.

#### 1.5. Changing actions of local anesthetics when injected into inflamed tissue.

#### 1.6. Combinations of local anesthetics with vasoconstrictors (epinephrine, phenylephrine, fenypressin): advantages, disadvantages, contraindications.

#### 1.7. Local and toxic effects of local anesthetics, preventive measures.

#### 2. Astringent drugs: tannin, zinc oxide, oak bark broth, sage leaves infusion.

#### 3. Mucilaginous drugs: amylum and flax seeds mucilages, sucralfate.

#### 4. Absorbent drugs: activated carbon, talc.

#### 5. Irritant drugs: mustard plasters, refined turpentine oil, menthol, ammonia solution.



**As a result, you should be able to:**

- Explain that means a local anesthesia, which types of local anesthesia are used for different purposes.
- Describe the mechanism of action of local anesthetics.
  - Identify anesthetics used for the surface, wire and infiltration anesthesia.
- Dependence of local anesthetics on the state of the sodium channel (open, closed or inactivated), and the frequency of discharges in the nerve fibers.
- Explain the dependence of the speed and force the action of local anesthetics from pH of the tissue, and the pK of substance.
- Identify 4 factors that determine the sensitivity of nerve fibers to local anesthetics.
- Identify the main manifestations of local and systemic toxicity of local anesthetics.

**Write out the following drugs:** procaine (suppository), lidocaine (solution), articaine (solution), ropivacaine (solution).

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## FINAL LESSON ON DRUGS AFFECTING PERIPHERAL NERVOUS SYSTEM

**Objective:** To systematize and consolidate the knowledge of the pharmacological properties and medical use of drugs affecting the peripheral innervation.

During the preparation for the final lesson you should repeat classification, pharmacodynamics, pharmacokinetics, indications and contraindications of the following drug groups:

1. Cholinomimetic and anticholinesterase drugs.
2. Cholinergic antagonist drugs.
3. Adrenergic and antiadrenergic drugs.
4. Drugs affecting the afferent nerve endings (anesthetics, astringents, mucilaginous drugs, absorbents, irritants).

**Write out the following drugs:** pilocarpine, neostigmine, atropine, pirenzepine, tolterodine, trihexyphenidyl, clonidine, propranolol, atenolol, metoprolol, nadolol, bisoprolol, carvedilol, artocaine, lidocaine, procaine.

### Questions for individual study:

1. Draw schematic of neural and mediator organization of the efferent peripheral nervous system (PNS), and indicate at it the sympathetic and parasympathetic divisions of the autonomic nervous system, somatic nerve fibers; specify mediators, types and subtypes of receptors.
2. List the effects caused by increased activity of the sympathetic division of the autonomic nervous system.
3. List the effects caused by increased tone of parasympathetic autonomic nervous system.
4. Draw a generalized scheme of the cholinergic synapses structure, possible levels of pharmacologic management of cholinergic transmission, explain examples of agents which act presynaptically and postsynaptically.
5. Draw a generalized scheme of the adrenergic synapse structure, possible levels of pharmacologic management of adrenergic transmission, explain examples of agents which act presynaptically and postsynaptically.
6. The types and subtypes of cholinergic receptors, their primary localization, effects of pharmacological stimulation.
7. The molecular mechanisms of signal transduction upon activation of muscarinic ( $M_1$ ,  $M_2$ ,  $M_3$ ) and nicotinic ( $N_n$  and  $N_m$ ) receptors.
8. The types and subtypes of adrenergic receptors, their primary localization, effects of pharmacological stimulation.
9. The molecular mechanisms of signal transduction upon activation of  $\alpha_1$ -,  $\alpha_2$ -,  $\beta_1$ -,  $\beta_2$ -,  $\beta_3$ -adrenergic receptors.
10. Dopamine receptors, their primary localization, effects of pharmacological stimulation of peripheral  $D_1$ - and  $D_2$  receptors.
11. Explain the importance of receptor heterogeneity in drug action.
12. Presynaptic receptors, their role in signal transmission in cholinergic and adrenergic synapses.
13. The classification of cholinomimetic drugs (groups and preparations).
14. Muscarinic agonists, classification, pharmacological effects (effects on the eyes, heart, blood vessels, smooth muscle organs, exocrine gland).
15. Anticholinesterase agents, classification, mechanism of action, pharmacological effects.

16. The medical use of muscarinic agonists and anticholinesterase agents (major indications), side effects.
17. The effects of overdose and poisoning by muscarinic agonists and anticholinesterase agents, antidote therapy.
18. Drugs which stimulate acetylcholine release, mechanism of action, clinical application.
19. Nicotinic agonists, pharmacological effects, risks associated with tabagism. Drugs used for controlling smoking, substantiate their effect.
20. Cholinergic antagonists, classification (groups and preparations).
21. Muscarinic antagonists: classification, pharmacological effects on the example of atropine overdose and poisoning.
22. Mydriatics (cholinoblockers) of varying duration of action.
23. Clinical use of muscarinic antagonists. Features and application of quaternary M-blockers.
24. Side and toxic effects of muscarinic antagonists, treatment of poisoning with atropine-like substances.
25. Peripheral muscle relaxants (curariform means): classification, mechanisms of action.
26. Clinical application of curariform means side effects and hazards.
27. Antagonists of curariform drugs, principle of their action, application.
28. Ganglionic blockages, their spectrum of action, clinical use, side effects.
29. Adrenergic agonists, classification (groups and preparations).
30. Catecholaminic drugs: epinephrine, norepinephrine, dopamine, dobutamine, isoproterenol, their spectrum of receptor action, pharmacological effects, clinical use, side effects.
31. Alpha-agonists: classification, pharmacological effects, clinical application, side effects.
32. Alpha-agonists with selective action on the urethral sphincter, application, side effects.
33. Adrenergic agonists with primary beta-1-stimulating effect: preparations, localization of action, pharmacological effects, clinical application, contraindications.
34. Beta2-agonists: preparations, pharmacological effects, clinical application, side effects.
35. Pharmacological effects of stimulation of peripheral dopamine receptors ( $D_1$  and  $D_2$ ), clinical significance of these effects on the example of dopamine.
36. Adrenergic antagonists, classification (groups and preparations).
37. Alpha-blockers: classification, pharmacological effects, role of the selectivity of action, clinical application, side effects.
38. Beta-adrenergic antagonists, classification (groups and preparations).
39. The pharmacological effects of beta-blockers, role of selectivity, clinical use, side effects.
40. The clinical significance of cardioselectivity in beta-blockers action.
41. Beta-blockers with additional alpha-blocking effect: drugs, features of action, clinical use.
42. Beta-blockers with improved lipophilicity, locally anesthetic and vasodilating properties: give examples, substantiate clinical significance of these additional features.
43. Beta-blockers with ISA: give examples to clarify relationship of the ISA with partial agonism against beta-receptors, substantiate the clinical significance of the ISA.
44. Local anesthetics: Classification according the chemical structure, the use for various types of local anesthesia, speed of onset and duration of action.
45. The mechanism of action of local anesthetics, connection between effect and physicochemical properties of local anesthetic, tissue condition (effect of inflammation), dependence of action on the structure and properties of nerve fibers.
46. Side effects and hazards arising from the use of local anesthetics.
47. Astringents, mucilaginous drugs, absorbents, irritants: preparations, mechanism of action and the use in medicine.

## **DRUGS AFFECTING THE FUNCTIONS OF EFFECTOR ORGANS AND SYSTEMS**

### **LESSON 13. DIURETIC DRUGS**

#### **Key questions:**

1. Diuretics: definition, classification according to the localization of action in nephron, strength and speed of onset and duration of effect.
  - 1.1. Carbonic anhydrase inhibitors (acting on the proximal renal tubules) — acetazolamide.
  - 1.2. Loop diuretics (acting on the ascending part of loop of Henle): furosemide, bumetanide, torasemide.
  - 1.3. Thiazide (hydrochlorothiazide, bendroflumethiazide) and thiazide-like (chlorthalidone, indapamide, xipamid, metolazone) diuretics acting on the initial part of the distal renal tubules.
  - 1.4. Potassium-sparing diuretics (acting on the distal renal tubules and collector renal tubules): sodium channels inhibitors (triamterene, amiloride), aldosterone antagonists (spironolactone, eplerenone).
  - 1.5. Osmotic diuretics (acting on the proximal renal tubules, the descending part of the loop of Henle and collector renal tubules) — mannitol.
  - 1.6. Side effects of diuretics, including water-electrolyte and metabolic disorders.
  - 1.7. Use of diuretics: arterial hypertension, chronic heart failure, edemas, oliguric renal failure, acute intoxications, hyperaldosteronism, glaucoma, etc
  - 1.8. Criteria for diuretics selection:
    - speed of onset and time to maximum diuretic effect;
    - the duration and intensity of the effect;
    - the level of electrolytes and blood coagulation potential;
    - glomerular filtration rate;
    - methods and mechanisms of excretion.
  - 1.9. Combined use of diuretics. Rational combination of different diuretics and diuretics with drugs of other pharmacological groups.
  - 1.10. Absolute contraindications to the use of diuretics
2. Drugs that increase the glomerular filtration: xanthines, cardiac glycosides, dopamine; mechanism of action, clinical use.
3. Uricosuric drugs: sulfinpyrazone, probenecid, benzbromaron, losartan, fenofibrate, indacrinone, ticrynafen (rarely use).
4. Antagonists of the antidiuretic hormone (aquaretics), acting on the collector renal tubules: demeclocycline, conivaptan, tolvaptan
5. Agonists of the antidiuretic hormone — desmopressin.

**As a result, you should be able to:**

- Name the 5 major types of diuretics and specify the location of their action.
- Specify the main indications for use and side effects of acetazolamide, thiazides, loop and potassium-sparing diuretics.
- To characterize the 2 drugs that reduce potassium loss with sodium diuresis.
- Specify how you can reduce calcium excretion in urolithiasis.
- Approach to the treatment of acute severe hypercalcemia in patients with advanced carcinoma.
- Specify what should be appointed with nephrogenic diabetes to reduce the volume of urine.
- Specify what should be assigned to increase the excretion of water at a syndrome of excessive secretion of ADH.

**Write out the following drugs:** hydrochlorothiazide (tablets), furosemide (solution), chlorthalidone (tablets), spironolactone (tablets).

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## LESSON 14. ANTIHYPERTENSIVE DRUGS

### Key questions:

1. The main pharmacological approaches to the management of arterial blood pressure.
2. Classification of antihypertensive drugs:

#### 2.1. Diuretics:

- thiazide and thiazide-like (hydrochlorothiazide, indapamide, chlorthalidone, metolazone);
- loop (furosemide, bumetanide, torasemide);
- potassium-sparing (amiloride, triamterene, spironolactone).

#### 2.2. Inhibitors of the renin-angiotensin-aldosterone system (RAAS).

##### 2.2.1. Inhibitors of angiotensin-converting enzyme (ACE):

- short-term action (3 times a day) — captopril;
- average-term action (1–2 times a day) — enalapril, benazepril, quinapril, moexipril, ramipril;
- long-term action (once per day): lisinopril, fosinopril, perindopril, trandolapril.

##### 2.2.2. Angiotensin receptors AT<sub>1</sub> antagonists (ARB, angiotensin II antagonists):

losartan, valsartan, candesartan, azilsartan, irbesartan, olmesartan, telmisartan.

##### 2.2.3. Combined drugs of RAAS inhibitors with diuretics and/or CCB, proof of the benefits and use of such combinations.

##### 2.2.4. Renin inhibitor — aliskiren.

#### 2.3. Sympathoplegic drugs.

##### 2.3.1. Central $\alpha_2$ -adrenergic and I<sub>1</sub>-imidazoline receptors agonists: moxonidine, clonidine, guanfacine, methyldopa.

##### 2.3.2. $\beta$ -adrenergic antagonists: nonselective — propranolol, nadolol, timolol; cardioselective — atenolol, bisoprolol, betaxolol, metoprolol; with additional NO-dependent vasodilatation — nebivolol; with ISA — acebutolol, carteolol, penbutolol, pindolol.

##### 2.3.3. Mixed-action adrenergic antagonists: carvedilol, labetalol, proxodolol.

##### 2.3.4. $\alpha$ -adrenergic antagonists: doxazosin, prazosin, terazosin, nicergoline.

##### 2.3.5. Sympatholytics: reserpine, guanethidine, guanadrel (rarely use).

##### 2.3.6. Ganglionic blockers: trimethaphan, hexamethonium (rarely use).

#### 2.4. Calcium L-type channel blockers (CCBs):

- vasodilating (CCB with the predominant effect on the blood vessels) — dihydropyridine derivatives: nifedipine and its retard forms, amlodipine, felodipine, nicardipine, nisoldipine, nitrendipine, lacidipine, lecanidipine (except nimodipine);
- bradycardic (CCB with the predominant effect on the heart): phenylalkylamin derivatives — verapamil, gallopamil; benzothiazepine derivatives — diltiazem.

#### 2.5. Vasodilators:

- arteriolar — minoxidil, hydralazine, diazoxide;

- arteriolar and venous — sodium nitroprusside, nitroglycerine, magnesium sulfate, bendazol (dibazol).
3. Molecular and hemodynamic mechanisms of action of antihypertensive drugs, side effects, dosage regimen, contraindications and precautions for their use.
  4. The choice of drugs for the individual therapy of arterial hypertension:
    - 1st line drugs (standard therapy): ACE inhibitors, blockers, thiazide diuretics, CCBs, beta-blockers (mono- or combination therapy);
    - adjuvants: alpha blockers, renin inhibitors, vasodilators, sympatholytic (in addition to group 1);
    - hypertension + ChHF: RAAS inhibitors, aldosterone antagonists, diuretics, beta-blockers;
    - hypertension in pregnant women: methyldopa (traditional first-choice drug), labetalol (fewer side effects in comparison methyldopa), clonidine, beta blockers (except atenolol), CCBs (except nifedipine); RAAS inhibitors are contraindicated;
    - hypertension + postinfarction period: beta-blockers without the ISA, RAAS inhibitors, thiazides;
    - hypertension + ischemic heart disease: beta-blockers, CCBs (retard forms), RAAS inhibitors, diuretics;
    - hypertension in the elderly: CCB (!) + other 1st line drugs;
    - hypertension in chronic kidney disease: RAAS inhibitors (with caution), thiazides;
    - metabolic syndrome (obesity + hypertension + insulin resistance): thiazides (!), RAAS inhibitors, CCBs.
    - hypertension + erectile dysfunction: avoid alpha 2 and I1 agonists (central action);
    - hypertension + diabetes: preferred RAAS inhibitors (ACE inhibitors, ARB), chlorthalidone, in old age — CCBs.
    - hypertension in children and adolescents (mostly secondary): inhibitors of the RAAS, CCB, beta-blockers, thiazides.
  5. Drugs for the emergency control of arterial blood pressure.
    - 5.1. Relief of hypertensive crises: captopril, enalaprilat, labetalol, clonidine, nicardipine, hydralazine, nitroglycerin, sodium nitroprusside, esmolol, fenoldopam, magnesium sulfate, bendazol (applied depending on the clinical condition of the patient). Dangers of acute decline of blood pressure (development of renal, cerebral and coronary ischemia).
    - 5.2. Prevention of rupture of an aortic aneurism:  $\beta$ -adrenergic antagonists, vasodilators.
    - 5.3. Control blood pressure in severe heart failure: ACE inhibitors, myotropic vasodilators,  $\alpha$ -adrenergic antagonists, CCBs.
    - 5.4. Controlled hypotension — sodium nitroprusside, trimethaphan.
    - 5.5. Control blood pressure in pheochromocytoma — doxazosin, prazosin, terazosin.
    - 5.6. Agents used in pulmonary arterial hypertension — sildenafil, tadalafil.

**As a result, you should be able to:**

- Name 4 main groups of antihypertensive agents, give examples of drugs.
- Identify main target of action of sympatoplegic agents, give examples of drugs acting on these targets.
- Identify differences in action between three types of RAAS inhibitors.
- Identify compensatory reactions of the body (if they occurred) resulting from the action of each of the main 4 groups of antihypertensive drugs.
- Identify main diuretics used in hypertension and prove their effectiveness.
- Identify the main antihypertensive vasodilators and describe their effects.
- Identify 4 mechanisms of action of vasodilators.
- Identify preferred combinations of antihypertensive drugs.
- Identify preferred drugs for treatment of systolic hypertension.
- Identify preferred drugs for treatment hypertension in pregnant women.
- Identify the main side effects of antihypertensive drugs prototypes.

**Write out the following drugs:** indapamide (coated tablets), enalapril (tablets), lisinopril (tablets), losartan (tablets), candesartan (tablets), amlodipine (tablets), diltiazem (coated tablets), nebivolol (tablets), carvedilol (tablets), doxazosin (tablets), moxonidine (tablets), clonidine (tablets).

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## **LESSON 15. ANTIANGINAL AND OTHER ANTIISCHEMIC DRUGS. HYPOLIPIDEMIC DRUGS**

1. The concept of ischemic heart disease (IHD), its pathogenesis and clinical forms. Basic approaches to pharmacotherapy of IHD and angina pectoris.
2. Classification of drugs used in insufficiency of coronary circulation.
3. Antianginal drugs. Pharmacodynamics, pharmacokinetics, indications, side effects.
  - 3.1.  $\beta$ -adrenergic antagonists: propranolol, atenolol, bisoprolol, metoprolol, nadolol, oxprenolol, acebutolol; comparative characteristics.
  - 3.2. Calcium-channel blockers (CCB): verapamil, diltiazem, nifedipine (retard forms with delayed release of the active substance), amlodipin, nicardipine, felodipine; comparative characteristics.
  - 3.3. Organic nitrates and nitrate-like drugs:
    - organic nitrates: nitroglycerin, isosorbide dinitrate, isosorbide mononitrate; comparative characteristics.
    - nitrate classification according duration: short (1 h), moderately prolonged (up to 6 h) and long-acting (from 6 to 24 h);
    - medicinal forms for relief and prevention of angina attacks;
    - tolerance to nitrates and way of its overcoming;
    - sydnonimines of nitrate-like action — molsidomine.
  - 3.4. Comparative position of  $\beta$ -blockers, nitrates and CCBs as drugs for relief and prevention of angina attacks.
  - 3.5. Other antiischemic drugs.
    - 3.5.1. Potassium channel activators — nicorandil.
    - 3.5.2. Inhibitors of sinus node  $I_f$ -channels — ivabradine.
    - 3.5.3. Metabolic means: trimetazidine, ranolazine, mildronate, ubidecarenone (coenzyme Q).
    - 3.5.4. Drugs of reflex action — validol.
  - 3.6. Dangers of use of myotropic vasodilators with angina pectoris. Coronary steal phenomenon (steal the oxygen of the myocardium).
  - 3.7. Principles and criteria of drug selection for relief and prevention of angina attacks: clinical form of IHD; heart rate; BP level; presence of heart failure; impairments of hepatic and renal functions; hyperlipidemia; pregnancy.
  - 3.8. Drugs used for the treatment of myocardial infarction.
    - 3.8.1. Drugs for restoration of coronary blood flow: thrombolytic drugs, anticoagulants, antiaggregants.
    - 3.8.2. Drugs for limitation the size of impairment focus — nitroglycerine.
    - 3.8.3. Drugs for pain relief: narcotic analgesics, droperidol.
    - 3.8.4. Beta-blockers: in the acute phase of myocardial infarction (atenolol, metoprolol) in the early phase of healing (acebutolol, metoprolol, propranolol, timolol). Indications and risks of use at myocardial infarction.

### 3.8.5. Drugs for the treatment of myocardial infarction complications:

- cardiogenic shock — dopamin, norepinephrin, phenylephrine; rhythm disturbances — antiarrhythmic drugs; acute heart failure — dopamine, dobutamine, nitroglycerine, sodium nitroprusside, furosemide.

## 4. Hypolipidemic drugs: classification, mechanism of action, indications for use and side effects.

### 4.1. Sequestrants of bile acids and drugs inhibiting cholesterol absorption in the intestine: cholestyramine, colestipol, ezetimibe.

### 4.2. Drugs lowering the formation of atherogenic lipoproteins:

- nicotinic acid (niacin, vitamin PP) and its derivatives (enduracin);
- statins — inhibitors of an early phase of sterol synthesis (3-hydroxy-3-methylglutaryl-CoA reductase): atorvastatin, simvastatin;
- fibric acid derivatives (fibrates) — lipoprotein lipase activators: gemfibrozil, fenofibrate (lipanthyl 200 M long-term form);
- antioxidants and oxidized-low density lipoprotein (LDL) inhibitors in foamy cells — probucol.

### 4.2.1. Physiological correctors of lipid exchange containing essential phospholipids and unsaturated fatty acids, raising the high density lipoprotein (HDL) level: essentielle, lipostabil.

### 4.3. Essential phospholipids and unsaturated fatty acids, which increase HDL: Essentiale, lipostabil.

## As a result, you should be able to:

- Describe the pathophysiology of angina pectoris, vasospastic angina and unstable angina.
- Name the main determinants of consumption and oxygen supply of the myocardium.
- Specify the main pharmacological approaches to the prevention and relief of anginal pain.
- Name the 3 main classes of antianginal agents and their representatives.
- Name the latest and auxiliary antianginal agents.
- Compare the therapeutic and adverse effects of nitrates, beta-blockers, and CCBs used for angina pectoris.
- Explain why the nitrate combination with beta-blockers and CCBs can be more effective than when either of them used alone.
- To explain why the combination of nitrates and sildenafil (when used for erectile dysfunction) are potentially dangerous.
- To substantiate the basic principles of the treatment of myocardial infarction and identify the main groups of drugs used for this purpose.
- Name the main groups of lipid-lowering agents, indications for their use and side effects.

**Write out the following drugs:** atenolol (tablets), nitroglycerin (sublingual), isosorbide dinitrate (retard), nicorandil (tablets), verapamil (solution), amlodipine (tablets), atorvastatin (tablets), ezetimibe (tablets).

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## LESSON 16. DRUGS USED FOR THE TREATMENT OF HEART FAILURE

Pathophysiology of heart failure (HF). Understanding the clinical symptoms, forms of disease, methods of pharmacological intervention. Main groups of drugs used in acute and chronic HF.

1. Agents acting on the renin–angiotensin system (RAAS).
  - 1.1. Angiotensin-converting-enzyme (ACE) inhibitors:
    - short-term action (6–12 hours) — captopril;
    - average-term action (12–24 hours) — enalapril;
    - long-term action ( $\geq 24$  hours): lisinopril, perindopril, fosinopril, ramipril.
  - 1.2. Angiotensin II antagonists: losartan, irbesartan, valsartan, candesartan.
  - 1.3. Aldosterone receptors antagonists: spironolactone, eplerenone.
  - 1.4. Mechanisms of action of RAAS inhibitors in chronic HF and pharmacological effects: influence on afterload (total peripheral vascular resistance), preload, blood pressure in pulmonary circulation, heart rate and cardiac output, myocardial remodeling and mortality.
  - 1.5. Therapeutic use and side effects of RAAS inhibitors:
    - in chronic heart failure,
    - in postmyocardial infarction period for preventing myocardial hypertrophy;
  - 1.6. Vasopeptidase inhibitors — omapatrilat. Pharmacodynamics, use in chronic HF.
2. Diuretics.
  - 2.1. Characteristic features of use of diuretics (thiazide, loop) in chronic HF.
  - 2.2. Influence of diuretics (hydrochlorothiazide, indapamide, furosemide, torasemide) on the quality of life and life expectancy, chronic HF course and prognosis.
3.  $\beta$ -adrenergic antagonists:
  - cardioselective: bisoprolol, metoprolol, nebivolol;
  - mixed ( $\beta_1$ ,  $\beta_2$ ,  $\alpha_1$ -adrenergic antagonists) — carvedilol;
  - specific features of  $\beta$ -adrenergic antagonists action in chronic HF, indications, contraindications, side and toxic effects.
4. Drugs with positive inotropic effect (increasing myocardial contractility).

Classification.

  - 4.1. Cardiac glycosides (CG):
    - short-term action — strophanthin;
    - average-term action — digoxin;
    - long-term action — digitoxin.
  - 4.2.  $\beta$ -adrenomimetics: dopamine, dobutamine.
  - 4.3. Phosphodiesterase inhibitors: milrinone, enoximone, theophylline drugs.
  - 4.4. Other cardiotonic agents: levosimendan.
  - 4.5. History of cardiac glycoside discovery and use (W. Withering, E. V. Pelikan). Their sources. Basic structural determinants of pharmacological activity.
  - 4.6. The mechanism of CG action on contractile and bioelectric functions of the heart (heart force and heart rate, conduction, excitability, automatism, myocardial

bioenergy, parasympathetic tone, sensitivity to sympathetic stimulation). ECG changes under CG influence.

4.7. The essence of CG therapeutic action in cardiac decompensation (influence on stroke and minute blood volume, arterial and venous pressure, blood flow rate, diuresis). Areas of CG use.

4.8. CG pharmacokinetics.

4.9. Side and toxic effects of CG (arrhythmogenic effect, influence on the gastrointestinal tract, neurotoxicity). Withdrawal phenomenon. Possible causes of digitalis intoxications in view of effect onset rate, width of therapeutic range, cumulative properties.

4.10. Factors increasing CG toxicity: hypopotassemia, alkalosis, hypoxia, hypercalcemia, hypomagnesemia, hypothyroidism, hyponatremia; drugs: verapamil, quinidine, corticosteroids, thiazide and loop diuretics. Principles of treatment of digitalis intoxications.

4.11. Nonglycoside inotropic drugs. Mechanisms of action. Indications and contraindications to use. Side effects. Comparative characteristics with cardiac glycosides.

5. Peripheral vasodilators, features of action and use in HF.

5.1. Vasodilators of direct action: venous (isosorbide dinitrate); arteriolar (hydralazine); mixed (sodium nitroprusside).

5.2. CCBs — amlodipine (other CCBs should be avoided in patients with reduced ejection fraction).

5.3.  $\alpha_1$ -adrenergic antagonists: prazosin, doxazosin.

6. Metabolic drugs used in HF: inosine, pyridoxine, anabolic steroids.

**As a result, you should be able to:**

- Describe the strategy for treatment of acute and chronic heart failure, list the main groups of drugs used for this purpose.
- Describe the mechanism of action of cardiac glycosides and their main effects. Explain why cardiac glycosides today, is not a means of first choice for the treatment of chronic HF.
- Describe the nature and mechanism of the toxic effect of cardiac glycosides on the heart.
- Explain beneficial effects in chronic HF of diuretics, vasodilators, ACE inhibitors and other means of non-inotropic type of action.
- Explain useful effects of beta-blockers in chronic HF and name drugs used for this purpose.
- To substantiate use of aldosterone antagonists in chronic HF.
- List the other inotropic agents used in heart failure.

**Write out the following drugs:** furosemide (tablets), lisinopril (tablets), ramipril (tablets), candesartan (tablets), bisoprolol (tablets), carvedilol (tablets), digoxin (solution), spironolactone (tablets).

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## LESSON 17. ANTIARRHYTHMIC DRUGS

1. Causes and pathophysiology of arrhythmias.
2. Mechanisms of tachyarrhythmias; heightened automaticity, reverse pulse input (re-entry), trigger automaticity.
3. Main pharmacological approaches to treatment of arrhythmias based on the management of ionic currents and generation of action potential in the heart.
4. Drugs used in tachyarrhythmias.
  - 4.1. Classification (Vaughan Williams classification).
    - 4.1.1. Class I — sodium-channel blockers (membrane stabilizers):
      - class IA — increasing effective refractory period (ERP) (quinidine-like AAD): procainamide, disopyramide, quinidine;
      - class IB — decreasing ERP: lidocaine, mexiletine, phenytoin;
      - class IC — does not significantly affect ERP: flecainide, propafenone, moracizine (moricizine), etacizin.
    - 4.1.2. Class II —  $\beta$ -adrenergic antagonists: propranolol, nadolol, timolol, metoprolol, atenolol, oxprenolol, esmolol.
    - 4.1.3. Class III — potassium channel blockers (prolonging repolarisation and an ERP): amiodarone, sotalol ( $\beta$ -adrenergic antagonist), dronedarone, dofetilide, ibutilide.
    - 4.1.4. Class IV — CCBs (bradycardiac): verapamil, diltiazem.
  - 4.2. Basic mechanisms of antiarrhythmic action of the above-mentioned drugs: influence on ionic currents, action potential, rate of spontaneous diastolic depolarisation, rest potential, threshold potential, ERP of pacemaker cells, conducting system and cardiomyocytes.
  - 4.3. Influence of AAD on the basic heart functions (automatism, excitability, conduction, contractility), BP, stroke volume, neurovegetative innervation, ECG.
  - 4.4. Other AAD used in tachyarrhythmias: adenosine, digoxin, ivabradin, ranolazine, magnesium sulfate, potassium and magnesium combined drugs.
  - 4.5. Indications for AAD administration:
    - supraventricular arrhythmias — adenosine, digoxin, verapamil, etc.;
    - supraventricular and ventricular arrhythmias — amiodarone,  $\beta$ -adrenergic antagonists, disopyramide, procainamide, flecainide, propafenone, etc.;
    - ventricular arrhythmias — lidocaine, mexiletine, moracizine, etc.
  - 4.6. Arrhythmogenic (proarrhythmic) and other AAD side effects and their correction.
  - 4.7. Contraindications for AAD administration.
  - 4.8. Combined use of AAD and their interaction with other drugs (cardiac glycosides, indirect anticoagulants, diuretics, potassium and calcium drugs).
  - 4.9. Criteria for AAD selection: type of arrhythmia, impact on electrophysiological component of arrhythmia (vulnerable parameter and a pharmacological target), cost (during long-term therapy).
5. The drugs used in bradyarrhythmias:
  - M-cholinergic antagonists — atropine;
  - adrenomimetics — epinephrine, isoprenaline.



**As a result, you should be able to:**

- Name basic mechanisms of tachyarrhythmias and their relationship with the processes of generation and conduction of impulses in the heart.
- Name 4 main groups of AAD and other drugs used in tachyarrhythmias.
- Describe differences in the effects of the 4 groups of AAD and adenosine on heart action potentials and ionic currents.
- Name the 2–3 or more representatives of each of these groups.
- Name basic indications for use AAD from these 4 groups and adenosine.
- Name basic tools used in supraventricular arrhythmias.
- Name basic tools used in ventricular arrhythmias.
- Name main side effects of antiarrhythmic agents.
- Name agents used in bradyarrhythmias, substantiate their action.
- Explain how hyperpotassemia, hypopotassemia or antiarrhythmic agents may trigger arrhythmias.

**Write out the following drugs:** procainamide (solution), lidocaine (solution), flecainide (tablets), oxprenolol (tablets), amiodarone (tablets, solution), sotalol (coated tablets), verapamil (dragee).

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## LESSON 18. FINAL LESSON ON DRUGS AFFECTING THE CARDIOVASCULAR SYSTEM AND KIDNEY RENAL FUNCTION

**Objective:** To systematize and consolidate knowledge on the pharmacological properties of drugs acting on the function of kidneys and cardiovascular system; to systematize and consolidate skills of writing out the main drugs of the above-mentioned groups in prescriptions. While preparing for the lesson it is necessary to revise the classification, mechanisms of action, peculiarities of pharmacokinetics, main and side effects, indications and contraindications for drug administration of the following groups:

1. Diuretics.
2. Antihypertensive drugs.
3. Antianginal and hypolipidemic drugs.
4. Drugs used for the treatment of heart failure.
5. Antiarrhythmic drugs.
6. Drugs acting on regional blood flow (material of the lecture).

**Be able to write out the following drugs:** amiodarone, atenolol, atorvastatin, bisoprolol, candesartan, carvedilol, clonidine, digoxin, diltiazem, doxazosin, enalapril, furosemide, hydrochlorothiazide, indapamide, isosorbide dinitrate, lidocaine, lisinopril, losartan, metoprolol, moxonidine, nebivolol, nicorandil, nitroglycerin (sublingual), procainamide, ramipril, sotalol, spironolactone, verapamil.

### Questions for individual study:

1. Diuretics, definition. Classification of diuretics according to the site and character of their action in the nephron. Classification of diuretics according to their efficiency.
2. List thiazide and thiazide-like diuretics; loop diuretics; potassium-sparing diuretics.
3. Draw a scheme of a nephron and indicate on it the action site of diuretics enhancing the filtration of primary urine; carbonic anhydrase inhibitors; loop diuretics; thiazide and thiazide-like diuretics; potassium-sparing diuretics; aquaretics.
4. Mechanism of action of osmotic; loop; thiazide and thiazide-like diuretics; spironolactone; potassium-sparing diuretics; demeclocycline.
5. Arrange the following drugs in decreasing order according to their diuretic action power: spironolactone, chlorthalidone, furosemide, hydrochlorothiazide, mannitol.
6. Effect of loop; potassium-sparing; thiazide and thiazide-like diuretics on electrolyte excretion.
7. Side effects of loop; potassium-sparing; thiazide and thiazide-like diuretics.
8. Indications for administration of carbonic anhydrase inhibitors; osmotic; potassium-sparing; loop; thiazide and thiazide-like diuretics.
9. Contraindications to the administration of osmotic; loop; thiazide and thiazide-like diuretics.
10. Principles of pharmacotherapy of heart failure. Purposes of heart failure treatment.
11. Groups of drugs used for the treatment of heart failure.
12. List angiotensin-converting-enzyme (ACE) inhibitors. Explain why ACE inhibitors are used for the treatment of chronic heart failure.
13. Give proof of using diuretics for the treatment of heart failure.
14. Give proof of using vasodilators for the treatment of heart failure (groups, drugs).
15. Side effects of calcium channel blockers that limit their use for the treatment of heart failure.
16. Drugs with positive inotropic effect on the heart (groups, drugs).
17. Mechanism of positive inotropic effect of cardiac glycosides, essence of cardiac glycosides therapeutic effect in cardiac decompensation.
18. List cardiac effects of cardiac glycosides, the characteristic changes of ECG while using cardiac glycosides.
19. List extracardiac effects of cardiac glycosides.
20. Indications and contraindications for administration of cardiac glycosides. Side effects of cardiac glycosides.
21. Symptoms of the intoxication with cardiac glycosides required their withdrawal.
22. Antiarrhythmic drugs used for the treatment of glycosidic arrhythmia.
23. Drugs used for electrolyte balance correction in case of intoxication with cardiac glycosides.
24. Give proof of administering  $\beta$ -adrenergic antagonists for the treatment of chronic heart failure, name drugs.
25. Metabolic drugs used for the treatment of heart failure.
26. Antiarrhythmic drugs for the treatment of tachyarrhythmia (groups, drugs).
27. Antiarrhythmic drugs for the treatment of bradyarrhythmia (groups, drugs).
28. AAD class I, groups, drugs, mechanism of action at arrhythmias, indications for use.
29. Differences in IA, IB, IC subclasses in their effect on AP phase of Purkinje fibers.
30. AAD class II, drugs, mechanism of action at arrhythmias, indications for use.
31. AAD class III, drugs, mechanism of action at arrhythmias, indications for use, side effects.

32. AAD class IV, drugs, mechanism of action at arrhythmias, indications for use, side effects.
33. Extrasystematic agents of treatment tachyarrhythmias (adenosine, preparations of potassium, magnesium, digoxin), their mechanism of action at arrhythmia, indications for use.
34. Arrhythmogenic effect of AAD, its causes, arrhythmogenic and non-arrhythmogenic AAD.
35. Effect of antiarrhythmic drugs of subgroups I A, I B, I C, groups II, III, IV on the basic cardiac functions.
36. Determinants of systolic and diastolic arterial blood pressure (ABP).
37. Mechanisms of controlling normal ABP and in case of arterial hypertension.
38. Aims of antihypertensive therapy.
39. Antihypertensives of the 1st line, groups, drugs.
40. Antihypertensives of the 2nd line, groups, drugs.
41. Diuretics used for the treatment of arterial hypertension, groups, drugs, mechanism of antihypertensive action.
42. Side effects of diuretics used in hypertension and their prevention.
43. ACE inhibitors, drugs, mechanism of antihypertensive action, side effects, risk of use, contraindications.
44. Angiotensin receptor blockers, drugs, mechanism of antihypertensive action, side effects, contraindications.
45. CCBs used as antihypertensives, drugs, mechanism of action, side effects, contraindications.
46. Sympathoplegic drugs, used as antihypertensives (groups, drugs).
47. Mechanism of  $\beta$ -adrenergic antagonists antihypertensive action, preferred drugs.
48. Alpha<sub>1</sub>-blockers in hypertension, drugs, mechanism of action, indications for use, side effects.
49. Drugs used for relief of hypertensive crises. The risks associated the acute fall of blood pressure under these conditions.
50. Antihypertensives used at pregnancy.
51. Preferable combinations of antihypertensive drugs, substantiate it, provide examples.
52. Determinants of myocardial oxygen consumption and myocardial oxygen supply.
53. Principles of antianginal pharmacotherapy.
54. Use of  $\beta$ -blockers in angina pectoris, drugs, mechanism of anti-anginal action, selection criteria.
55. Use of CCBs in angina pectoris, drugs, mechanism of anti-anginal action, selection criteria.
56. Use of organic nitrates in angina pectoris, drugs, mechanism of anti-anginal action, selection criteria.
57. Side effects of nitrates.
58. Metabolic drugs used for IHD.
59. Main drugs used for the treatment of myocardial infarction and their complications.
60. Hypolipidemic drugs (groups; drugs).
61. Hypolipidemic mechanisms of action of nicotinic acid; statins; fibrates.
62. Side effects of nicotinic acid; statins; fibrates.
63. Drugs used for the treatment of to treat erectile dysfunction (groups; drugs).
64. Phlebotonics, list the drugs, indications for use.
65. Drugs used for pulmonary hypertension.
66. Principles of pharmacotherapy of peripheral blood flow disturbance (Raynaud's disease, vibration disease; claudication).

67. Write out the the prescriptions for:

- A thiazide diuretic for treatment AH.
- A potassium-sparing diuretic.
- An ACE inhibitor drug for treatment AH.
- A CCB of long-term action for treatment AH.
- A  $\beta$ -adrenergic antagonist for treatment AH.
- Drug for the prophylaxis of angina attacks from beta-blocker group.
- Drug for the prophylaxis of angina attacks from CCBs.
- Remedy for relief angina from nitrates group.
- The medicine of choice for the treatment of chronic HF.
- A  $\beta$ -adrenergic antagonist for the treatment of chronic HF.
- An inotropic drug for the treatment of chronic HF.
- An aldosterone antagonist for the treatment of chronic HF.
- Diuretic for therapy decompensation of chronic HF.
- AAD 1st class for the treatment of supraventricular tachyarrhythmias.
- AAD 1st class for the control of ventricular fibrillation at myocardial infarction.
- AAD 2nd class for the treatment of supraventricular tachyarrhythmias.
- AAD 3rd class with polytropic effect.
- AAD 4th class to control supraventricular arrhythmias.
- Lipid-lowering agents from statin group.

## LESSON 19. DRUGS AFFECTING BLOOD SYSTEM

### HEMOPOIESIS MODULATORS

#### 1. Drugs for the treatment of anemias

##### 1.1. Drugs used for the treatment of iron-deficiency (hypochromic) anemias:

- iron drugs to be administered orally — ferrous sulfate and other iron (II) salts;
- iron drugs to be administered parenterally — iron (III) polyisomaltosate (i/m); iron (III) sucrose complex(i/v);
- drugs combining iron with folic acid, ascorbic acid, cyanocobalamin, cobalt and other components — (feful, ferroplex, speisferron and others);

##### 1.1.1. Causes of hypochromic anemias. Principles of pharmacotherapy.

##### 1.1.2. Pharmacodynamics and pharmacokinetics of iron drugs; side and toxic effects.

##### 1.1.3. Poisoning with iron drugs and aid measures — deferoxamine.

##### 1.2. Drugs used for megaloblastic (hyperchromic) anemias: cyanocobalamin, folic acid. Biological role of vitamins B<sub>9</sub> and B<sub>12</sub>, physiological need, causes of hypovitaminoses, therapeutical use (indications, dosing, routes of administration, side effects).

##### 1.3. Drugs used for hypoplastic, hemolytic, renal anemias: erythropoietins alfa and beta; darbepoetin alfa, antilymphocyte globulin; pyridoxine; glucocorticosteroids.

#### 2. Drugs used for leucopenia:

- colony-stimulating factors: molgramostim, filgrastim, lenograstim;
- pyrimidine derivatives: methyluracil, pentoxil.

#### 3. Drugs inhibiting hemopoiesis — anticancer drugs: hydroxycarbamide, methylthiouracil, bleomycin, etoposide, etc.)

### HEMOSTASIS MODULATORS

#### 4. Antithrombotic drugs

##### 4.1. Antiplatelet drugs (antiaggregants).

#### 4.1.1. Drugs affecting arachidonic acid metabolism:

- I type cyclooxygenase (COX-1) inhibitors — acetylsalicylic acid (low doses);
- thromboxane synthesis inhibitors — dazoxiben.

#### 4.1.2. Drugs increasing cyclic adenosine monophosphate (cAMP) in the thrombocytes:

- phosphodiesterase inhibitors: pentoxifylline, dipyridamole;
- adenylate cyclase stimulants: epoprostenol (prostacyclin), alprostadil (prostaglandin E<sub>1</sub> (PGE<sub>1</sub>) drug).

#### 4.1.3. Thrombocyte receptor antagonists:

- blockers of adenosine diphosphate (ADP) receptors on thrombocyte membranes: clopidogrel, ticlopidine, prasugrel, ticagrelor;
- glycoprotein thrombocyte receptor antagonists (GP IIb/IIIa): abciximab, eptifibatide, tirofiban.

### 4.2. Anticoagulants

#### 4.2.1. Direct anticoagulants

##### a) for parenteral use:

- heparins: unfractionated heparin — heparin, low-molecular-weight heparins (fractionated) — dalteparin, nadroparin, enoxaparin, tinzaparin;
- heparinoids — sulodexide, danaparoid;
- hirudins (direct thrombin inhibitors) — lepirudin, bivalirudin, argatroban;
- direct factor Xa inhibitor — fondaparinux;
- plasma drugs — antithrombin III.

##### b) for oral use:

- direct thrombin inhibitors — dabigatran;
- direct Xa factor inhibitors — rivaroxaban, apixaban.

#### 4.2.2. Indirect anticoagulants (to be administered orally) — warfarin, phenindione, acenocoumarol.

#### 4.2.3. Heparin antagonists — protamine sulfate.

### 4.3. Thrombolytic drugs (fibrinolytics)

#### 4.3.1. Direct fibrinolytics — fibrinolysin.

#### 4.3.2. Indirect fibrinolytics — streptokinase, urokinase, tissue plasminogen activator (abbreviated t-PA or PLAT) and its recombinant forms: alteplase, tenecteplase.

Principles of the treatment and prevention of acute arterial and venous thromboses.

### 5. Haemostatic drugs

#### 5.1. Thrombopoietin receptor agonist — eltrombopag (thrombopoietin).

#### 5.2. Platelet aggregation stimulants (aggregants) — etamsylate, calcium salts.

#### 5.3. Indirect coagulants — vitamin K drugs: phytomenadione, menadione.

#### 5.4. Fibrinolytic inhibitors:

- amino acids — tranexamic acid;
- plasma protease inhibitors — aprotinin.

#### 5.5. Plasma drugs — fibrinogen, protein C concentrate, blood clotting factors VII, VIII, and IX.

#### 5.6. Recombinant factor VIIa — eptacog alfa (activated).

#### 5.7. Local drugs to stop bleeding: thrombin, tachocomb, beriplast, haemostatic sponge, alufer (Bel), membrana fibrinosa isogena, gelplastan; desmopressin.

Principles of drug actions of the given groups, administration, side and toxic effects.

**Write out the following drugs:** erythropoietins beta (bottles), alteplase (bottles), dabigatran (capsules), rivaroxaban (coated tablets), tranexamic acid (solution), clopidogrel (coated tablets), enoxaparin (solution), warfarin (tablets).

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## TOPIC FOR INDIVIDUAL STUDY. VITAMIN DRUGS

### Main questions:

1. Definition of vitamins; classification; sources. Causes of hypovitaminoses; pathogenesis of vitamin deficiency. Types of vitamin therapy.
2. Water-soluble vitamin drugs: thiamine, benfotiamine, riboflavin, flavinat, calcium pantothenate, folic acid, nicotinic acid, pyridoxine, cyanocobalamin, ascorbic acid, rutin, quercetin.
3. Fat-soluble vitamin drugs: retinol, ergocalciferol, alfacalcidol, phytomenadione, menadione, tocopherol. Hypervitaminosis caused by the treatment of retinol and ergocalciferol.
4. Vitamin-like compound drugs: choline chloride, calcium pangamate, methionine methylsulfonium chloride, inosine.
5. Polyvitamins and combined drugs: «Undevit», «Centrum», «Supradin».

**Write out the following drugs:** alfacalcidol (solution for oral use), retinol (dragee), thiamine (solution), folic acid (tablets).

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# DRUGS AFFECTING THE CENTRAL NERVOUS SYSTEM

## LESSON 20. GENERAL ANESTHETICS. ETHYL ALCOHOL. ANTICONVULSANTS

### 1. General anesthetics (GA)

- 1.1. The definition of general anesthesia (narcosis). A history of the discovery of anesthesia (diethyl ether). The concept of inhalation anesthesia and non inhalation anesthesia. Varieties of anesthesia (basic, combined, introductory, reinforcing).
- 1.2. The determinants of the depth of anesthesia (the concentration or partial pressure of GA in the CNS).
- 1.3. The determinants of development speed and anesthesia recovery:
  - concentration of GA in the inspired air;
  - alveolar ventilation;
  - alveole-blood transfer;
  - blood-tissue transfer.
- 1.4. Stages of anesthesia.
- 1.5. The requirements for an ideal anesthetic.
- 1.6. The concept of the activity of inhalation GA (minimum alveolar concentration — MAC). Clinical use.
- 1.7. Molecular and neurophysiological mechanisms of action of GA.
- 1.8. The main classes of GA
  - 1.8.1. Drugs for inhalation anesthesia:
    - liquid volatiles — halothane (fluothane), isoflurane, sevoflurane;
    - gases — nitrous oxide.
  - Comparative characteristics of inhalation GA.
  - 1.8.2. Drugs for non inhalation (intravenous) anesthesia:
    - barbiturates — sodium thiopental;
    - non barbiturates GA — propofol, etomidate, ketamine (dissociative anesthesia).
  - Comparative characteristics of non inhalation GA according to the duration, development speed and anesthesia recovery, side and toxic effects.

### 2. Ethyl alcohol (ethanol)

- 2.1. Local and resorptive effects of ethyl alcohol; use in medicine.
- 2.2. Acute intoxication with ethyl alcohol. Medical aid.
- 2.3. Chronic intoxication with ethyl alcohol (alcoholism). Principles and drugs for alcoholism: disulfiram (teturam, radoter, esperal), apomorphine, acamprosate.

### 3. Anticonvulsants (antiepileptic drugs)

- 3.1. Drugs effective in generalized seizures:
  - tonic-clonic seizures — sodium valproate, carbamazepine, phenytoin, phenobarbital, primidone, lamotrigine, topiramate;
  - absence seizures — ethosuximide, sodium valproate;
  - myoclonic seizures — sodium valproate, ethosuximide, lamotrigine.
- 3.2. Drugs effective in partial seizures (simple, complex, secondary generalized): carbamazepine, sodium valproate, phenytoin, lamotrigine, levetiracetam, topiramate, gabapentin, pregabalin, vigabatrin, tiagabine, zonisamide, retigabine.

3.3. Drugs effective in status epilepticus: lorazepam, clonazepam, diazepam, phenytoin.

3.4. Drugs for the relief of seizures of any etiology: diazepam, clonazepam, magnesium sulfate, GA, antipsychotic drugs, muscle relaxants, paracetamol (hyperthermic convulsions).

Mechanisms of anticonvulsant action. Principles of use. Side effects.

#### 4. Antiparkinsonian drugs

4.1. Dopaminergic drugs: levodopa, amantadine, selegiline, rasagiline, bromocriptine, pramipexole, ropinirole, rotigotine.

4.2. DOPA-decarboxylase inhibitors: carbidopa, benserazide and their combination with levodopa — Nacom, Madopar. COMT inhibitors — entacapone.

4.3. Central cholinergic antagonists: trihexyphenidyl, biperiden.

Principles of drug correction of extrapyramidal disorders. Mechanisms of action and side effects of antiparkinsonian drugs.

#### 5. Drugs to reduce spasticity — central muscle relaxants: baclofen, tizanidine, tolperisone.

**Write out the following drugs:** sodium valproate (tablets), carbamazepine (tablets), topiramate (capsules), ethosuximide (oral solution), amantadine (tablets), nacom (tablets), entacapone (coated tablets), trihexyphenidyl (tablets), tolperisone (dragee).

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## LESSON 21. ANALGETIC DRUGS

1. General concept of pain and pain relief
  - 1.1. Nociceptive system: specific and nonspecific ways of conducting sensation of pain; pain mediators.
  - 1.2. Antinociceptive system: antinociceptive system mediators and their precursors; opiate receptors — localization, heterogeneity ( $\mu$ ,  $\kappa$ ,  $\delta$ ,  $\sigma$ ), effects of their activation.
2. Narcotic analgetics (opioids) and their antagonists
  - 2.1. Opioid basic pharmacological effects:
    - molecular and cellular mechanisms of action;
    - influence on the CNS (analgesia, euphoria, sedative action, respiratory depression, depression of cough reflex, hypothermal and emetic action, myosis, increase of intracranial pressure, muscular rigidity);
    - cardiovascular effects;
    - influence on the gastro-intestinal tract;
    - urogenital effects;
    - endocrine effects.
  - 2.2. Opioids pharmacokinetics.
  - 2.3. Opioids basic groups and their characteristics.
    - 2.3.1. Full agonists of opioid receptors:
      - natural opium alkaloids (phenanthrene derivatives) — morphine, codeine, dihydrocodeine;
      - phenylpiperidines — trimeperidine, fentanyl;
      - diphenylpropylamines — methadone.
    - 2.3.2. Partial agonists of opioid receptors — buprenorphine.
    - 2.3.3. Agonists-antagonists of opioid receptors — pentazocine, nalbuphine.
    - 2.3.4. Analgetics with mixed (opioid and nonopioid) mechanisms of action — tramadol, tapentadol.
    - 2.3.5. Opioid antagonists — naloxone, naltrexone.
  - 2.4. The fields of medical use: acute and chronic pains, cough, diarrhea, pulmonary edema, premedication in anaesthesia, neuroleptanalgesia.
  - 2.5. Opioid acute poisoning and medical aid measures.
  - 2.6. Side and toxic effects. Chronic toxicity and drug abuse (narcomania, morphinism). Narcomania and abstinent syndrome treatment.
  - 2.7. Drug interaction with sedative-hypnogenic and antipsychotic drugs, cholinergic antagonists,  $\alpha$ -adrenergic antagonists, MAO inhibitors, tricyclic antidepressants, amphetamine.
3. Nonnarcotic analgetics
  - 3.1. Nefopam (central analgetic).
  - 3.2. Neuroleptanalgesic — fentanyl + droperidol (talamonal).
  - 3.3. Analgetics-antipyretics:
    - central cyclooxygenase (COX) inhibitors — paracetamol;

- cyclooxygenase inhibitors in peripheral tissues and the CNS (peripheral COX inhibitors): acetylsalicylic acid, ibuprofen, ketorolac, metamizole (analgin);
- drugs for treating malignant hyperthermia — dantrolene.

Mechanisms of analgesic and antipyretic actions. Use in medicine: indications, side-effects, contraindications. Comparative characteristics of nonnarcotic and narcotic analgetics.

#### 4. Combined analgetics

4.1. Spasmoanalgetics — baralgin, spasmolgon; novigan.

4.2. Combined drugs, containing analgetics:

- metamizole + caffeine + thiamine (Benalgin);
- paracetamol + propyphenazone + caffeine (Saridon);
- paracetamol + ibuprofen (Brustan);
- paracetamol + caffeine + codeine (Proxol forte);
- dextropropoxifen + paracetamol (Co-proxamol);
- metamizole + paracetamol + caffeine + codeine + phenobarbital (Pentalgin ICN);
- metamizole + naproxen + caffeine + codeine + phenobarbital (Pentalgin-N).

#### 5. Drugs, used in neuropathic painful syndromes

##### 5.1. Migraine.

5.1.1. Drugs for the treatment of acute seizures:

- nonnarcotic analgetics — acetylsalicylic acid, paracetamol and others;
- Serotonine agonists ( $S_1$  (5HT<sub>1</sub>)-receptors) — sumatriptan, naratriptan;
- Ergot alkaloids — ergotamine;
- Antiemetics — metoclopramide, domperidone.

5.1.2. Seizures prophylaxis — pizotifen,  $\beta$ -adrenergic antagonists, tricyclic antidepressants, sodium valproate, calcium channel blockers, cyproheptadine.

5.2. Neuralgias: postherpetic, trifacial and glossopharyngeal nerves, etc. — carbamazepine, phenytoin, sodium valproate, tricyclic antidepressants.

5.3. Acute and chronic painful syndromes (auxiliary drugs):

- clonidine (myocardial infarction, tumors, postoperative pains, etc.);
- amitriptyline (chronic pains, tumours, phantom pains, etc.);
- ketamine (tumors);
- calcitonin (tumor bones metastases);
- octreotide (hormone-secreting tumors of gastrointestinal area and pancreas);
- glucocorticosteroids (compressive neuropathy);
- benzofurocaine (pancreatitis, peritonitis, acute pleurisy, colics, etc.);
- other drugs with analgetic effect — baclofen (GABA (gamma-aminobutyric acid)-ergic drug), diphenhydramine (antihistamine drug).

**Write out the following drugs:** tramadol (suppositories), fentanyl (systema therapeuticum transcutaneum — STT), ergotamine (solution), sumatriptan (coated tablets).

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## LESSON 22. PSYCHOTROPIC DRUGS. PART I

Psychopharmacology in medicine, everyday and social life. Basic groups of psychotropic drugs.

### 1. Anxiolytic and sedative-hypnogenic drugs

1.1. Anxiolytic, sedative and hypnogenic effects — essence, similarity and differences.

1.2. Chemical classes and pharmacological groups of drugs used in psychoneurotic disorders and sleep impairments.

1.2.1. Anxiolytics (tranquilizers).

1.2.1.1. Benzodiazepines:

- an average-term action ( $T_{1/2}$  5–24 hours) — alprazolam, lopazepam, phenazepam;
- a long-term action ( $T_{1/2} > 24$  hours) — chlórdiazepoxide, diazepam;
- daytime tranquilizers (without sedative component) — oxazepam (an average-term action), medazepam, dipotassium clorazepate (a long-term action).

1.2.1.2. Nonbenzodiazepine anxiolytics (atypical) — buspirone; fabomotizole; mebicar; phenibut.

1.2.2. Benzodiazepine antagonists — flumazenil.

1.2.3. Sedative-hypnogenic drugs:

1.2.3.1. Sedative (obtundent) drugs:

- herbal drugs of valerian, motherwort, balm (mellissa), kava;
- combined drugs — corvalol.

1.2.3.2. Hypnogenic drugs (hypnotic) drugs (recommended period of drugs use — no more than 3 weeks):

- benzodiazepines with the marked hypnotic effect:
  - a short-term action ( $T_{1/2} < 5$  hours) — triazolam;
  - an average-term action — temazepam, lormetazepam;
  - a long-term action — nitrazepam, flunitrazepam, flurazepam;
- nonbenzodiazepines — zaleplon ( $T_{1/2}$  — 1 hours, take up to 2 weeks); zolpidem ( $T_{1/2}$  — 2 hours, take up to 4 weeks); zopiclone ( $T_{1/2}$  — 5–6 hours, take up to 4 weeks);
- antihistamine drugs — diphenhydramine, promethazine;
- aliphatic derivatives — chloral hydrate, triclofos sodium, clomethiazole;
- barbiturates — amobarbital (for the treatment of severe obstinate (hard-to-treat) insomnia in patients taken barbiturates).

1.2.3.3. Drugs used in biorhythm disorders (when changing time zones) — melatonin, ramelteon, tasimelteon, fabomotizole.

1.3. Pharmacological effects, neurophysiological and molecular mechanisms of action of anxiolytic and sedative-hypnogenic drugs. Pharmacokinetics. Side and toxic effects. The fields of anxiolytic and sedative-hypnogenic drug use, the limits of their use.

### 2. Antipsychotic drugs (neuroleptics, APD)

2.1. Neuroleptic distinctive features as a special class of psychopharmacological drugs. The main discovery milestones and creation of neuroleptics. The concept of neuroleptia.

2.2. Modern antipsychotic drugs:

2.2.1. First generation

- phenothiazine derivatives: chlorpromazine — aliphatic derivatives; periciazine, thioridazine, pipotiazine — piperidine derivatives; fluphenazine, trifluoperazine — piperazine derivatives;
- butyrophenone derivatives — haloperidol, benperidol (additionally taken to control antisocial sexual behavior);

- thioxanthene derivatives — flupentixol, zuclopenthixol;
  - benzamide derivatives — sulpiride, levosulpiride;
- 2.2.2. Second generation (atypical antipsychotic drugs) — amisulpiride, clozapine, olanzapine, risperidone, paliperidone, quetiapine. Aripiprazole.
- 2.3. Neurophysiological effects and APD mechanisms of action. APD pharmacokinetics. Principals of APD use. Use of depot injection medicinal forms. Side and toxic effects (influence on the CNS, vegetative functions, endocrine system).

**Write out the following drugs:** triazolam (tablets), nitrazepam (tablets), zolpidem (tablets), alprazolam (tablets), phenazepam (tablets), diazepam (tablets, solution), medazepam (tablets), chlorpromazine (solution), haloperidol (solution), flupentixol (dragee), clozapine (tablets).

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## LESSON 23. PSYCHOTROPIC DRUGS. PART II

### 1. Antidepressants (thymoleptics)

#### 1.1. Nonselective monoamine reuptake inhibitors.

##### 1.1.1. Noradrenalin and serotonin reuptake inhibitors.

- tricyclic antidepressants — imipramine, amitriptyline, doxepin, dosulepine, amoxapine.

##### 1.1.2. Other antidepressants:

- venlafaxine (inhibit serotonin and noradrenalin reuptake, without antimuscarine and sedative effects);
- reboxetine (selective noradrenalin reuptake inhibitor), duloxetine (inhibit serotonin and noradrenalin reuptake);
- agomelatine (melatonin receptors agonist and selective antagonist of serotonin);
- flupentixol (antipsychotic);
- mirtazapine (blocks presynaptic  $\alpha_2$ -adrenoreceptors in serotonergic and noradrenalinergic synapses);
- mianserine (blocks presynaptic  $\alpha_2$ -adrenoreceptors and 5HT<sub>2</sub>-serotonine receptors);
- tianeptine (strengthens neuronal serotonin reuptake);
- trazodone (weakens central amphetamine effects and peripheral noradrenaline effects, but strengthens the effects of serotonin precursor, selectively inhibits serotonin reuptake).

#### 1.2. Selective serotonin reuptake inhibitors: fluoxetine, sertraline, paroxetine.

#### 1.3. Monoamine oxidase (MAO) inhibitors:

- nonselective — phenelzine, iproclazide (with irreversible effect);
- MAO-A inhibitors — moclobemide (with reversible effect).

#### 1.4. Herbal drugs with mild antidepressant effect: hypericum (St. John's wort) herb (negrustin), hypericin.

Effects of antidepressants on monoaminergic mechanisms of neuronal transmission, receptor and postreceptor effects. Pharmacokinetics of antidepressants. Side effects induced by histamine, muscarine and  $\alpha_2$ -adrenoreceptor blocks. Use in medicine: indications and contraindications.

### 2. Psychostimulants:

- methylxanthines — caffeine;
- arylalkylamines — mesocarb, methylphenidate, amphetamine;
- eugeroic — modafinil, armodafinil, solfiamfetol, pitolisant.

### 3. Normothymic (antimanic) drugs

#### 3.1. Lithium salts — lithium carbonate, lithium oxybate, etc.

#### 3.2. Anticonvulsants — carbamazepine, sodium valproate.

#### 3.3. Antipsychotic drugs and benzodiazepines.

Pharmacokinetics and mechanisms of action of lithium salts. Use of lithium salts in medicine: indications, side effects, contraindications.

### 4. Nootropic drugs (neurometabolic stimulants, neuroprotectors)

#### 4.1. Mainly improving metabolic processes: piracetam, piritinol, meclofenoxate, cerebrolysin.

#### 4.2. Mainly improving cerebral blood flow: vinpocetine, nimodipine.

- 4.3. Activators of central cholinergic processes: donepezil hydrochloride, rivastigmine.  
 4.4. Activators of central dopaminergic processes — memantine (blocks potential-dependant NMDA-receptors).  
 4.5. Monoclonal antibody against amyloid-beta — aducanumab.

Pharmacodynamics and pharmacologic effects. Use in medicine — disorders of intellectual, mnestic and cognitive functions of different genesis: cerebral atherosclerosis, cerebral blood flow disorder, age, Alzheimer's disease, etc. Side effects and contraindications.

## 5. Tonics

### 5.1. Tonics and adaptogens:

- herbal drugs — ginseng tincture, schizandra (magnolia-vine) tincture, eleutherococ liquid extract, rhodiola liquid extract, echinopanax (devil's club) tincture;
- animal drugs — pantocrin, rantarine.

### 5.2. Cerebrospinal function stimulants — strychnine, securinine.

Molecular mechanisms of action, pharmacological effects of tonics and psychostimulants. Use in medicine: indications, side effects, restrictions.

## 6. Analeptics: almitrine, doxapram, bemegride, aethimisol, caffeine sodium benzoate.

Mechanisms of action, pharmacological effects. Use in medicine: indications, side effects, contraindications.

**Write out the following drugs:** amitriptyline (solution), fluoxetine (capsules), sertraline (tablets), tianeptine (tablets), mesocarb (tablets), methylphenidate (tablets), doxapram (solution).

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## DRUGS CONTROLLING METABOLIC AND IMMUNE DISORDERS

### LESSON 24. HORMONAL AND ANTIHORMONAL DRUGS. PART I

#### 1. Hypothalamic and pituitary (hypophysis) hormones

##### 1.1. Hypothalamic hormones and their synthetic analogues:

- sermorelin — somatorelin synthetic analogue; octreotide, lanreotide — somatostatine synthetic analogues;
- gonadorelin and its synthetic analogues: goserelin, triptorelin, buserelin;
- protirelin — synthetic analogue of thyrotropin-releasing hormone.

##### 1.2. Hormones of the anterior pituitary lobe (adenohypophysis), their synthetic analogues and antagonists:

- growth hormone — somatropin; mecasermin — human recombinant insulin-like growth factor 1 (hrIGF-1); growth hormone receptor antagonist — pegvisomant;
- corticotropins — tetracosactide;
- gonadotropins:
  - with follicle-stimulating activity — urofollitropin, follitropin alfa and beta;
  - with luteinizing activity — chorionic gonadotropin, choriogonadotropin alpha, lutropin alfa;
  - menotropins (FSH & LH, ratio 1:1).
- thyrotropic hormone — thyrotropin alfa;
- prolactin inhibitor — bromocriptin;
- gonadotropic hormone inhibitor — danazol.

1.3. Posterior pituitary lobe (neurohypophysis) hormone drugs and their synthetic analogues: oxytocin, terlipressin ( $V_1$  vasopressin receptor agonist), desmopressin ( $V_2$  vasopressin receptor agonist).

2. Pineal gland (epiphysis) hormone drugs — melatonin.

Pharmacological effects of pituitary and pineal gland hormone drugs. Use in medicine.

3. Thyroid and antithyroid hormone drugs:

3.1. Thyroid hormone drugs: sodium levothyroxine ( $T_4$ ), liothyronine ( $T_3$ ).

3.2. Antithyroid drugs:

- thioamides — thiamazole, propylthiouracil;
- iodine drugs, radioactive iodine;
- $\beta$ -adrenergic antagonists (propranolol, etc), calcium channel blockers.

Principles of action of thyroid and antithyroid drugs, indications, side effects and complications.

4. Pancreatic hormones and antidiabetic drugs

4.1. Insulin drugs

4.1.1. Human insulins:

- short-term action — ultra-short-acting (insulin lispro), short-acting — human insulin;
- average-term action: insulin-zinc suspension combined (amorphous + crystalline), insulin isophane;
- long-term action: insulin-zinc suspension (crystalline), insulin glargine.

4.1.2. Animal insulins:

- short-term action: insulin neutral for injections (monosuinsulin);
- average-term action: insulin zinc suspension combined (amorphous + crystalline), insulin zinc suspension (amorphous) (semilong), insulin isophane;
- long-term action: insulin zinc suspension (crystalline) (ultra long).

4.1.3. Biphasic insulins. Pharmacodynamics and pharmacokinetics of insulin drugs.

Comparative characteristics of different kinds of insulin drugs. Principles of use. Side effects and their prophylaxis.

4.2. Oral hypoglycemic drugs.

4.2.1. Sulfonylurea derivatives — glybenclamide, gliclazide, glipizide, gliquidone.

4.2.2. Biguanides — metformin.

4.2.3. Other drugs:

- stimulants postprandial insulin secretion — repaglinide, nateglinide;
- glucagon-like peptide-1 agonists — exenatide, liraglutide;
- dipeptidyl peptidase-4 inhibitor (increased secretion of glucose-dependent insulin only in individuals with type 2 diabetes) — sitagliptin, vildagliptin, saxagliptin;
- $\gamma$ -receptor (PPAR) agonists, activate peroxisome proliferation (increase tissue sensitivity to insulin) — pioglitazone and rosiglitazone;
- intestinal  $\alpha$ -glucosidase inhibitor — acarbose, miglitol;
- sodium glucose transporter II and type (SGLT2) inhibitors — dapagliflozin, canagliflozin.

Principles and mechanisms of action of oral hypoglycemic drugs. Indications, side effects, restrictions in their use.

4.3. Insulin antagonists: glucagon, epinephrine, glucocorticoids, diazoxide (orally in case of chronic hypoglycemia).

**Write out the following drugs:** somatropin (powder), octreotide (solution), thiamazole (tablets), sodium levothyroxine (tablets), glybenclamide (tablets), vildagliptin (tablets), metformin (tablets).

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## LESSON 25. HORMONAL AND ANTIHORMONAL DRUGS. PART II

### 1. Adrenal cortex (adrenocortical) hormone drugs

#### 1.1. Glucocorticosteroids (GCS):

- short-term action — hydrocortisone, methylprednisolone, prednisolone;
- average-term action — triamcinolone;
- long-term action — dexamethasone, betamethasone;
- glucocorticoids for local application — triamcinolone (kenalog, ftorocort); fluocinolone acetonide (synaflanum), mometasone.

#### 1.2. Mineralocorticoid drugs — deoxycortone, fludrocortisone.

#### 1.3. Corticosteroid synthesis inhibitors — aminoglutethimide.

Pharmacodynamics of corticosteroid drugs. Pharmacological effects. Principles of GCS dosage. Use in medicine. Side effects and toxicity. Indications for mineralocorticoids and aminoglutethimide use.

### 2. Female sex hormones, their analogues and antagonists

#### 2.1. Estrogen drugs:

- steroid structure — estradiol, ethinyl estradiol;
- non-steroid structure — hexestrol (synestrol), diethylstilbestrol;
- estrogen receptors selective modulators — raloxifene, clomifene, tamoxifene.

#### 2.2. Gestagen drugs: progesterone, hydroxyprogesterone, medroxyprogesterone, norethisterone, dydrogesterone. Progestine antagonist — mifepristone.

Physiological role of estrogens and gestagens, their synthesis and secretion regulation. Pharmacologic effects and pharmacodynamics of estrogen and gestagen drugs. Use in medicine.

#### 2.3. Contraceptives.

##### 2.3.1. Combined oral contraceptives:

- monophase — Cilest, Marvelon, Regulon, etc.; Diane-35;
- biphasic — Anteovin, etc.;
- triphasic — Tri-merci, Tri-regol etc.

##### 2.3.2. Containing only progestins:

- oral — norethisterone (Micronor), etc.;
- implantable, depot drugs — levonorgestrel (Norplant).

##### 2.3.3. Postcoital contraceptives — levonorgestrel (Postinor).

#### 2.4. Estrogen and progestin antagonists — tamoxifen, clomiphene, mifepristone.

Principles of action of different contraceptive groups, indications, side effects and precautions in their prescription.

### 3. Medications affecting the muscles of the uterus

#### 3.1. Uterus muscle stimulants

- Medications that stimulate rhythmic contractions of the myometrium: oxytocin and analogs (urofollitropin, carbetocin, demoxytocin), prostaglandins (dinoprost, dinoprostone, carboprost, alprostadil), antigestagens (mifepristone);
- Medications that stimulate tonic contractions of the myometrium: methylergometrine.

#### 3.2. Medications relaxing the muscles of the uterus

- Medications that reduce the contractile activity of the myometrium:  $\beta_2$ -adrenergic agents (hexoprenaline, phenoterol, terbutaline, ritodrin, salmeterol, salbutamol); gestagens (hydroxyprogesterone caproate, dydrogesterone, chorionic gonadotropin);  $\text{Ca}^{2+}$  channel blockers (nifedipine); oxytocin receptor antagonists (atosiban); magnesium sulfate.

- Means that lower the tone of the cervix: M-anticholinergics (atropine), antispasmodics of myotropic action (drotaverine).

The mechanisms of action of agents affecting the myometrium. The use of drugs that affect the myometrium (induction and stimulation of labor, stopping uterine bleeding, preventing premature birth). Complications arising from the use of drugs that affect the myometrium and their prevention.

#### 4. Male sex hormones and their derivatives

- 4.1. Androgen drugs — testosterone and its aethers, methyltestosterone, mesterolone.
- 4.2. Anabolic steroids — nandrolone (retabolil), etc.
- 4.3. Antiandrogen drugs — flutamide.

Principles of action. Indications, dangerous and side effects.

#### 5. Hormonal regulators of mineral homeostasis and other drugs, influencing on bone tissue metabolism.

- 5.1. Parathyroid hormones — teriparatide (parathyroid hormone recombinant fragment).
- 5.2. Antiparathyroid hormones — calcitonin, paricalcitol.
- 5.3. Bisphosphonates — alendronic acid, risedronic acid, zoledronic acid.
- 5.4. Vitamin D and analogues — alfacalcidol.

Principles of pharmacologic management of bone tissue metabolism, the role of parathyroid regulation. Mechanisms of action of bisphosphonates, indications and restrictions.

**Write out the following drugs:** methylprednisolone (tablets), dexamethasone (tablets), fludrocortisone (tablets, ophthalmic ointment), estradiol (tablets), progesterone (solution), norethisterone (tablets), testosterone (solution), nandrolone (solution), cyproterone acetate (tablets, solution), alendronic acid (tablets), calcitonin (solution, nasal spray), paricalcitol (solution).

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This prescription is valid for 30 days <div style="text-align: right;">* leaflet of yellow color</div>		

<b>PRESCRIPTION</b>		<b>АБ №</b> «__» ____ 20__ (the date of prescription)
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## LESSON 26. ANTI-INFLAMMATORY AND ANTI-GOUT DRUGS

### 1. Anti-inflammatory drugs

#### 1.1. Non-steroidal anti-inflammatory drugs (NSAIDs).

##### 1.1.1. Nonselective cyclooxygenase (COX) inhibitors:

- salicylic acid derivatives — acetylsalicylic acid (in small doses is a nonselective COX-1 inhibitor), diflunisal;
- anthranilic acid derivatives (fenamates) — mefenamic acid;
- arylacetic acid derivatives: diclofenac, aceclofenac;
- arylpropionic acid derivatives: ibuprofen, naproxen;
- indoleacetic derivatives: indomethacin, sulindac;
- pyrazolidinedione derivatives — phenylbutazone;
- oxicams — piroxicam.

##### 1.1.2. Selective COX-2 inhibitors:

- relatively selective COX-2 inhibitors: meloxicam, nimesulide, nabumetone (prodrug);
- highly selective COX-2 inhibitors: celecoxib, valdecoxib.

##### 1.1.3. Combined drugs — Arthrotec (diclofenac + misoprostol).

##### 1.1.4. Pharmacological effects of NSAIDs. Mechanisms of anti-inflammatory effect — the effect on the mediators and inflammatory cells, including:

- synthesis of prostaglandins (COX-1 and COX-2), monoamines (histamine, serotonin), kinins, acid mucopolysaccharides, proliferation of fibroblasts;

- activity of NF- $\kappa$ B nuclear transcription factor (regulates the synthesis of anti-inflammatory cytokines);
- cartilage metabolism.

1.1.5. Indications for use of NSAIDs, side effects (effects on the gastrointestinal tract, kidneys, central nervous system, bronchi, Reye's syndrome in children), preventive measures.

## 1.2. Steroidal anti-inflammatory drugs — glucocorticosteroids (GCS).

### 1.2.1. Systemic glucocorticosteroids:

- short-term action: prednisolone, methylprednisolone;
- average-term action: triamcinolone;
- long-term action: dexamethasone, betamethasone;

1.2.2. Glucocorticosteroids for intra-articular injections — soluble salts of hydrocortisone, methylprednisolone, prednisolone, dexamethasone.

### 1.2.3. Pharmacological effects of GSC. Mechanisms of anti-inflammatory action:

- influence on the synthesis of prostaglandins and leukotrienes;
- regulation of the activity of genes coding the synthesis of anti-inflammatory cytokines (IL-1 and IL-6, TNF- $\alpha$  and GM-CSF, etc.) and metalloproteinases;
- modulating effect on the release of endothelin, the synthesis of hyaluronic acid, the induction of NO synthase.

1.2.4. Indications and contraindications for use. Basic injections schemes, side effects and the measures to prevent them:

## 1.3. Development areas of anti-inflammatory drugs that control the progression of systemic connective tissue diseases:

- monoclonal antibodies against membrane antigens of immunocompetent cells and inflammatory cytokines;
- soluble cytokine receptors and cytokine release inhibitors;
- anti-inflammatory cytokines;
- drugs inhibiting the generation of reactive oxygen and nitrogen species.

## 2. Anti-gout drugs

### 2.1. Drugs for relief of acute gout attacks:

- colchicine, NSAIDs — indometacin, naproxen, diclofenac, etc.
- GSC — prednisolone, methylprednisolone, etc.

### 2.2. Drugs for the treatment of gout:

- uric acid synthesis inhibitors — allopurinol, febuxostat;
- uricosuric drugs — sulfinpyrazone, probenecid, aethamidum;
- mixed type — urodanum.

Definition, classification, mechanism of action, indications and contraindications to the use and side effects of anti-gout drugs.

**Write out the following drugs:** prednisolone (ointment), arthrotec (tablets), allopurinol (tablets), sulfinpyrazone (tablets).

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## LESSON 27. ANTIALLERGIC AND IMMUNOMODULATING DRUGS

### 1. Drugs used for allergic reaction of immediate type (immediate type hypersensitivity)

#### 1.1. Glucocorticosteroids (GCS):

##### 1.1.1. Systemic GCS:

- short-term action: hydrocortisone, methylprednisolone, prednisolone;
- average-term action: triamcinolone;
- long-term action: dexamethasone, betamethasone.

##### 1.1.2. Glucocorticoids for local application: fluticasone, beclomethasone, budesonide, mometasone, fluocinolone acetonide.

Mechanisms of antiallergic action, influence on mediators and allergy cells:

- processes of prostaglandins and leukotrienes synthesis;
- FC-receptors on the surface of cells, basophils, macrophages and other mesenchymal cellular elements;
- activity of components of complement system (C3-C8);
- T- and B-lymphocyte cooperation, leucocyte migrations.

Indications and contraindications.

#### 1.2. Antagonists of leukotriene receptors: zafirlukast, montelukast.

#### 1.3. Mast cell membrane stabilizers: chromoglycic acid, nedocromil, ketotifen.

#### 1.4. Antihistamine drugs:

##### 1.4.1. Histamine H<sub>1</sub>-receptors antagonists:

- first generation: diphenhydramine, promethazine, clemastine, quifenadine;

- second generation: loratadine, desloratadine, fexofenadine, cetirizine;
- histamine H<sub>1</sub>-receptors antagonists with antiserotonin activity — cyproheptadine.

#### 1.4.2. Allergy mediator activity inhibitors — fenspiride.

Pharmacodynamics of antihistamine drugs. Comparative characteristics. Use in medicine, side effects.

1.5. Antiallergic effect of theophylline drugs (aminophylline, teotard, euphyllong) and adrenomimetics (epinephrine, ephedrine, salbutamol), their administration.

1.6. Drugs used for anaphylactic shock: epinephrine, salbutamol, GCS, dopamine, antihistamine drugs.

2. Drugs used for allergic reactions of delayed type (delayed type hypersensitivity) — autoimmune processes, tissue incompatibility

2.1. Disease-modifying antirheumatic drugs — DMARDs (slow effect):

- gold salts — auranofin;
- penicillamine;
- aminoquinolines — chloroquine;
- sulphasalazine.

2.2. Immunosuppressants:

- GCS;
- cytotoxic drugs: azathioprine, methotrexate, leflunomide, cyclophosphamide;
- drugs, inhibiting interleukin-2 expression or action: cyclosporine, tacrolimus, sirolimus;
- polyclonal antibodies drugs: antilymphocyte immunoglobulins;
- monoclonal antibodies drugs: basiliximab, daclizumab — interleukin-2 receptor antagonists.

2.3. Non-steroidal anti-inflammatory drugs (see Lesson 9).

Pharmacodynamics, main pharmacological effects of DMARDs and immunosuppressants. Their use. Side and toxic effects.

3. Immunomodulators

3.1. Exogenous:

- microbial — IRS-19, broncho-munal, ribomunil;
- herbal — echinacea drugs (Immunal); Belarussian combined herbal drugs — Ehingin, Trimunal.

3.2. Exogenous immunoregulatory peptides:

- thymic peptide drugs: thymalin, tactivin;
- cytokines: betaleukine, aldesleukin;
- interferons: gamma interferon, thiloron (interferonogen);
- immunoglobulin drugs — normal human immunoglobulin.

3.3. Synthetic immunomodulators: thymogen, inosine, pranobex.

Mechanisms of immunomodulator action (influence on the monocyte-macrophage system cells, T- and B-lymphocytes, cytokine synthesis, antibody formation, use in medicine, side effects and precautions.

**Write out the following drugs:** diphenhydramine (suppositories, solution), promethazine (solution), prednisolone (tablets), penicillamine (capsules), methotrexate (coated tablets), thymogen (solution), tilorone (tablets).

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# CHEMOTHERAPEUTIC DRUGS

## LESSONS 28, 29. ANTIMICROBIAL DRUGS. ANTIBIOTICS

1. General issues of chemotherapy of infections
  - 1.1. Definition of chemotherapeutic drugs, their general characteristics, classification.
  - 1.2. History of discovery and use of antimicrobial drugs. Antibiotics. Biological significance of antibiosis (works by D. Romanovsky, P. Erlich, G. Domagk, A. Fleming, G. Flory, E. Chain, Z. Yermolyeva, S. Waxman). Role of antibiotics in medicine and biology.
  - 1.3. Basic definitions of chemotherapy of infections:
    - empirical (probable) antimicrobial therapy, combined antimicrobial therapy, antimicrobial chemoprophylaxis;
    - antibiotic, probiotic (eubiotic);
    - bactericidal / bacteriostatic effect;
    - first-line (drugs of choice) and second-line drugs;
    - minimal inhibitory concentration, minimal bactericidal concentration;
    - postantibiotic effect;
    - sensitivity/resistance of infectious agents;
    - nosocomial infection, superinfection, mixed infection, dysbacteriosis.
  - 1.4. Characteristic differences between chemotherapeutic drugs and pharmacological drugs of other pharmacotherapeutic groups.
  - 1.5. Modern sources of obtaining and prospective trends of antimicrobial drugs development.
  - 1.6. Criteria and principles of rational chemotherapy of infections.
  - 1.7. Clinical and microbiological indications for determining the infectious agent sensitivity to antibiotics.
  - 1.8. Principles of combined antibiotic therapy. Rational combinations of antimicrobial drugs.
  - 1.9. Critical analysis of reasons for inefficient antimicrobial therapy.
  - 1.10. The concept of the properties of an «ideal» antimicrobial drug as criteria for selection of new antimicrobial drugs.
  - 1.11. Principles of antibiotic classification.
  - 1.12. Basic mechanisms of antibiotic action.
  - 1.13. Side effects and complications of antibiotic therapy, their prevention and treatment.
  - 1.14. Resistance of microorganisms to antibiotics; mechanisms and ways to decrease it.
2. Antibiotics inhibiting the synthesis of bacterial cellular wall (bactericidal)
  - 2.1.  $\beta$ -LACTAM:
    - 2.1.1. Penicillins:
      - biosynthetic penicillins: for parenteral administration — benzylpenicillin (sodium and potassium salts), benzylpenicillin procaine, benzathine benzylpenicillin (Bicillin-1); for oral administration — phenoxymethylpenicillin (Penicillin V);
      - isoxazolympenicillins (antistaphylococcal penicillins resistant to  $\beta$ -lactamases): flucloxacillin, cloxacillin, oxacillin;

- aminopenicillins (broad spectrum): amoxicillin, ampicillin, co-amoxiclav;
- carboxypenicillins (antipseudomonal): ticarcillin+clavulanic acid;
- ureidopenicillins (antipseudomonal): piperacillin+tazobactam;
- mecillanams (active to gram-negative (G-) flora, inefficient against pseudomonads); pivmecillinam.

2.1.2. Cephalosporins and cephamycins — classification by antimicrobial spectrum, resistance to  $\beta$ -lactamases and routes of administration (parenteral / oral administration):

- *1<sup>st</sup> generation* — relatively narrow spectrum, highly effective against G+ bacteria and cocci (except enterococci, methicillin resistant staphylococci (MRSA)), considerably less active against G- flora (escherichia coli, klebsiella pneumoniae, indole negative proteus): cephradine, cefazolin / *cephalexin*, *cephradine*, *cefadroxil*.
- *2<sup>nd</sup> generation* — broad spectrum, more active against G- flora (hemophilic bacillus, neisserias, enterobacterias, indol-positive proteus, klebsiella, moraxella, serratia), resistant to  $\beta$ -lactamases: cefuroxime, cefoxitin (cephamycin) / *cefactor*, *cefuroxime axetil*.
- *3<sup>rd</sup> generation* — broad spectrum, highly effective against G- flora, including that producing  $\beta$ -lactamases; active against pseudomonads, acinetobacter, citrobacter; penetrating the CNS: cefotaxime, ceftazidime, ceftriaxone / *cefixime*, *cefpodoxime*.
- *4<sup>th</sup> generation* — broad spectrum, highly effective against bacteroids and other anaerobic bacteria; highly resistant to broad spectrum  $\beta$ -lactamases; in terms of their efficacy against G- flora are equal to the 3<sup>rd</sup> generation of cephalosporins; in terms of their efficacy against G+ flora are less efficient than the 1<sup>st</sup> generation of cephalosporins: cefepime, cefpirome / —.
- Combined drugs of cephalosporins with  $\beta$ -lactamase inhibitors: Sulperazon (cefoperazone + sulbactam).

2.1.3. Carbapenems: imipenem, meropenem, ertapenem (ultrabroad spectrum).

2.1.4. *Other cephalosporins and penems* — ceftobiprole, ceftaroline fosamil.

2.1.5. Monobactams: aztreonam (active against G- bacteria).

2.2. GLYCOPEPTIDES: vancomycin, teicoplanin (active against G+ bacteria).

2.3. Cycloserine (antituberculous antibiotic).

3. Antibiotics that interfere with plasma membrane structure (bactericidal).

3.1. POLYPEPTIDES: polymyxin B, colistin.

3.2. POLYENES: nystatin, amphotericin B.

4. Antibiotics inhibiting RNA synthesis (bactericidal).

4.1. ANSAMYCINS: rifampicin, rifabutin.

4.2. Griseofulvin (fungistatic).

5. Antibiotics inhibiting protein synthesis (bacteriostatic).

5.1. AMINOGLYCOSIDES — bactericidal (exception):

- 1<sup>st</sup> generation — streptomycin, neomycin;
- 2<sup>nd</sup> generation — gentamicin;
- 3<sup>rd</sup> generation — amikacin, tobramycin;
- other aminoglycosides — netilmicin.



## 5.2. TETRACYCLINES:

- biosynthetic: tetracycline, oxytetracycline;
- semisynthetic: doxycycline, lymecycline, tigecycline, minocycline.

## 5.3. MACROLIDES AND AZALIDES:

- 14-membered: erythromycin, clarithromycin, telithromycin;
- 15-membered (azalides): azithromycin;
- 16-membered: spiramycin.

## 5.4. AMPHENICOLS — chloramphenicol (levomycetin).

## 5.5. LINCOSAMIDES: clindamycin, lincomycin.

## 5.6. STEROIDAL ANTIBIOTICS — fusidic acid (Fusidin).

## 5.7. OXAZOLIDINONES — linezolid (G- flora + MRSA + vancomycin- resistant enterococci).

## 5.8. STREPTOGRAMINS — quinupristin / dalfopristin.

## 5.9. Some other antibacterial agents: daptomycin, rifaximin, fidaxomicin, spectinomycin.

The characteristic of each group of antibiotics should include:

- classification of the drugs of this group;
- characteristics of the antimicrobial effect (bactericidal / bacteriostatic), targets and mechanisms of action;
- general characteristic of the antimicrobial spectrum;
- peculiarities of pharmacokinetics, route of administration, medicinal forms;
- main indications for clinical use;
- side and toxic effects, ways of their prevention and treatment.

## LESSON 28 — questions 1–2.

**Write out the following drugs:** benzylpenicillin (bottles), benzathine benzylpenicillin (bottles), amoxicillin (tablets, capsules, oral suspension), phenoxymethylpenicillin (tablets), piperacillin (bottles), cephalexin (capsules, oral suspension), cefuroxime (bottles), cefaclor (powder for oral suspension), ceftazidime (bottles), cefotaxime (bottles), cefepime (bottles), imipenem (bottles), doripenem (bottles), vancomycin (capsules).

## LESSON 29 — questions 3–5.

**Write out the following drugs:** doxycycline (coated tablets, powder for injections), gentamicin (ointment, solution), amikacin (solution, gel), chloramphenicol (eye drops), clarithromycin (powder for suspension), azithromycin (syrup), clindamycin (syrup), colistin (powder for inhalations), nystatin (suppositories), rifampicin (capsules, solution).

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## LESSON 30. SYNTHETIC ANTIMICROBIAL DRUGS

### 1. Sulfonamide drugs (sulfonamides) and trimethoprim

#### 1.1. The history of sulfonamide therapy discovery and development.

#### 1.2. Classification based on location and duration:

##### 1.2.1. Systemic sulfonamides:

- short-term action ( $T_{1/2} < 10$  hours): sulfanilamide (streptocide), sulfadimidine (sulfadimezinum);
- average-term action ( $T_{1/2} — 10–24$  hours) — sulfadiazine;
- long-term action ( $T_{1/2} — 24–48$  hours and longer): sulfamethoxypyridazine, sulfadimethoxine, sulfadoxine (in combination with pyrimethamine is a drug of choice in the treatment of malaria caused by *Plasmodium falciparum*, resistant to chloroquine), sulfalene.
- combination of sulfanilamides with trimethoprim — co-trimoxazole (Bactrim, Biseptol, Sumetrolim — trimethoprim + sulfamethoxazole), etc. Mechanisms to increase antimicrobial activity and antimicrobial spectrum expansion.

##### 1.2.2. Sulfonamides, acting in the lumen of the intestine: phthalylsulfathiazole (phthalazol), phthalylsulfapyridazine (phthazin); salazosulfanilamides — sulfasalazine, etc.

##### 1.2.3. Sulfonamides for local application: sulfacetamide, silver sulfadiazine, mafenide.

### 2. Oxyquinolines: nitroxoline, chlorquinaldol.

### 3. Nitrofurans: nitrofurantoin, furazolidone, furagin.

### 4. Quinolones: nalidixic acid, oxolinic acid, pipemidic acid.

### 5. Fluoroquinolones: ciprofloxacin, ofloxacin, norfloxacin, sparfloxacin, levofloxacin, moxifloxacin, gatifloxacin etc.

### 6. Nitroimidazoles: metronidazole, tinidazole.

### 7. Methenamine.

Pharmacodynamics and pharmacokinetics of synthetic antimicrobial drugs. The antimicrobial spectrum. Indications for use, side and toxic effects and their prevention. Contraindications. Features of urinary antiseptics.

**Write out the following drugs:** sulfacetamide (ointment), co-trimoxazole (oral suspension, tablets), nitrofurantoin tablets), pipemidic acid (suppositories), levofloxacin (tablets), ciprofloxacin (coated tablets), moxifloxacin (tablets), metronidazole (tablets, solution).

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## LESSON 31. ANTIMYCOBACTERIAL AND ANTIFUNGAL DRUGS

### 1. Antimycobacterial drugs

#### 1.1. Antituberculosis drugs.

1.1.1. First drugs: isoniazid, rifampicin, ethambutol, pyrazinamide, streptomycin.

1.1.2. Reserve drugs: bedaquiline, delamanid, capreomycin, kanamycin, amikacin; ethionamide, prothionamide; cycloserine, fluoroquinolones; azithromycin, clarithromycin; rifabutin; thioacetazone; clofazimine; PAS (para-aminosalicylic acid).

#### 1.2. Antileprotic drugs: dapsone, clofazimine, rifampicin.

The principles of tuberculosis pharmacotherapy. The mechanisms of action of antituberculosis drugs, side effects and their prevention. The concept of hemoprophylaxis of tuberculosis.

### 2. Antifungal (antimycotic) drugs

#### 2.1. Destroying the cell wall of the fungus.

2.1.1. Polyene antibiotics: amphotericin B, nystatin, natamycin, mycoheptin.

#### 2.1.2. Azoles:

- imidazole derivatives for local and system application: ketoconazole, miconazole; for local application: clotrimazole, econazole, tioconazole, etc.;
- triazole derivatives: fluconazole, itraconazole, posaconazole, voriconazole, isavuconazole.

2.1.3. Allylamines — terbinafine.

2.1.4. Morpholines — amorolfine (for local application only).

#### 2.2. Inhibiting fungal cell mitosis — griseofulvin (an antibiotic).

#### 2.3. Inhibiting the synthesis of DNA — flucytosine.

Pharmacodynamics and the spectrum of antifungal activity. Pharmacokinetics (for the drugs of systemic application), medicinal forms. Side effects, toxicity.

**Write out the following drugs:** isoniazid (tablets, solution), rifampicin (capsules, solution), streptomycin (bottles), ethambutol (tablets, capsules), amphotericin B (powder, ointment), griseofulvin (suspension, liniment), terbinafine (cream, gel, tablets), itraconazole (soluiotn).

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## LESSON 32. ANTIPROTOZOAL AND ANTIVIRAL DRUGS

### 2.4. Antiprotozoal drugs.

#### 2.4.1. Antimalarial drugs.

2.4.2. Hematoshizotropic drugs (affecting erythrocyte schizonts): chloroquine, mefloquine, quinine, artesunate (i/v), artemether (i/m), artenser + lumefantrine (Riamet), pyrimethamine, pyrimethamine + sulfadoxine (Fansidar).

#### 2.4.3. Histoshizotropic drugs:

- affecting pre-erythrocytic (primary tissue) forms: pyrimethamine, proguanil, proguanil + atovaquone (Maloron);
- affecting exoerythrocytic (secondary tissue) forms — primaquine.

#### 2.4.4. Gamontotropic drugs (affect sexual forms):

- gamontocide — primaquine;
- gamontostatic — pyrimethamine (sporontocide action).

#### 2.4.5. Doxycycline, clindamycin. Features of use in the treatment of malaria.

The principles of chemotherapy of malaria, the concept of individual and social malaria chemoprophylaxis. The principles of action of antimalarial drugs, side and toxic effects.

### 2.5. Drugs for the treatment of amoebiasis.

2.5.1. At any location of amoebas: metronidazole, tinidazole.

2.5.2. At intestinal location of amoebas:

- direct action (effective in case of the localization of amoebas in the lumen of the intestine) — diloxanide, chiniofon;
- indirect action (effective in case of the localization of amoebas in the lumen and the wall of the intestine) — doxycycline.

#### 2.5.3. Drugs affecting the tissue forms of amoebas:

- in case of the localization of amoebas in the wall of the intestine and liver — emetine;
- in case of the localization of amoebas in the liver — chloroquine.

The principles of chemotherapy of amoebiasis.

#### 2.6. Drugs for the treatment of trichomoniasis:

- for oral application — tinidazole;
- for oral and intravaginal application: metronidazole, trichomonacid, furazolidone;
- for intravaginal application: povidone-iodine, policresulen.

The principles of chemotherapy of trichomoniasis.

#### 2.7. Drugs for the treatment of giardiasis: metronidazole, tinidazole, mepacrine, furazolidone.

#### 2.8. Drugs for the treatment of toxoplasmosis: pyrimethamine combined with sulfonamides (sulfadiazine or sulfadimidine) and combined with antibiotics (clindamycin, clarithromycin, azithromycin).

#### 2.9. Drugs for the treatment of leishmaniasis:

- for the treatment of visceral and cutaneous leishmaniasis: sodium stibogluconate, amphotericin B, pentamidine isethionate;
- for the treatment of cutaneous leishmaniasis: mepacrine, monomycin.

#### 2.10. Drugs for the treatment of pneumocystosis: co-trimoxazole, pentamidine isethionate (inhaled), atovaquone, dapsone + trimethoprim, clindamycin + primaquine.

### 2. Antiviral drugs.

#### 2.1. Inhibitors of adsorption, penetration and deproteinization (stripping) of viruses.

##### 2.1.1. Gamma globulins against measles, hepatitis B, rabies, and cytomegalovirus infection.

##### 2.1.2. Anti-influenza drugs:

- aminoadamantanes — rimantadine (remantadine);
- neuraminidase inhibitors — oseltamivir, zanamivir.

#### 2.2. Inhibitors of intracellular synthesis of viral components.

##### • Inhibitors of nucleic acid synthesis.

##### 2.2.1. Antiherpetic drugs:

- nucleoside analogues: acyclovir, famciclovir, valacyclovir; penciclovir, idoxuridine;
- phosphonoformic acid derivative — foscarnet.

##### 2.2.2. Drugs for the treatment of HIV infection:

- attachment and fusion inhibitors: enfuvirtide — inhibitor of fusion (the process of tightening of the virus particles to the lymphocytes), inhibitors of CC5 (chemokine) receptor — maraviroc;
- reverse transcriptase inhibitors (nucleoside analogues): zidovudine, emtricitabine, lamivudine, didanosine, abacavir, tenofovir;

- reverse transcriptase inhibitors of a non-nucleoside structure: nevirapine, efavirenz, etravirine, rilpivirine;
- integrase inhibitors: raltegravir, dolutegravir, elvitegravir;
- protease inhibitors (PI): saquinavir, fosamprenavir, tipranavir, darunavir;
- pharmacokinetic boosters (PI enhancers): ritonavir, cobicistat;
- combined formulations: cobicistat + elvitegravir + emtricitabine; tenofovir + emtricitabine + efavirenz or rilpivirine etc.

#### 2.2.3. Antiviral drugs for cytomegalovirus:

- nucleoside analogues — ganciclovir, valganciclovir;
- phosphonoformic acid derivative — foscarnet;
- cidofovir (for the treatment of CMV retinitis in patients with AIDS).

#### 2.2.4. Drugs used in respiratory syncytial infection:

- ribavirin (ribofuranosyl-triazole-carboxamide);
- palivizumab (monoclonal antibodies for the prevention of respiratory syncytial infections in children at high risk of disease).

### 2.3. Inhibitors of RNA and late viral proteins synthesis:

- interferons — low-molecular-weight glycoproteins: interferon alpha, interferon alpha-2a, interferon alpha-2b — monocytic, interferon beta (fibroblastic), interferon gamma-1b (T-lymphocytic);
- interferonogens: tilorone, arbidol;
- inhibitors of the late viral proteins synthesis — thiosemicarbazone derivatives — metisazon (for the prevention and treatment of smallpox (variola)).

### 2.4. Inhibitors of virus self-assemblance — rifampicin.

### 2.5. Virucidal drugs for local application: oxoline, tebprofen, butaminofen (Belarusian), bonafton (used topically and orally).

### 2.6. Agents for treatment of chronic hepatitis B: peginterferon alfa or interferon alfa (in some cases, peginterferon alfa-2a), entecavir or tenofovir, adefovir dipivoxil, lamivudine or telbivudine.

### 2.7. Agents for treatment of chronic hepatitis C: ribavirin + peginterferon alfa, boceprevir or telaprevir (genotype 1) or sofosbuvir (genotype 1–5 or 6) in combination with ribavirin and peginterferon alfa necessarily; simeprevir, daclatasvir.

### 2.8. Other antiviral agents: remdesivir (an inhibitor of RNA-dependent RNA polymerase treatment of smallpox in humans).

Features of a virus as the pharmacodynamic target. Problems of viral infections pharmacotherapy. The mechanisms of action of antiviral drugs. The characteristics of drugs for the treatment of influenza, cytomegalovirus, respiratory syncytial and herpetic infection, HIV infection. Pharmacodynamics of interferons and interferonogens. Medicinal forms, the principles of antiviral drugs use.

**Write out the following drugs:** chloroquine (tablets, solution), mefloquine (tablets), metronidazole (tablets, suppositories, solution), tinidazole (tablets), rimantadine (tablets), acyclovir (bottles, tablets), zidovudine (capsules), tenofovir (coated tablets), nevirapine (tablets, suspension), raltegravir (tablets), darunavir (coated tablets), enfuvirtide (bottles).

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## TOPICS FOR INDIVIDUAL STUDY. ANTISEPTICS AND DISINFECTANTS. ANTICANCER DRUGS

### ANTHELMINTIC AGENTS

Classification of antihelminthic drugs

1. Antinematodal agents — mebendazole, albendazole, thiabendazole, levamisole, pyrantel, piperazine, ivermectin, diethylcarbamazine.
2. Anticestodals and antitrepatodals — praziquantel, niclosamide.
3. Drugs used in extra-intestinal helminths — chloxylum, diethylcarbamazine.
4. The mechanisms of damaging effect at helminths. Principles of chemotherapy of parasitic infestations. A therapeutic target of anthelmintics. Pharmacokinetics, pharmacodynamics and side effects of anthelmintic drugs.

### ECTOPARASITICIDES

1. Permethrin.
2. Lindane (Gamma benzene hexachloride).
3. Benzyl benzoate.
4. Crotamiton.
5. Sulfur.
6. Dicophane (DDT).
7. Ivermectin.

### ANTICANCER (ANTIBLASTOMIC) DRUGS

1. Cytotoxic drugs.
  - 1.1. Alkylating drugs: cyclophosphamide, carmustine, melphalan; platinum drugs — cisplatin, carboplatin, oxaliplatin.
  - 1.2. Antimetabolites: methotrexate, mercaptopurine, fluorouracil, cytarabine, capecitabine.
  - 1.3. Drugs that arrests mitosis (herbal alkaloids): vincristine, vinblastine, paclitaxel, docetaxel, etoposide, irinotecan.
  - 1.4. Antibiotics: doxorubicin, bleomycin, mitomycin.
2. Hormones and their antagonists: tamoxifen, letrozole, anastrozole, cyproterone acetate, flutamide, finasteride, goserelin, aminoglutethimide.
3. Enzymes — L-asparaginase.
4. Cytokines — IL-2 (aldesleukin).
5. Monoclonal antibodies: trastuzumab, rituximab, bevacizumab etc.
6. Tyrosine kinase inhibitor: imatinib.
7. The principles of chemotherapy of malignant neoplastic diseases.
8. Mechanisms of action of anticancer drugs.
9. Features of the spectrum of anticancer action of alkylating drugs, antimetabolites, platinum drugs, antibiotics, hormones and antagonists of hormones, enzymes.
10. Complications arising from the use of anticancer drugs, their prevention and treatment.

### ANTISEPTICS AND DISINFECTANTS

1. The concept of antisepsis (antiseptic) and disinfection. The differences of antiseptics from other antibacterial drugs. Requirements for antiseptics.
2. Classification of antiseptics according to their chemical structure.
  - 2.1. Antiseptic of aromatic series:
    - phenol derivatives, phenol, resorcinol (resorcin), birch tar, biklotimol;
    - nitrofurane derivatives — nitrofurazone;

- dyes: brilliant green, methylthioninium chloride;
  - biguanides — chlorhexidine.
- 2.2. Antiseptics of aliphatic series:
    - aldehydes: formaldehyde, glutaraldehyde;
    - alcohols: ethyl alcohol, isopropyl alcohol;
    - detergents: cetylpyridinium chloride, benzalkonium chloride, miramistin.
  - 2.3. Acids and bases: boric acid, ammonia drugs.
  - 2.4. Oxidizers: hydrogen peroxide, potassium permanganate.
  - 2.5. Polyguanidines: biopag, phosphag, ecopag.
  - 2.6. Metal compounds — silver proteinate (protargol), silver sulfadiazine, zinc sulfate, zinc oxide.
  - 2.7. Other antiseptics: hexetidine (faringosept) ambazone.
  - 2.8. Preparations of vegetable origin: leaves cranberries and bearberry, marigold flowers, chamomile flowers, herb hypericum, hlorofillipt, salvini.
3. The conditions determining the antimicrobial activity of antiseptics, the mechanisms of action of antiseptics of different chemical groups.
  4. Features of the use of certain antiseptics. The principles of the treatment of acute poisonings with antiseptics.

### LESSON 33. FINAL LESSON ON CHEMOTHERAPEUTIC DRUGS

**Objective:** To systematize and consolidate the knowledge of pharmacological properties, indications, principles of use of chemotherapeutic drugs. Consolidate the skills of writing prescriptions for basic chemotherapeutic drugs.

When preparing for the final class on chemotherapeutic drugs it is recommended to review the material of the following lessons:

- Antimicrobial drugs. Antibiotics.
- Synthetic antimicrobial drugs.
- Antimycobacterial and antifungal drugs.
- Antiprotozoal and antiviral drugs.

**Be able to write out in various medicinal forms:** co-trimoxazole, nitrofurantoin, ofloxacin, ciprofloxacin, metronidazole, benzylpenicillin procaine, cephazolin, cefaclor, ceftazidime, cefepime, imipenem, vancomycin, doxycycline, gentamicin, amikacin, chloramphenicol, clarithromycin, azithromycin, clindamycin, isoniazid, rifampicin, streptomycin, ethambutol, chloroquine, griseofulvin, terbinafine, itraconazole, rimantadine, acyclovir, zidovudine, nevirapine, raltegravir, enfuvirtide.

#### Questions for individual study:

1. Definition of chemotherapeutic drugs.
2. Difference of chemotherapeutic drugs from antiseptics and disinfectants.
3. Essence of concepts: empirical (probable) antimicrobial therapy, combined antimicrobial therapy, antimicrobial chemoprophylaxis; antibiotic, probiotic (eubiotic); bactericidal and bacteriostatic effect; first-line (drugs of choice) and second-line drugs; minimal inhibitory concentration and minimal bactericidal concentration; sensitivity and resistance of infectious agents, postantibiotic effect.
4. Determinants of selective toxicity of chemotherapeutic drugs.
5. Essence of differences of pharmacodynamic and chemotherapeutic action.
6. Principles of a rational chemotherapy of infections.

7. Indications for the combined antibiotic therapy.
8. Principles of the combined antibiotic therapy.
9. Principles of classification of antibiotics.
10. The basic mechanisms of antibiotic action.
11. Name the side effects of antibiotics caused by their allergic action.
12. Name the side effects and the complications of an antibiotic therapy connected with their pharmacodynamic action.
13. Name the side effects and the complications of an antibiotic therapy connected with their chemotherapeutic action.
14. Mechanisms of development of a resistance of microorganisms to antibiotics.
15. Ways to decrease a resistance of microorganisms to antibiotics.
16. The reasons of an inefficiency of antimicrobial therapy.
17. Name the groups of the antibiotics inhibiting the synthesis of bacterial cellular wall, antibiotics that interfere with plasma membrane structure; inhibiting RNA synthesis; inhibiting protein synthesis; with bactericidal action on based microbial cells; with bactericidal action on sharing microbial cells; bacteriostatic antibiotics;  $\beta$ -lactam antibiotics.
18. Classification of penicillins.
19. Classification of cephalosporins.
20. Name the basic antibiotics of monobactams and carbapenems; glycopeptides and polypeptides; ansamycins and amphenicols; aminoglycosides; tetracyclines and lincosamides; macrolides and azalides.
21. Name the antifungal antibiotics.
22. Specify the accessory to group, an antimicrobial spectrum, resistance to  $\beta$ -lactamases and a route of administration of the following antibiotics:
  - cephalazolin, cephalexin, cephradine;
  - cefuroxime, cefoxitin, cefuroxime axetil, cefaclor;
  - cefotaxime, ceftazidime, cefixime, ceftriaxone;
  - cefepime, cefpirome.
23. Specify the accessory to group, features of distribution, an antimicrobial spectrum and side effects of fusidic acid.
24. Specify the accessory to group, an antimicrobial spectrum of cycloserine.
25. Name the first-line drugs for the treatment of the infections caused by methicillin resistant staphylococci.
26. Name the groups of chemotherapeutic drugs active against intracellular microorganisms.
27. Name the basic chemotherapeutic drugs active against anaerobes.
28. Name the chemotherapeutic drugs with high antipseudomonal activity.
29. Indications for tetracyclines; chloramphenicol; streptomycin; carbapenems.
30. The characteristic of imipenem and meropenem on an antimicrobial spectrum, resistance to  $\beta$ -lactamases and dehydropeptidase 1.
31. The side effects of penicillins; cephalosporins; carbapenems; aminoglycosides; tetracyclines; chloramphenicol; macrolides.
32. Name the groups of synthetic antimicrobial drugs.
33. The classification of sulfonamides on duration of action.
34. Name the sulfonamides acting in the lumen of the intestine.
35. Name the sulfonamides for local application.
36. The features of therapeutic action of sulfonamides combined with salicylic acid.
37. Indications for sulfasalazine.

38. The mechanism of the antimicrobial action of sulfonamides.
39. An antibacterial spectrum of sulfonamides.
40. The mechanism of the antimicrobial action of trimethoprim.
41. How chemotherapeutic properties of sulfonamides will change at their combination with trimethoprim and why?
42. Name the sulfonamides the most dangerous concerning crystalluria.
43. The complications of therapy by sulfonamides.
44. Why do local anesthetics decrease bacteriostatic action of sulfonamides?
45. The precautions for therapy by sulfonamides.
46. Name the drugs of 8-oxyquinoline derivatives.
47. An antimicrobial spectrum of chlorquinaldol and nitroxoline.
48. The features of pharmacokinetics of 8-oxyquinoline derivatives with nitro group and containing halogens.
49. Indications for chlorquinaldol and nitroxoline.
50. The side effects of chlorquinaldol and nitroxoline.
51. Name the drugs of nitrofurans.
52. The mechanism of action of nitrofurans.
53. Indications for furazolidone and nitrofurantoin.
54. Why is it necessary to limit the use of the products containing a lot of tyramine during the treatment by furazolidone?
55. The influence of furazolidone on a metabolism of ethyl alcohol.
56. Complications during therapy by nitrofurantoin.
57. The side effects of furazolidone.
58. The side effects of nalidixic acid.
59. Indications for quinolones.
60. Basic difference of fluoroquinolones from quinolones frames radically changing their pharmacological properties and the antimicrobial action.
61. Name the widely used fluoroquinolones in clinical practice.
62. The mechanism of action of fluoroquinolones.
63. The antimicrobial spectrum of fluoroquinolones.
64. The pharmacokinetic properties of fluoroquinolones.
65. Indications for fluoroquinolones.
66. The side effects of fluoroquinolones.
67. Absolute contraindications for fluoroquinolones.
68. Name the drugs of nitroimidazoles.
69. The mechanism of action of metronidazole.
70. An antibacterial and antiprotozoal spectrum of metronidazole.
71. The pharmacokinetics of metronidazole.
72. Indications for metronidazole.
73. The side effects of metronidazole.
74. Name targets of action of antimalarial drugs.
75. Name the drugs influencing on erythrocyte schizonts; pre-erythrocytic forms of a malarial plasmodium; on sexual forms of a malarial plasmodium.
76. The principles of use of antimalarial drugs for individual chemoprophylaxis, treatments of malaria; for prophylaxis of relapses of malaria (radical treatment); social chemoprophylaxis.



77. Name the antimalarial drugs for individual chemoprophylaxis, treatments of malaria; for prophylaxis of relapses of malaria (radical treatment); social chemoprophylaxis.
78. What kind of a malarial plasmodium does not create exoerythrocytic forms?
79. What form of malaria does not relapse after treatment and why?
80. Name the drugs, efficient at any localization of amoebas; at intestinal localization of amoebas; acting on the tissue forms of amoebas.
81. The mechanism of action of chiniofon.
82. The pharmacokinetic properties of chiniofon used for the treatment of amoebiasis.
83. The pharmacokinetic properties of diloxanide.
84. The side effects of chiniofon; emetine; diloxanide.
85. Name the drugs for the treatment of trichomoniasis for oral application; for oral and intravaginal application; for intravaginal application.
86. The principles of the treatment of trichomoniasis.
87. Name the drugs for the treatment of giardiasis.
88. The mechanism of action of mepacrine.
89. The side effects of mepacrine.
90. The drugs for the treatment of toxoplasmosis.
91. The peculiarities of drug use for the treatment of toxoplasmosis associated with HIV infection.
92. The peculiarities of drug use for the treatment of toxoplasmosis when there is a risk of infection of a fetus.
93. The drugs used for the treatment of visceral leishmaniasis; cutaneous leishmaniasis.
94. The side effects of sodium stibogluconate.
95. The side effects of pentamidine.
96. Name the drugs for the treatment of pneumocystosis.
97. Specify the problems of the pharmacotherapy of viral infections.
98. Stages of a virus reproduction as a target for action of antiviral drugs.
99. Name the inhibitors of adsorption, penetration and deproteinization (stripping) of viruses; inhibitors of nucleic acid synthesis; inhibitors of RNA and late viral proteins synthesis; inhibitors of virus self-assembly.
100. Name the anti-influenza drugs; antiherpetic drugs; antiviral drugs for cytomegalovirus; drugs for the treatment of HIV infection, Drugs used in respiratory syncytial infection; antiviral drugs of a broad spectrum of action.
101. Name the virucidal drugs for local application.
102. Name the gamma globulins for the treatment of viral infections.
103. The mechanism of action of aminoadamantanes, ribavirin, zidovudine, ganciclovir, foscarnet, acyclovir, nevirapine, saquinavir, interferons, tilorone.
104. Indications for acyclovir, idoxuridine, foscarnet, ganciclovir, zidovudine, rimantadine, ribavirin.
105. An antirabic drug.
106. First-line drug for the treatment of anogenital warts; herpetic keratitis, herpetic conjunctivitis.
107. Belarusian virucidal drug for local application.
108. First-line drug for the treatment of genital herpes.
109. The side effects of acyclovir, foscarnet, ganciclovir, zidovudine, aminoadamantanes, interferons, ribavirin.
110. An antibiotic with antiviral activity.

111. Efficiency and therapeutic potential of drugs for the treatment of HIV infection.
112. Name the basic antispirochetal drugs.
113. First-line drugs for the treatment of lues.
114. The principles of classification of antituberculosis drugs.
115. Name the first antituberculosis drugs.
116. Name the reserve antituberculosis drugs.
117. Name the most efficient antituberculosis drugs.
118. Name the antituberculosis drugs of average efficiency.
119. Name the antituberculosis drugs of low efficiency.
120. Name the most active synthetic antituberculosis drug.
121. Name the most active antituberculosis antibiotic.
122. Name the bacteriostatic antituberculosis drugs.
123. Name the antituberculosis drugs affecting micobacterias with intracellular localization.
124. Name the bactericidal antituberculosis drugs.
125. The mechanism of action of isoniazid; ethambutol; pyrazinamide; rifampicin; streptomycin.
126. Why treatment by isoniazid can be complicated by polyneuritis?
127. What drugs should be administered for prophylaxis of polyneuritis during treatment by isoniazid?
128. What antibacterial drugs are used for the treatment of lepra?
129. Kinds of chemoprophylaxis of tuberculosis.
130. Primary chemoprophylaxis of tuberculosis. Who to carry out at and which drugs to use?
131. Secondary chemoprophylaxis of tuberculosis. Who to carry out at and which drugs to use?
132. What is the difference between chemoprophylaxis and chemotherapy of tuberculosis?
133. The principles of a pharmacotherapy of tuberculosis.
134. Duration of tuberculosis treatment courses.
135. What and how does the duration of tuberculosis treatment changes depend on?
136. The side effects of isoniazid; ethambutol; pyrazinamide; rifampicin.
137. The prophylaxis of side effects of antituberculosis drugs.
138. The principles of the pharmacotherapy of mycoses.
139. Name the antifungal antibiotics.
140. Name the antifungal polyene antibiotics.
141. The mechanism of antifungal action of polyene antibiotics; griseofulvin; azoles.
142. Name the antifungal drugs — imidazole derivatives for local application.
143. Name the antifungal drugs — imidazole derivatives for systemic and local application.
144. Name the triazole derivatives.
145. Terbinafine, features of action and use.
146. Nystatin, features of action and use.
147. Why keratolytic and depilatory drugs are applied together with antifungal drug?
148. What fungi are less sensitive to polyene antibiotics: yeastlike microorganisms, causative agents of deep mycoses (coccidia, histoplasma, cryptococci and sporotrichum), mycelial fungi, dermatophytes?
149. What protozoa do polyene antibiotics affect?
150. What determines the choice of administration route of polyene antibiotics?
151. The difference of antiseptics from disinfectants.
152. The difference of antiseptics from other antibacterial drugs.
153. The requirements for antiseptics.

154. The classification of antiseptics according to their chemical structure (groups, drugs).
155. Name the antiseptics of detergents; metal compounds; halogen compounds; acids and bases; aromatic compounds; aliphatic derivatives; oxidizers; nitrofurans derivatives; dyes; biguanides.
156. The mechanism of action of the antiseptics of detergents; metal compounds; halogen compounds; acids and bases; aromatic compounds; aliphatic derivatives; oxidizers; nitrofurans derivatives; dyes; biguanides.
157. The features of use of the antiseptics of detergents; metal compounds; halogen compounds; acids and bases; aromatic compounds; aliphatic derivatives; oxidizers; nitrofurans derivatives; dyes; biguanides.
158. The principles of the treatment of acute poisonings with antiseptics.
159. The principles of chemotherapy of malignant neoplastic diseases.
160. Main anticancer drugs (groups, drugs).
161. Name the anticancer drugs of different groups: alkylating drugs; antimetabolites; drugs that arrest mitosis; antibiotics; enzymes; platinum drugs.
162. The mechanisms of action of anticancer drugs of different groups: alkylating drugs; antimetabolites; drugs that arrest mitosis; antibiotics; enzymes; platinum drugs.
163. The features of a spectrum of anticancer action of alkylating drugs; antimetabolites; antibiotics; enzymes; platinum drugs.
164. The side effects of anticancer drugs of different groups: alkylating drugs; antimetabolites; drugs that arrest mitosis; antibiotics; enzymes; platinum drugs.
165. The complications and consequences of anticancer chemotherapy.

## LESSON 34. DRUGS AFFECTING THE RESPIRATORY SYSTEM

1. Bronchodilators and other drugs used in bronchial asthma (BA)
  - 1.1. Principles of pharmacotherapy of BA and relieving of asthmatic attacks.
  - 1.2. The major classes of pharmacological drugs used in BA. Mechanisms of action, the main pharmacological effects, side effects, contraindications.
    - 1.2.1. Adrenergic agonists:
      - Selective  $\beta_2$ -adrenomimetics: short-term action (up to 3–4 hours) — salbutamol, terbutaline, fenoterol; long-term action (up to 10–12 hours) — salmeterol, formoterol.
      - Other adrenomimetics — epinephrine (emergency treatment of acute allergic and anaphylactic reactions), ephedrine.
    - 1.2.2. M-cholinergic antagonists: short-term action (3–4 times a day) — ipratropium bromide; long-term action (once a day) — aclidinium, glycopyrronium, tiotropium.
    - 1.2.3. Theophylline drugs:
      - to relieve asthmatic attacks — aminophylline (euphyllin);
      - long-term action — teotard, teodur, teodur-24, euphyllong.
    - 1.2.4. Antiallergic drugs:
      - mediators of allergy release inhibitors — cromoglicic acid and its sodium salt, nedocromil, ketotifen;
      - leukotriene receptor antagonists — montelukast, zafirlukast;
      - phosphodiesterase IV inhibitors — roflumilast.

- 1.2.5. Glucocorticosteroids — beclomethasone, budesonide, fluticasone, mometasone.
- 1.2.6. Combined bronchodilators:
  - salmeterol + fluticasone (Seretide);
  - formoterol + budesonide (Symbicort);
  - formoterol + beclomethasone (Fostair);
  - fenoterol + ipratropium bromide (Berodual);
  - fenoterol + cromoglicic acid (Ditek).
- 1.2.7. Other drugs for the treatment of BA — monoclonal antibodies bind with IgE receptors (omalizumab), antihistamines, hyposensitization drugs (allergen extracts), methotrexate, etc.
2. Respiratory stimulants and surfactants
  - 2.1. Stimulants of respiration — almitrine (peripheral respiratory analeptic); doxapram, nikethamide, aethimizolum, bemegride (stimulants of the respiratory center).
  - 2.2. Surfactants — beractant, poractant alpha and stimulants of their synthesis — ambroxol.
3. Expectorant and mucolytic drugs
  - 3.1. Drugs to facilitate sputum discharge:
    - reflex action — herbal drugs: ipecacuanha, thermopsis, polygala, Althaea officinalis, licorice;
    - resorptive action — potassium iodide, sodium iodide, terpin hydrate, guaifenesin (with additional mucolytic action), herbal drugs: thyme herb, anise oil, eucalyptus oil, etc.
  - 3.2. Drugs reducing the viscosity and elasticity of sputum:
    - synthetic mucolytic (secretolytic) drugs: carbocysteine, acetylcysteine, bromhexine, ambroxol, mesna;
    - enzymes: dornase alfa.
4. Antitussives drugs
  - 4.1. Drugs of central action:
    - narcotic (opioid) — codeine, morphine;
    - nonnarcotic — dextromethorphan, oxeladin, pholcodin (containing dextromethorphan, terpin hydrate, levomenthol).
  - 4.2. Drugs of peripheral action — prenoxdiazine, pronilid.
5. Decongestants
  - 5.1. Local intranasal decongestants:
    - short-term action (up to 4–6 hours) — naphazoline;
    - average-term action (up to 8–10 hours) — xylometazoline;
    - long-term action (more than 12 hours) — oxymetazoline;
    - corticosteroids (nasal spray) — fluticasone, mometasone.
  - 5.2. Systemic decongestants — pseudoephedrine.
6. Drugs, used for the treatment of pulmonary edema
  - 6.1. Narcotic analgesics (trimepiridine, morphine, fentanyl) and neuroleptics (droperidol, haloperidol) — elimination of pain syndrome, anxiety, tachypnea, decrease venous return of blood to the heart.
  - 6.2. Diuretics (furosemide, toxic pulmonary edema — mannitol) — decrease in blood volume, reducing the load on the heart, tissue dehydration (mannitol).
  - 6.3. Drugs with positive inotropic effect (dobutamine, dopamine, digoxin).

- 6.4. Glucocorticosteroids (prednisolone, hydrocortisone) — bronchial spasmolytic and antiallergic effects.
- 6.5. Nitrates and nitrate-like drugs (nitroglycerin, isosorbide dinitrate) — reduction of the hydrostatic pressure in the pulmonary vessels and reduction of preload on the heart.
- 6.6. Ganglionic blockers (hexamethonium) — reduction of the hydrostatic pressure in the pulmonary vessels (rarely used).
- 6.7. Aminophylline — eliminating of bronchospasm and improving of alveolar ventilation.
- 6.8. Oxygen therapy, correction of acid-base balance, defoamers (ethyl alcohol).
7. Drugs that induce lung diseases
  - 7.1. Acetylsalicylic acid and other NSAIDs — aspirin asthma and pneumonites.
  - 7.2. M-cholinomimetics and  $\beta$ -adrenergic antagonists (including eye drops — pilocarpine, timolol) — bronchospasm.
  - 7.3. ACE inhibitors — dry cough.
  - 7.4. Amiodarone — chronic interstitial pneumonites with fibrosis.
  - 7.5. Cytostatics — pulmonary fibrosis.

**Write out the following drugs:** codeine (powder for oral use), formoterol (powder for inhalations), berodual (aerosol), aminophylline (solution), ketotifen (syrup), terbutaline (powder for inhalations), montelukast (chewable tablets), dornase alfa (solution for nebulizer).

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		The doctor's prescription is valid from «___» _____ 20___	
Full name of the patient		_____	
Date of Birth		_____	
Full name of the doctor		_____	
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Signature of the doctor Doctor's personal stamp			
This prescription is valid for 30 days, 60 days (cross out the unnecessary)			

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This prescription is valid for 30 days, 60 days (cross out the unnecessary)			

## LESSON 35. DRUGS AFFECTING THE GASTROINTESTINAL TRACT. PART I

### 1. Drugs affecting appetite and the processes of digestion

#### 1.1. Antianorexic drugs (stimulating appetite):

- reflex action — bitters (wormwood tincture, the sap of plantain);
- central action — cyproheptadine;
- stimulating anabolic processes — insulin, anabolic steroids (nandrolone).

#### 1.2. Drugs that improve the processes of digestion:

- enzymes — pepsin, tilactase;
- hydrochloric acid;
- a combination of enzymatic and acidic drugs (acidin-pepsinum, gastric juice).

#### 1.3. Drugs for the treatment of obesity:

##### 1.3.1. Drugs affecting the gastrointestinal tract (GIT):

- antienzymes — orlistat;
- increasing the volume of intestinal contents — methylcellulose.

##### 1.3.2. Anorexigenic drugs of central action:

- sympathomimetics: phenylpropanolamine and phentermine; dexfenfluramine and phentermine — risks (development of heart failure, pulmonary hypertension) and restriction of their use.

##### 1.3.3. Hypoglycemic drugs (oral) — metformin, acarbose.

2. Antispastic and other drugs affecting gastrointestinal motility
  - 2.1. Drugs reducing the tone and motility.
    - 2.1.1. Cholinergic antagonists:
      - tertiary amines — dicycloverine, atropine and other belladonna alkaloids;
      - quaternary ammonium compounds — hyoscine butylbromide, propantheline.
    - 2.1.2. Spasmolytics of myotropic action: drotaverine, papaverine, mebeverine, pinaverium bromide.
  - 2.2. Stimulants of motility:
    - 2.2.1. Cholinomimetics — pyridostigmine bromide, neostigmine.
    - 2.2.2. Dopamine antagonists — metoclopramide, domperidone.
3. Emetic and antiemetic drugs
  - 3.1. Emetics — apomorphine, syrup of ipecacuanha, hypertensive (15 %) sodium chloride solution.
  - 3.2. Antiemetics:
    - 3.2.1.  $S_3$  ( $5HT_3$ )-serotonin receptors antagonists — ondansetron, granisetron, tropisetron.
    - 3.2.2. Dopamine  $D_2$ -receptors antagonists — metoclopramide, domperidone, dimethpramid, thiethylperazine.
    - 3.2.3. Histamine  $H_1$ -receptors antagonists — promethazine.
    - 3.2.4. Drugs against sickness syndrome — scopolamine (hyoscine hydrobromide), tablets «Aeron».
    - 3.2.5. Other antiemetic drugs — nabilone (synthetic cannabinoid), dexamethasone, aprepitant (blocker of neurokinin 1 ( $NK_1$ ) receptors).

The selection of drugs depending on the mechanism of vomiting and features of its antiemetic action.

- 4. Antidiarrheal drugs
  - 4.1. Opiate receptor agonists — loperamide, eluxadolone, diphenoxylate, codeine, Cophenotrop (diphenoxylate + atropine, 100:1).
  - 4.2. Adsorbent drugs — activated carbon, ion exchange resins (cholestyramine), diosmectite (smecta).
  - 4.3. Astringents — oak bark, bilberry fruits, hypericum herb, chamomile flowers, sage leaf.
- 5. Laxative drugs.
  - 5.1. Drugs causing chemical irritation of the intestine:
    - 5.1.1. The group of anthraquinones — drugs of senna (sennosides A and B) and rhubarb.
    - 5.1.2. Other drugs — bisacodyl, castor oil, phenolphthalein, sodium picosulfate.
  - 5.2. Drugs, causing mechanical irritation of the intestine:
    - 5.2.1. With osmotic properties — magnesium sulfate, sodium sulfate, lactulose, macrogols.
    - 5.2.2. Increasing the volume of the contents of the intestine (bulk laxatives) — methylcellulose, ispaghula.
  - 5.3. Drugs softening stool — liquid paraffin, vaseline oil.
  - 5.4. Peripheral opioid receptor antagonists — methylnaltrexone bromide.
  - 5.5. Other agents used in constipation — linaclotide (agonist of guanylate cyclase-C receptors), lubiprostone (chloride channel activator), prucalopride — selective agonist of serotonin  $5HT_4$  receptors.

Localization of action and the onset rate of laxative effect. Indications and contraindications of laxatives use.

6. Drugs of local action applied in anal and rectal disorders.

6.1. Reduces pain — lidocaine (ointment).

6.2. Hemorrhoids drugs combined with corticosteroids — ultraprokt, perinal and others.

6.3. Rectal sclerosant — phenol.

6.4. Drugs used in anal fissures — local anesthetics, nitroglycerin (0.4 % ointment).

7. Antiflatulent (antifoaming) drugs

7.1. Herbal drugs — the fruit of fennel, dill, caraway.

7.2. Synthetic drugs — simethicone, dimethicone, simethicone + alverin (Meteospazmyl).

8. Agents for treatment inflammatory bowel disease (ulcerative colitis and Crohn's disease) — aminosalicylates (sulfasalazine, mesalazine, balsalazide), corticosteroids, immunosuppressive agents, modulators of cytokines (including TNF- $\alpha$  inhibitors) — infliximab, adalimumab, golimumab; at food allergies — cromolyn sodium.

**Write out the following drugs:** platyphyllinum (suppository), aprepitant (capsules), ondansetron (syrup, tablets, suppository), metoclopramide (solution, tablets).

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## LESSON 36. DRUGS AFFECTING THE GASTROINTESTINAL TRACT. PART II

### 1. Drugs used in the hyperacidity of gastric content, reflux esophagitis, gastric ulcer and duodenal ulcer

#### 1.1. Drugs reducing the activity of acid-peptic factor.

##### 1.1.1. Antisecretory drugs:

- inhibitors of  $H^+-K^+-ATPase$  (of proton pump) — omeprazole, lansoprazole, pantoprazole, rabeprazole, esomeprazole;
- histamine  $H_2$ -receptors antagonists — famotidine, ranitidine, nizatidine;
- selective  $M_1$ -cholinergic antagonists — pirenzepine;
- prostaglandin analogues — misoprostol;
- gastrin receptor antagonists — proglumide.

The principles of the actions of the antisecretory drugs, comparative efficiency, speed and duration of action. Indications, side effects and their prevention.

##### 1.1.2. Antacids:

- containing aluminium and magnesium — aluminium hydroxide, aluminium phosphate (phosphalugel), magnesium hydroxide, magnesium carbonate, magnesium trisilicate;

- combined — aluminium–magnesium complexes (almagel, gastal, hydrotalcite, etc.), simethicone containing antacids (maalox plus, etc.), alginate containing antacids (acidex, gastrocot, gaviscon etc.);
- sodium bicarbonate.

Neutralizing activity, speed and duration of action of antacids. Side effects of antacids.

Precautions and restrictions of their use.

1.2. Drugs, which have a protective effect on the mucous membrane of the stomach and intestines (gastroprotectors):

- drugs forming a protective layer on the surface of the ulcer — sucralfate, bismuth tripotassium dicitrate;
- carbenoxolone.

1.3. Drugs, which have a bactericidal effect on *Helicobacter pylori* — a combination of antibiotics (clarithromycin, amoxicillin, metronidazole) and antisecretory drugs (omeprazole, rabeprazole, lansoprazole, pantoprazole, esomeprazole).

1.4. Other ulcer-healing drugs:

- reparants — solcoseryl, gastrofarm, sea buckthorn oil;
- nandrolone (anabolic steroids);
- drugs of vitamins A, U;
- dalargin.

2. Hepatotropic drugs

2.1. Bile-expelling drugs.

2.1.1. Cholesecretics (choleretics):

- bile acid drugs — dehydrocholic acid, allohol, cholenzym;
- synthetic choleretics — osalmid, cyclovalone, hydroxymethyl nicotinamide;
- herbal drugs — corn silk, sandy everlasting, rose hips, common tansy;
- hydrocholeretics — mineral water.

2.1.2. Cholekinetics (cholagogue):

- true cholekinetics — cholecystokinin, magnesium sulfate, barberry drugs;
- spasmolytics — drotaverine, papaverine, M-cholinergic antagonists.

2.1.3. Drugs with bile-expelling and spasmolytic action — himecromone.

2.2. Hepatoprotectors: betaine, methionine, essentielle, silibinin, silibor.

2.3. Cholelitholytic drugs — ursodeoxycholic acid.

3. Drugs affecting the function of the pancreas

3.1. Stimulants of secretion — dilute hydrochloric acid.

3.2. Pancreatic enzyme replacement therapy (PERT) — pancreatin; panzinorm, festal.

3.3. Drugs decreasing the secretion — M-cholinergic antagonists, antacid drugs.

3.4. Inhibitors of proteolysis — aprotinin, ovomisin.

3.5. Diagnostic drugs — secretin, cholecystokinin.

Principles of pharmacotherapy of acute and chronic pancreatitis.

**Write out the following drugs:** esomeprazole (coated tablets), pirenzepine (solution), metoclopramide (tablets), misoprostol (tablets).

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## LESSON 37. DRUG-TO-DRUG INTERACTION

**Objective:** To study the main ways of interaction, mechanisms and possible effects of drug-to-drug interactions.

1. Combined administration of drugs (polypharmacotherapy or combined therapy, polypragmasia). Drug interaction (definition).
2. Indications for combined pharmacotherapy.
3. Possible results of drug-to-drug interaction (synergism, antagonism, their types).
4. Pharmacodynamic properties of drugs increasing the rate of clinically significant interactions.
5. The main mechanisms of drug-to-drug interaction.
  - 5.1. Pharmaceutical interaction. Requirements to carry out infusion therapy.
  - 5.2. Pharmacological interaction (types).
    - 5.2.1. Pharmacokinetic interaction:
      - 5.2.1.1. At the absorption stage:
        - during enteral administration (determining factors — acidity, direct interaction in the lumen of the gastrointestinal tract, motility activity of the gastrointestinal tract, changes in intestinal flora, changes in absorption mechanisms);
        - during parenteral administration (ways of the absorption control).
      - 5.2.1.2. During distribution and storage:
        - direct interaction in blood plasma;
        - competitive exclusion from the connections with blood plasma albumins;
        - exclusion from the connections with tissue proteins.

5.2.1.3. During the process of metabolism:

- hepatic microsomal enzyme induction;
- hepatic microsomal enzyme inhibition;
- disulfiram-like reactions.

5.2.1.4. During the process of elimination:

- by passive diffusion;
- by active transport.

5.2.2. Pharmacodynamic interaction

- at the level of specific receptors;
- at the level of enzymes;
- at the level of ion channels;
- at the level of transport systems.

Examples of clinically significant drug interactions.

## **TOPIC FOR INDIVIDUAL STUDY. PRINCIPLES OF THE TREATMENT OF ACUTE DRUG POISONING. EMERGENCY AID DRUGS**

1. Therapeutic principles of acute drug poisoning.

1.1. Classification of drugs according to their toxicity and hazards (List A, List B), storage conditions of drugs and their dispensing from the pharmacy.

1.2. The concept of toxicokinetics and toxicodynamics. Quantitative assessment of toxic effect.

1.3. The main mechanisms of toxic effect of drugs.

1.4. Principles of the treatment of acute drug poisoning:

- emergency first aid;
- slowing-down of absorption and detoxification of unabsorbed poison;
- accelerated elimination, inactivation of absorbed poison;
- restoration of physiological functions.

1.5. First aid tactics depending on the way the poison gets into the organism.

1.6. Antidotes, definition, classification.

1.6.1. Toxicotropic antidotes:

- acting on physical and chemical principles: activated carbon;
- acting on chemical principle: unitiol, mecaptide, dexrazoxane, calcium trisodium pentetate, penicillamine.

1.6.2. Toxicokinetic antidotes (accelerating biotransformation of poisons): trimedoxime bromide, methylene blue (methylthioninium chloride), sodium thiosulfate, ethyl alcohol, antioxidants.

1.6.3. Pharmacological antagonists: atropine, naloxone, esmolol, flumazenil, acetylcysteine, etc.

1.6.4. Specific antitoxin sera: monovalent anti-digoxin, anti-botulinum, anti-ophidic sera.

1.7. The main mechanisms of antidote action. Principles of use.

Name the drug of choice for the treatment of poisoning with the drugs named below; explain the mechanism of action:

- barbiturates;
- benzodiazepine sedative-hypnogenic drugs;
- paracetamol;

- heparin;
- non-depolarizing muscle relaxants (pancuronium bromide, etc);
- narcotic analgesics;
- neuroleptics (extrapyramidal effects);
- cardiac glycosides (negative chronotropic effect).

## 2. Emergency aid drugs.

- 2.1. Emergency aid drugs for acute heart failure.
- 2.2. Emergency aid drugs for angina.
- 2.3. Emergency aid drugs for hypertensive crises.
- 2.4. Emergency aid drugs for bronchospasms.
- 2.5. Emergency aid drugs for acute hypoglycemia.
- 2.6. Emergency aid drugs for anaphylactic shock.

Emergency aid principles in case of the above-mentioned conditions, drugs of choice, medicinal forms and routes of administration.

# EXAMINATION QUESTIONS

## CHAPTER I. GENERAL PHARMACOLOGY AND PRESCRIPTION

1. Essence of pharmacology as a science. Parts and fields of modern pharmacology. The main terms and concepts of pharmacology — pharmacological activity, action, efficiency.
2. Sources and stages of drug development. Drugs — generics, placebo effects. Definition of such concepts as medicinal agent (medicinal drug, drug), medicinal substance, medicinal form.
3. Routes of drug administration into the body and their characteristic. Presystemic drug elimination.
4. Drug transfer through biological barriers and their types. The main factors influencing on the drug transfer in the body.
5. Drug transfer of variable ionization substances through membranes (Henderson-Hasselbach's equation of ionization). Principles of transfer management.
6. Drug transfer in the body. Aqueous diffusion and lipid diffusion (Fick's diffusion equation). Active transport.
7. Central postulate of pharmacokinetics: concentration of medicinal substance in blood plasma — the main parameter for management of the pharmacological effect. The tasks solved on the basis of this postulate.
8. Pharmacokinetic models (one-compartment and two-compartment), quantitative laws of absorption and drug elimination.
9. Bioavailability of drugs — definition, essence, quantitative expression, determinants.
10. Drug distribution in the body: compartments, ligands, the main determinants of distribution.
11. Elimination rate constant, its essence, dimension, connection with other pharmacokinetic parameters.
12. Excretion half-life of drugs, its essence, dimension, connection with other pharmacokinetic parameters.
13. Clearance as the main parameter of pharmacokinetics for management of the dosing regimen. Its essence, dimension and connection with other pharmacokinetic parameters.
14. Dose. Types of doses. Units of drug dosage. Aims of drug dosage, ways and variants of administration of drugs, dosing interval.
15. Administration of drugs at the constant rate. Kinetics of drug concentration in blood. Steady-state concentration of drug in the blood ( $C_{ss}$ ), achievement time, its calculation and management.
16. Discrete administration of drugs. Kinetics of drug concentration in the blood, therapeutic and toxic ranges (intervals) of concentrations. Calculation of steady-state concentration ( $C_{ss}$ ), limits of fluctuations and its management. Choice of interval of discrete doses administration.
17. Load (initial) dose. Therapeutic essence, calculation using other pharmacokinetic parameters, conditions and restrictions of its use.
18. Maintaining doses, their therapeutic essence and calculation of an optimal dosing regimen.
19. Individual, age and sex differences of pharmacokinetics of drugs. Amendments in the calculation of individual values of volume of distribution.

20. Renal clearance of drugs, mechanisms, their quantitative and qualitative characteristics.
21. The factors influencing on renal clearance of drugs. Dependence of renal clearance on physical and chemical properties of drugs.
22. Hepatic clearance of drugs, its determinants and restrictions. Enterohepatic circulation of drugs.
23. Correction of drug therapy at liver and kidneys diseases. General approaches. Correction of dosing regimen under the control of general clearance.
24. Correction of the dosing regimen of drugs under control of residual renal function.
25. Factors changing the drugs clearance. Strategy of individual drug therapy.
26. Biotransformation of drugs, its biological sense, main orientation and influence on drug activities. The main phases of metabolic transformations of drugs in an organism.
27. Clinical value of a biotransformation of drugs. Factors influencing on their biotransformation. Metabolic drug interactions.
28. Routes and mechanisms of elimination of drugs. Possibilities of management of elimination processes of drugs.
29. The concept of receptors in pharmacology: molecular nature of receptors, signal mechanisms of action of drugs (types of the transmembrane signaling and the secondary intermediaries).
30. Physical-chemical and chemical mechanisms of action of drugs.
31. Selectivity and specificity of drugs effects. Therapeutic, side and toxic effects of drugs, their nature from positions of the concept of receptors. Therapeutic strategy of struggle against side and toxic effects of drugs.
32. Terms and concepts of quantitative pharmacology: effect, efficiency, activity, agonist (full, partial), antagonist. Clinical difference between activity and efficiency of drugs.
33. Quantitative patterns of pharmacological effect. Law of diminishing of biological systems response. Clark-Ariens model and its consequences. General view of the concentration — effect dependence in normal and log-normal (half-logarithmic) coordinates.
34. Gradual and quantum assesment of the effect, essence and clinical use. Quantitative assesment of the drug activity and efficiency in experimental and clinical practices.
35. Types of drug effects. Change of drug action at continuous administration.
36. The dependence of action of drugs on age, sex, specific features of an organism. The influence of daily rhythms.
37. Variability in the drug actions. Hypo- and a hyperreactivity, tolerance and tachyphylaxis, hypersensitivity and idiosyncrasy. Reasons of variability of action of drugs and rational strategy of therapy.
38. Assessment of safety of drugs. Therapeutic index and standard safety margins.
39. Pharmacokinetic drug interactions (examples).
40. Pharmacodynamic drug interactions. Antagonism, synergism, their types. The nature of the effect changes of drugs (activity, efficiency) depending on the type of antagonism.
41. Side and toxic effects of drugs. Teratogenic, embryotoxic, mutagenic actions of drugs. Medical and social aspects of the struggle with drug abuse, narcomania and alcoholism. The concept of toxicomania.
42. Pharmaceutical drug interactions. Precautions during infusion therapy.
43. Types of pharmacotherapy. Deontological problems of pharmacotherapy.
44. Basic principles of treatment and prevention of medicinal substances poisoning. Antidote therapy (examples).

45. Prescription and its structure. General rules for writing out a prescription. State regulation of writing out and dispensing drugs.
46. Rules of writing out narcotic, poisonous and potent substances.
47. Drugs under control. Drugs prohibited for prescribing.

## **CHAPTER II. SPECIAL PHARMACOLOGY**

Characteristics of each group of drugs should include:

- classification with indicating of drugs;
- mechanism of action;
- pharmacological effects;
- main pharmacokinetic characteristics of the drugs of the group;
- use in clinical medicine (indications);
- main side and toxic effects;
- main contraindications.

For antimicrobial drugs in addition to know:

- antimicrobial spectrum;
- effect (bactericidal / bacteriostatic);
- tactics of rational dosing.

1. The scheme of the functional organization of the peripheral nervous system. Excitation transmission in cholinergic and adrenergic synapses.
2. Astringent, mucilaginous drugs, absorbents and irritants.
3. Local anesthetic drugs.
4. M, N-cholinomimetics and stimulants of endogenic acetylcholine release.
5. Anticholinesterase drugs. Acute poisoning and medical aid.
6. M-cholinomimetics.
7. N-cholinomimetics. Nicotinomimetics use in smoking control.
8. M-cholinergic antagonists.
9. Ganglionic blockers.
10. Muscle relaxant drugs (curare-type).
11. Adrenomimetics.
12. Adrenergic antagonists.
13. Sympathomimetics and sympatholytics.
14. General concept of pain and pain relief. Drugs, used in neuropathic painful syndromes.
15. General anesthetics. Definition. Determinants of depth, speed of development and anesthesia recovery. The requirements for an ideal anesthetic.
16. Drugs for inhalation anesthesia.
17. Drugs for non inhalation anesthesia.
18. Ethyl alcohol. Acute and chronic poisoning. Treatment.
19. Narcotic analgesics. Acute and chronic poisoning. Principles of the treatment and medical aid.
20. Nonnarcotic analgesics and antipyretics.
21. Sedative-hypnogenic drugs. Acute poisoning and medical aid.
22. Anticonvulsants.
23. Antiparkinsonian drugs and drugs for the treatment of spasticity.
24. Psychopharmacology. The classification of psychotropic drugs. Tonics.
25. Antipsychotic drugs.



26. Antidepressants (thymoleptics). Normothymic (antimanic) drugs.
27. Anxiolytic drugs.
28. Psychostimulants, actoprotectors, analeptics.
29. Nootropic drugs.
30. Drugs for the prevention and relief of bronchospasm.
31. Antitussives, expectorant and mucolytic drugs.
32. Diuretics.
33. Principles of pharmacotherapy of pulmonary edema.
34. Principles of pharmacotherapy of heart failure (specify groups of drugs). Drugs reducing the load on the heart.
35. Drugs with positive inotropic effects. Cardiac glycoside intoxication, medical aid.
36. Antiarrhythmic drugs.
37. Principles of IHD pharmacotherapy. Antianginal drugs.
38. Principles of pharmacotherapy of acute myocardial infarction.
39. Antihypertensive sympathoplegic drugs. Principles of pharmacotherapy of arterial hypertension (specify groups of drugs).
40. Antihypertensive drugs that affect electrolyte balance, renin-angiotensin system.
41. Myotropic vasodilators, calcium channel blockers.
42. Drugs affecting hematopoiesis and regeneration.
43. Antithrombotic drugs.
44. Haemostatic drugs.
45. Drugs affecting appetite and the processes of digestion.
46. Principles of pharmacotherapy of gastric ulcer and duodenal ulcer. Antiulcerogenic drugs.
47. Stimulants of motility of the gastrointestinal tract. Antispastic and antidiarrheal drugs.
48. Drugs affecting the exocrine and endocrine functions of the pancreas.
49. Emetic and antiemetic drugs.
50. Hepatotropic drugs.
51. Laxative and antiflatulent (antifoaming) drugs.
52. Drugs affecting myometrium tone and activity.
53. Hypothalamic and pituitary (hypophysis) hormones.
54. Thyroid hormone drugs. Antithyroid drugs.
55. Drugs, influencing on calcium and bone tissue metabolism.
56. Female sex hormones and their antagonists. Oral contraceptives.
57. Androgen and antiandrogen drugs. Anabolic steroids.
58. Adrenal cortex (adrenocortical) hormone drugs and their synthetic analogues. Corticosteroid synthesis inhibitors.
59. Hypolipidemic drugs.
60. Water-soluble vitamin drugs.
61. Fat-soluble vitamin drugs and vitamin-like compound drugs.
62. Anti-inflammatory drugs.
63. Anti-gout drugs.
64. Principles of pharmacotherapy of collagenoses. Disease-modifying antirheumatic drugs.
65. Antiallergic drugs. Antihistamine drugs.
66. Immunomodulators (immunostimulators, immunosuppressants).
67. Basic principles of chemotherapy. Principles of classification of antibiotics.

68. Antiseptics and disinfectants. General characteristics, the differences of antiseptics from antimicrobial drugs. Main groups of antiseptics: metal compounds, halogen compounds, oxidizers, dyes, aliphatic, aromatic and nitrofurans derivatives, detergents, acids and bases, polyguanidines.
69. Antimicrobial drugs. General characteristics. Basic definitions of chemotherapy of infections.
70. Penicillins.
71. Cephalosporins.
72. Carbapenems and monobactams.
73. Macrolides and azalides. Streptogramins.
74. Tetracyclines and aminoglycosides.
75. Aminoglycosides.
76. Lincosamides. Fusidic acid. Oxazolidinones.
77. Glycopeptides and polypeptides.
78. Side effects of antibiotics. Rational combinations of antibacterial drugs.
79. Sulfonamide drugs.
80. Synthetic antimicrobial drugs: nitrofurans, oxyquinolines, quinolones, fluoroquinolones, nitroimidazoles.
81. Antituberculosis drugs.
82. Antiviral drugs.
83. Antimalarial drugs and drugs for the treatment of amoebiasis.
84. Drugs for the treatment of giardiasis, trichomoniasis, toxoplasmosis, leishmaniasis, pneumocystosis.
85. Antifungal (antimycotic) drugs.
86. Anthelmintic drugs. Drugs for the treatment of scabies and pediculosis.
87. Anticancer (antiblastic) drugs.

### **CHAPTER III. LIST OF DRUGS OF CHAPTER II**

1. —
2. Tannin, sage leaves infusion, activated carbon, menthol, ammonia solution.
3. Benzocaine (anestezine), procaine (novocaine), tetracaine, lidocaine, bupivacaine, articaine.
4. Acetylcholine chloride, carbachol, itopride.
5. Neostigmine, pyridostigmine bromide, edrophonium, donepezil hydrochloride, trimedoxime bromide.
6. Pilocarpine, bethanechol.
7. Nicotine, cytisine, anabasine.
8. Atropine, hyoscyne hydrobromide (scopolamine), homatropine, tropicamide, propantheline bromide, dicycloverine, pirenzepine, darifenacin, tolterodine.
9. Trimethaphan, hexamethonium.
10. Atracurium besylate, pipecuronium bromide, suxamethonium chloride.
11. Epinephrine (adrenalin hydrochloride), norepinephrine (noradrenaline hydrotartrate), phenylephrine, dobutamine, salbutamol, isoprenaline.
12. Prazosin, propranolol, nadolol, pindolol, atenolol, metoprolol, nebivolol, acebutolol, labetalol.
13. Ephedrine, guanethidine, reserpine.

14. Sumatriptan, ergotamine, paracetamol, propranolol; tricyclic antidepressants, carbamazepine, clonidine, ketamine.
15. —
16. Halothane (fluothane), isoflurane, sevoflurane, dinitrogen monoxide (nitrous oxide).
17. Sodium thiopental, propofol, ketamine.
18. Ethyl alcohol. Disulfiram (teturam).
19. Morphine, trimipridine, fentanyl, buprenorphine, pentazocine, methadone, codeine, naloxone, naltrexone.
20. Tramadol, nefopam, paracetamol, acetylsalicylic acid, ibuprofen, ketorolac, dantrolene.
21. Nitrazepam, temazepam, triazolam, zolpidem, zopiclone, herbal drugs of motherwort and valerian.
22. Carbamazepine, phenytoin, ethosuximide, sodium valproate, lamotrigine, clonazepam, diazepam, lorazepam, phenobarbital, magnesium sulfate, antipsychotic drugs, muscle relaxants.
23. Levodopa, levodopa + carbidopa, levodopa + benserazide, trihexyphenidyl, biperiden. Tolperisone, tizanidine.
24. Eleutherococ liquid extract, ginseng tincture, pantocrin.
25. Chlorpromazine, thioridazine, fluphenazine, flupentixol, haloperidol, benperidol, chlorpromazine, clozapine, risperidone.
26. Amitriptyline, clomipramine, venlafaxine, fluoxetine, maprotiline, tianeptine, moclobemide. Lithium carbonate.
27. Alprazolam, diazepam, chlordiazepoxide, oxazepam, medazepam, lorazepam, buspirone.
28. Caffeine, mesocarb, bemithyl. Almitrine, doxapram, nikethamide, bemegride, aethimizolum.
29. Piracetam, vinpocetine, nimodipine, donepezil hydrochloride, memantine.
30. Epinephrine, salbutamol, salmeterol, ipratropium bromide, theophylline, ketotifen, zafirlukast, beclomethasone.
31. Codeine, dextromethorphan, oxeladin, prenoxdiazine, pronilid (falimint). Thermopsis drugs, potassium iodide, acetylcysteine, dornase alfa, surfactant.
32. Hydrochlorothiazide, indapamide, chlorthalidone, furosemide, spironolactone, eplerenone, amiloride, mannitol.
33. Fentanyl, droperidol; furosemide, mannitol; dobutamine, dopamine, digoxin; isosorbide dinitrate, aminophylline, glucocorticoids, ethyl alcohol.
34. Inhibitors of the renin-angiotensin system, diuretics, vasodilators,  $\beta$ -adrenergic antagonists.
35. Strophanthin, digoxin, digitoxin. Dopamine, dobutamine. Milrinone. Potassium chloride, unithiol, atropine, lidocaine, Na<sub>2</sub>-EDTA.
36. Quinidine, procainamide, lidocaine, phenytoin, propafenone, atenolol, propranolol, amiodarone, sotalol, verapamil; atropine, isoprenaline.
37. Propranolol, atenolol; diltiazem, verapamil, amlodipine; nitroglycerin, nitroglycerin, isosorbide dinitrate, isosorbide mononitrate; nicorandil, ivabradine.
38. —
39. Propranolol, betaxolol, methyldopa, clonidine, moxonidine, guanethidine, doxazosin, labetalol, hexamethonium, hydralazine, minoxidil, sodium nitroprusside.
40. Indapamide, hydrochlorothiazide, aliskiren, captopril, enalapril, lisinopril, omapatrilat, losartan, irbesartan.

41. Papaverine, indapamide, minoxidil, sodium nitroprusside, diltiazem, verapamil, nifedipine, amlodipine.
42. Ferrous sulfate and other iron (II) salts, iron (III) sucrose complex, deferoxamine, cyanocobalamin, folic acid, erythropoietins alfa and beta, molgramostim, methyluracil, hydroxycarbamide and other anticancer drugs.
43. Acetylsalicylic acid, clopidogrel, ticlopidine, pentoxifylline, abciximab, epoprostenol, sodium heparin, calcium nadroparin, sodium enoxaparin, lepirudin, antithrombin III, dabigatran, rivaroxaban, warfarin, fibrinolysin, streptokinase, alteplase. Protamine sulfate.
44. Etamsylate, calcium salts, menadione, phytomenadione, tranexamic acid, blood clotting factor VIII and factor IX, thrombin, desmopressin.
45. Bitters, pepsin, hydrochloric acid, orlistat, methylcellulose, metformin, acarbose.
46. Aluminium hydroxide, magnesium hydroxide, pirenzepine, famotidine, omeprazole, bismuth tripotassium dicitrate, sucralfate, metronidazole, amoxicillin, clarithromycin.
47. Pyridostigmine bromide, dicycloverine, hyoscine butylbromide, loperamide, domperidone, metoclopramide.
48. Cholecystikinin, pancreatin, aprotinin, ovomin, insulin drugs, glybenclamide, metformin, acarbose, pioglitazone, repaglinide.
49. Apomorphine, ondansetron, metoclopramide, promethazine, hyoscine hydrobromide, nabilone, dexamethasone, aprepitant.
50. Allohohol, osalimid, essentielle, silibinin, ursodeoxycholic acid.
51. Drugs of senna, bisacodyl, sodium sulfate, magnesium sulfate, lactulose; the fruit of dill, simethicone.
52. Oxytocin, dinoprost, dinoprostone, misoprostol, ergometrine; salbutamol, hexoprenaline, atropine, nifedipine; mifepristone.
53. Sermorelin, octreotide; gonadorelin, goserelin; protirelin; tetracosactide, urofollitropin, chorionic gonadotropin, menotropins; oxytocin, desmopressin, terlipressin; pegvisomant, danazol.
54. Sodium levothyroxine ( $T_4$ ), liothyronine (triiodothyronine hydrochloride,  $T_3$ ), thiamazole, propylthiouracil, iodine drugs.
55. Teriparatide, calcitonin, paricalcitol, estrogens, ergocalciferol, alfacalcidol, alendronic acid.
56. Ethinyl estradiol, hexestrol, raloxifene; progesterone, norethisterone, levonorgestrel; tamoxifen, mifepristone.
57. Methyltestosterone, testosterone and its aethers, flutamide, nandrolone (retabolil).
58. Hydrocortisone, methylprednisolone, triamcinolone, dexamethasone, fludrocortisone, deoxycortone, aminoglutethimide.
59. Atorvastatin, simvastatin, nicotinic acid, cholestyramine, gemfibrozil, probucol, lipostabil.
60. Thiamine, riboflavin, calcium pantothenate, folic acid, nicotinic acid, pyridoxine, ascorbic acid, rutin.
61. Retinol, cholecalciferol, ergocalciferol, alfacalcidol, tocopherol, choline chloride, inosine.
62. Diclofenac, aceclofenac, ibuprofen, naproxen, indomethacin, meloxicam, celecoxib, nabumetone, prednisolone, methylprednisolone, dexamethasone, mometasone, fluocinolone acetonide.
63. Allopurinol, sulfinpyrazone, aethamidum, urodanum, colchicine.

64. Glucocorticoids, gold salts, penicillamine, sulfasalazine, methotrexate, azathioprine, chloroquine, hydroxychloroquine.
65. Diphenhydramine, promethazine, quifenadine, loratadine, dexamethasone, hydrocortisone, prednisolone, chromoglycic acid, montelukast, epinephrine.
66. IRS-19, ribomunil, gamma interferon, aldesleukin, thymogen, thyloron, echinacea drugs; azathioprine, methotrexate, cyclosporine, basiliximab, infliximab, abatacept.
67. —
68. Azelaic acid, ambazone, biclotymol, policresulen, picloxydine. Chloramine, iodine spirituous solution, povidone, chlorhexidine, chloroxylenol, hydrogen peroxide solution, potassium permanganate, brilliant green, methylthioninium chloride. Ethanol, formaldehyde, pure phenol, triclosan, nitrofurazone, glutaral, miramistin, boric acid, ammonia solution, incrasept-10A.
69. —
70. Benzylpenicillin (sodium and potassium salts), phenoxymethylpenicillin, benzathine benzylpenicillin (bicillin-1), procaine benzylpenicillin. Oxacillin, cloxacillin, amoxicillin, ampicillin, carbenicillin, piperacillin, pivmecillinam, co-amoxiclav.
71. Cefazolin, cephadrine, cefalexin; cefuroxime, cefoxitin, cefaclor; cefotaxime, ceftazidime, ceftriaxone, cefixime; cefepime; ceftobiprole.
72. Imipenem, meropenem, aztreonam.
73. Erythromycin, clarithromycin, telithromycin, azithromycin, spiramycin, quinupristin / dalbapristin.
74. Tetracycline, doxycycline. Chloramphenicol.
75. Streptomycin, gentamicin, amikacin, spectinomycin.
76. Lincomycin, clindamycin, fusidic acid, linezolid.
77. Vancomycin, teicoplanin. Polymyxins.
78. —
79. Sulfadimidine, sulfadiazine, sulfadimethoxine, co-trimoxazole, phthalylsulfathiazole (phthalazol), sulfacetamide, sulfasalazine.
80. Nitrofurantoin, nitroline, pipemidic acid, ciprofloxacin, ofloxacin, metronidazole.
81. Isoniazid, rifampicin, pyrazinamide, ethambutol, streptomycin. Levofloxacin, moxifloxacin; bedaquiline, delamanid.
82. Rimantadine (remantadine), oseltamivir, acyclovir, idoxuridine, maraviroc, zidovudine, nevirapine, raltegravir, indinavir, enfuvirtide, ganciclovir, ribavirin, entecavir, tenofovir, sofosbuvir, simeprevir, daclatasvir, interferons, tilorone, oxoline.
83. Chloroquine, mefloquine, primachinum, pyrimethamine, quinine, artemether, artesunate, metronidazole, tinidazole, chiniofon, doxycycline.
84. Metronidazole, tinidazole, trichomonad, pyrimethamine, mepacrine, sodium stibogluconate, pentamidine isethionate, co-trimoxazole, atovaquone.
85. Griseofulvin, clotrimazole, ketoconazole, fluconazole, voriconazole, itraconazole, ciclopirox, amphotericin B, nystatin, flucytosine, terbinafine.
86. Mebendazole, albendazole, pyrantel, piperazine, levamisole, ivermectin, praziquantel, niclosamide. Malathion, permethrin, phenothrin, sodium thiosulfate, benzyl benzoate.
87. Cyclophosphamide, busulfan, fluorouracil, cytarabine, vincristine, paclitaxel, etoposide, irinotecan, doxorubicin, cisplatin.

## LIST OF DRUGS FOR PRESCRIBING IN RECIPES ON EXAMS

For each drug you need to **know**:

- release form
- pharmacotherapeutic group
- basic indications for use
- side effects

1. Acyclovir (in bottles)
2. Alendronic acid (tablets)
3. Alfacalcidol (capsules, solution in oil)
4. Alprazolam (tablets)
5. Amikacin (solution in ampoules)
6. Amiodarone (solution in ampoules)
7. Atorvastatin (tablets)
8. Atropine (ointment)
9. Azithromycin (capsules, syrup)
10. Benzylpenicillin (in bottles)
11. Berodual (aerosol)
12. Bisoprolol (tablets)
13. Carbamazepine (tablets)
14. Carvedilol (tablets)
15. Cefaclor (capsules)
16. Ceftazidime (powder in bottles)
17. Chlorpromazine (dragee)
18. Ciprofloxacin (solution in bottles, coated tablets)
19. Clarithromycin (powder for suspension)
20. Clindamycin (capsules for children, syrup)
21. Clonidine (eye drops)
22. Clozapine (granules in sachets)
23. Co-trimoxazole (solution in ampoules)
24. Desloratadine (tablets)
25. Dexamethasone (tablets)
26. Diazepam (tablets)
27. Digoxin (solution in ampoules, solution in vials)
28. Diltiazem (coated tablets)
29. Diphenhydramine (solution in ampoules, suppositories)
30. Doxazosin (tablets)
31. Doxycycline (capsules, powder in ampoules)
32. Esomeprazole (tablets, powder in vials)
33. Ethosuximide (capsules)
34. Fluoxetine (capsules)
35. Flupentixol (oil solution in ampoules)
36. Furosemide (solution in ampoules)
37. Gentamicin (ointment, solution in ampoules, eye drops)
38. Glybenclamide (tablets)
39. Haloperidol (solution in ampoules)
40. Imipenem (powder for injections)
41. Indapamide (capsules, coated tablets)
42. Isosorbide mononitrate (tablets)

43. Ketotifen (syrup)
44. Levofloxacin (tablets)
45. Lidocaine (solution in ampoules)
46. Lisinopril (tablets)
47. Losartan (tablets)
48. Metformin (tablets)
49. Metoclopramide (solution in ampoules)
50. Metoprolol (tablets, coated tablets)
51. Metronidazole (suppositories, solution in bottles)
52. Nacom (tablets)
53. Nitrofurantoin (tablets)
54. Ondansetron (rectal suppositories, syrup)
55. Oseltamivir (capsules)
56. Perindopril (tablets)
57. Pilocarpine (ointment, solution in bottles)
58. Prednisolone (ointment)
59. Procainamide (solution in bottles)
60. Promethazine (coated tablets, dragee)
61. Propranolol (solution in ampoules)
62. Pyridostigmine bromide (solution in ampoules)
63. Rifampicin (capsules)
64. Salmeterol+Fluticasone, combined drug (aerosol)
65. Sodium levothyroxine (tablets)
66. Sodium valproate (tablets)
67. Sotalol (coated tablets)
68. Terbinafine (tablets, ointment, cream, gel, spray)
69. Terbutaline (solution in ampoules)
70. Tramadol (solution in ampoules, suppositories)
71. Trihexyphenidyl (tablets)
72. Vancomycin (capsules)
73. Warfarin (tablets)
74. Zidovudine (capsules)
75. Zolpidem (tablets)

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## GENERAL PRESCRIPTION

### INTRODUCTION

General Prescription contains the structure of the prescription, rules of making a prescription and writing out a prescription of some medicinal forms. It is the part that starts up the course in Pharmacology. Student after studying general prescription should be able to write out prescriptions for drug administration in different medicinal forms.

The authors suppose this material to be of help not only in the study of Pharmacology, but also as a source of information on the rules of writing out prescriptions in the future study of clinical medicine.

The main pharmacological concepts are as follows: medical substance, drug and medical form.

Medical substance is a specific chemical compound with pharmacological or/and biological effect.

Medicinal product is a pharmacological substance containing one or several medicinal substances used for treating some diseases.

Medicinal drug is medicinal product in definite drug formulation.

Due to the consistency, we can distinguish solid, liquid or soft medical formulation. There are medicinal forms for external or internal usage, for inhalations and injections according to administration routes.

### PHARMACOPEIA

Pharmacopeia (via Merriam-webster dict.) is a book describing drugs, chemicals and medical preparations, issued by an officially recognized authority and serving as a standard.

There exist two types of pharmacopeia: international and public.

International pharmacopeia consists of different types of recommendations and general principles of creating/distribution of different medicinal formulation and drugs. It's a type of informative paper. World Health Organization (WHO) is responsible for international pharmacopeia.

Public pharmacopeia is based on the international one and is an example of legislative paper. Each country has its own public pharmacopeia.

### PRESCRIPTIONS

Prescription is a written application of a medical doctor to a pharmacist which contains information about the drug in a definite formulation and description of administration route.

In the following piece of information, we are going to describe certain rules to write out a prescription correctly.

To write out a prescription, MD has to fulfill a special medical form. For addictive substances, MD has to use a pink-paper prescription form (the color may vary in different countries). The prescription should be fulfilled without any correction. In one prescribed form, not more than two normal drugs or one addictive substance can be prescribed.

Every prescription can be divided into five parts.

The 1<sup>st</sup> one — *inscription* (lat. inscription) — contains the information on date, the name, surname and age of the patient, as well as the name and surname of MD.

The 2<sup>nd</sup> one — *compellation* (lat. compellatio, invocatio) — is a compellation of MD to a pharmacist. MD writes ***Recipe (Rp.)*** here, which means “take”.

The 3<sup>rd</sup> part — *prescription* (lat. praescriptio) — is a list of medicinal substances of definite medicinal drug.

The 4<sup>th</sup> part — *subscription* (lat. subscriptio) — is an instruction to a pharmacist about medicinal formulation of the drug.

The 5<sup>th</sup> part — *signature, designation* (lat. signatura, designatio) — is instruction to the patient on the drug intake — the quantity of tablets, drops, milliliters, etc. and the frequency.

The first four parts are written by MD for a pharmacist in the Latin language, whereas the 5<sup>th</sup> one is addressed to the patient in one of national languages.

MD should finish the prescription with subscribing it and putting his own seal.

The names (trade names) of all active compounds and medicinal drugs, botanic names of drugs components should be written with a capital letter.

Doses of drugs should be written only in grams (for example 0.1, 0.002, 1.0, 10.0, etc.), units of activity (UA), international units (IU) or in milliliters for liquid medicinal formulations (0.2 ml, 2.0 ml, etc.).

In the last part of prescription, MD should write the information about:

1. The route of administration (orally, intravenously, subcutaneously, etc.)
2. The dose of a drug (1 tablet, 5 ml, one table-spoon, 6 drops, etc.)
3. The frequency of administration (2 times per day, every 8 hours, before meal, in the morning, etc.).

## SOLID MEDICINAL FORMS

**Powder** is free-flowing medicinal formulation resulting from mixing of one or several powdered medical substrates. There exist powders for external and internal usage; they can also be complex (powder mixture with two and more active compounds) and simple (one active compound). Powders can be divided and not divided into doses. If powder is divided, it can be written out in packs for internal use. Their weight ranges from 0.1 to 1.0 g.

Powders not divided into doses are usually prescribed for the whole treatment course, and their weight ranges from 5.0 to 100.0 g. In prescribing simple powders, MD should write the name of a drug, its dose and quantity of packs with it. If the weight of active compound is less than 0.1 gram we should add 0.3 gram (minimum) of some inactive substance (sugar or fructose).

Rp.:	Codeini phosphatis 0,015 Sacchari 0,3 M.f. pulvis D.t.d. N 10 S. Принимать внутрь по одному порошку 3 раза в день	R.	Codeine phosphate 0,015 Sugar 0,3 Mix to make powder Give such a dose in the amount 10 Label: Take orally one powder 3 times a day
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Rp.:	Kalii permanganatis 5,0 D.S. Порошок для приготовления раствора	R.	Potassium permanganate 5,0 Give. Label: Powder for solution
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Advantages of powders:

1. Precise dosing
2. Rather long shelf-life
3. Easy to prepare
4. Relatively inexpensive

**Astringent powder** — this powder is administered for external use. The composition of the powders is provided in Pharmacopoeia. They contain one or more medicinal substances mixed with inert powders (talc, starch). Talcum powder is harmful if inhaled since it may cause aspiration pneumonia or granuloma. Astringent powders are applied as an antiseptic and anti-inflammatory medication. *Baby powder* is an astringent powder used for preventing diaper rash in children, as a deodorant, and for other cosmetic purposes. Pediatricians generally prefer cornstarch to talc because it is unlikely to be easily inhaled. Baby powder can also be used as a shampoo, cleaning agent, and freshener. Powders are written out both official and mainly undivided.

Rp.:	Aspersiois Dermatoli 50,0 D.S. Присыпка для детей	R.	Dermatoli 50,0 Give. Label: Baby powder
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**Capsule** is a cover for different types of medicinal compounds in different medicinal formulations: liquids, powders, hydroscopic etc. Capsules prevent drugs from irritating the mucous

membrane, enamel and taste receptors. Capsules are prescribed for oral administration. They can be prepared from starch, gelatin or some other components. The two main types of capsules are:

- Hard-shelled capsules, which are typically made using gelatin and contain dry, powdered ingredients or miniature pellets made by processes of extrusion or spheronization. These pellets are made in two halves: a lower-diameter "body" that is filled and then sealed using a higher-diameter "cap".

- Soft-shelled capsules, primarily used for oils and for active ingredients that are dissolved or suspended in oil.

Rp.:	Chloramphenicoli 0,25 D.t.d. N 20 in capsulis gelatinosis S. Принимать внутрь по одной капсуле 3 раза в день	R.	Capsules of Chloramphenicol 0,25 in amount 20 Give. Label: Take orally 1 capsule 3 times a day
Rp.:	Capsulam Chloramphenicoli 0,25 D.t.d. N 20 S. Принимать внутрь по одной капсуле 3 раза в день		

**Pearl** is a kind of hard gelatin capsules. They have a circular shape and can contain small amounts of drugs. They are used when assigning into vitamin oils. Pearls are prescribed similarly to officinal capsules.

**Cachets** are a kind of hard starch capsules. They are intended for oral administration. Cachets have a larger volume, but they are rapidly dissolved in the stomach. In this regard, the drug is absorbed faster and has a more intensive effect. Cachets are prescribed as officinal capsules as well.

**Pellets implantable** are sterile capsules used for drug delivery implant, often hormones. When replanting under the skin pellet creates a depot from which the drug is slowly absorbed and has an effect for several months. Pellets are prescribed as officinal capsules as well.

**Spansules** are hard gelatin capsules which are filled with a mixture of several kinds of dragee or granules. Typically, each kind of granules is painted in different colors. One spansule may contain from 50 to 400 granules. Spansules are appointed for oral use and are prescribed as officinal capsules as well.

**Tablet** is an officinal pre-dosed preparation of solid medicinal formulation. Tablets can be prescribed for internal, sublingual, intravaginal usage or for the solution. They are stored in special packs called push-trough pack or blisters. Some tablets have special cover, they are called coated tablets. That cover protects the active component of a drug against acid gastric contents.

Tablets are simple and convenient to use. They provide an accurately measured dosage of the active ingredient in a convenient portable package, and can be designed to protect unstable medications or disguise unpalatable ingredients. Colored coatings, embossed markings and printing can be used to aid tablet recognition.

Rp.:	Phenacetini 0,3 D.t.d. N 10 in tabulettis S. Принимать внутрь по одной таблетке 3 раза в день	R.	Tablets of Phenacetin 0,3 in amount 10 Give. Label: Take orally one tablet three times a day
Rp.:	Tabulettas Phenacetini 0,3 N 10 D.S. Принимать внутрь по одной таблетке 3 раза в день		

  

Rp.:	Tabulettam Tetracyclini obductas 0,25 D.t.d. N 20 S. Принимать внутрь по одной таблетке 4 раза в день после еды	R.	Tetracycline coated tablets 0,25 in amount 20 Give. Label: Take orally one tablet 4 times a day after meal
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Most complex tablets have trade names. To write out a prescription of such tablets, MD should write the trade name of a drug in quotes without changing the suffix and then indicate the number of tablets.

Rp.:	Tabulettas «Nicoverinum» N 20 D.S. Принимать внутрь по одной таблетке два раза в день	R.	Nicoverin tablets in amount 20 Give. Label: Take orally one tablet two times a day
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**Sugar-coated pile** (dragee) is an officinal pre-dosed solid medicinal preparation. Dragee have more than one active compound, and to prevent unwanted pharmacological interaction we divide them by a layer of inert compound (sugar, etc.).

Rp.:	Dragee Chlorpromazini 0,25 D.t.d. N 20 S. Принимать по одному драже 3 раза в день	R.	Dragee of Chlorpromazine 0,25 in amount 20 Give. Label: Take 1 dragee three times a day
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**Microdragee** is a dosage form which is produced by coating a drug and an adhesive substance with small grains of sugar. With the aim of prolonged action, microdragee may be coated for retarding dissolution and absorption of the drug. It is possible to pick up a mixture of uncoated microdragee with different time-release drugs and prolongate its duration.

**Pellets** are small particles which have the form of grains. Graining make hygroscopic agents or mixtures more resistant to adverse environmental factors. The unpleasant smell or taste of drugs included in the granules can be adjusted by the addition of sugar or aromatic compounds. If necessary, they can be coated with protective films or membrane intended for indigestion. Pellets are dosed in pieces, by a special spoon or measuring cup. Sometimes, they are used for the preparation of solutions, syrups, medicines.

**Caramel** is a sort of solid medicinal formulation that contains a mixture of medicinal substances and additives (sugar, syrup, etc.).

**Pastilles** are produced in tablet form. They are slowly absorbed, and therefore can have a lasting effect on the oral mucosa, allowing their use in dentistry, for the treatment of sore throat and respiratory diseases. Pastilles are appointed for internal use in case of diseases of the gastrointestinal tract and for resorptive action. A pastille is prescribed as an officinal medicinal form.

**Solvets** are tablets, readily soluble in water. They are intended for the preparation of solutions used topically (as gargles, eye drops, nasal drops, etc.). Solvets are prescribed by the same rules as officinal tablets.

**Poultice** is a semi-solid mass. Poultices are intended for external use like an application. Usually such applications on the skin cause congestion, improve blood circulation, have anti-inflammatory, antiseptic and protective action. Poultices are prescribed as an officinal medicinal form.

**Lamellae** or disks are a form of eye and are used in ophthalmic practice. They consist of the drug substance, gelatin and water. Lamellae have the shape of a disk with a diameter of 3 mm and are placed for eyelid. Lamellae are prescribed by rules prescribing the officinal formulations.

**Salts** are effervescent powdered mixture consisting of drug substance, sodium hydrogen carbonate and tartaric or citric acid. When dissolving them in water, a large number of bubbles of carbon dioxide (the interaction with sodium hydrogen carbonate acid) are formed. The effervescent salts are written out as other officinal forms as well.

**Medicinal pencils** are designed for external use. They are shaped rod with a pointed ending. The dosage form of pencils includes substances with astringent or cauterizing action. They are applied for lubricating the skin or mucous membranes.

### Names of the solid drug forms

Russian	Latin	English
глоссета	glossetta	glossette
гранула	granulum	granule
драже	dragee	sugar-coated pile, dragee
карамель	caramel	caramel
карандаш лекарственный	stylus medicinalis	stylus, medicated pencil
капсула	capsula	capsule
кахета	cacheta	cachet
ламелля (диск глазной)	lamella	lamell (ophthalmic disc)
пастилка	trochiscus	pastille
пеллета	pelleta	pellet
перла	perla	pearl
порошок	pulvis	powder
припарка	cataplasma	poultiche
соль шипучая	sal effervescens	effervescent salt
сольвелла	solvella	solution-tablet
таблетка	tabuletta	tablet

### LIQUID MEDICINAL FORMULATIONS

**Solution** is a medicinal formulation received after dilution of solid, liquid or gaseous compounds in the water or other solvents. As a solvent, we can use distilled water, ethanol, glycerin and different oils.

We can write the concentration of a solution in different ways: in percentages, in ratio (for example 1 : 500), and sometimes in mass/volume ratio (for example 0.1 — 500 ml).

There exist two types of solutions: for **oral administration** and **for external use**.

Solutions **for external use** are as follows: lotions, eye, nose and ear drops. The volume of lotions is from 50 to 500 ml, drops usually prescribed in 5–10—20 ml.

Solutions may be prescribed by expanded manner — showing the number of solute and solvent or shortened — indicating the concentration.

Rp.:	Furacilini 0,1 Aquaе destillatae ad 500 ml M.D.S. Для полосканий горла	R.	Furacilin 0.1 Distilled water 500 ml Mix to make solution Give. Label: For gargle
Rp.:	Sol. Furacilini 0.02 % — 500 ml D.S. Для полосканий горла	R.	Solution of Furacilin 0.02 % — 500 ml Give. Label: For gargle
Rp.:	Sol. Furacilini 1 : 500 — 500 ml D.S. Для полосканий горла	R.	Solution of Furacilin 1 : 500 — 500 ml Give. Label: For gargle
Rp.:	Sol. Furacilini 0,1 — 500 ml D.S. Для полосканий горла	R.	Solution of Furacilin 0.1 — 500 ml Give. Label: For gargle

For external application and rinses can be used officinal solutions, the concentration of which is determined by Pharmacopoeia. In this case, only the name of solution and its quantity are prescribed. Such solutions are available in ready-official forms for external use.

**Colliers** are solutions of medicinal substances used as washes and lotions for the eyes.

**Collodion** is a nitrocellulose solution in alcohol and ether (1 : 7), to which are added drugs.

**Collutory** is a liquid mouthwash. Collutories are used as aqueous solutions of antiseptic and binders and usually have a complex structure.

**Gargles** are liquid preparations intended for rinsing the mouth and throat. They cannot be swallowed.

**Glycerin** is an antiseptic solution, and a binder in glycerol.

**Irrigation** is a liquid formulation intended for washing the surface of the skin and wounds.

**Lotions** are liquid preparations for application to the skin. They provide cooling or antiseptics. Some lotions are prepared specifically for flushing eyes, ears, nose and throat.

**Paints** are alcoholic, alcohol-aqueous or aqueous solutions of organic dyes intended for the lubrication of infected wounds.

**Spray** is an aqueous, alcoholic or oily solution of drugs for nose or throat. It is used by means of a track sprayer as well as for application to the skin.

**Oleates** are solutions of alkaloids or metal oxides in oleic acid.

**Soap** is a medical preparation based on a conventional soap with the addition of drugs.

**Applications** are the official medicines of liquid or pasty consistency, intended for application to the skin or to kill parasites.

**Liniment** is thick liquid or gelatinous mass, applied topically. Liniments can be solutions, emulsions or combined dispersions.

Solutions for oral administration. We can dose this type of solutions with different spoons: tea-spoon (5 ml), dessert-spoon (10 ml), table-spoon (15 ml). One drug is usually prescribed for 10–15 administrations. The range of the volume of the solution is from 50–60 ml to 180 ml.

Rp.:	Sol Natrii salicylatis 10 % — 180 ml D.S. Принимать внутрь по одной столовой ложке три раза в день	R.	Solution of Sodium salicylate 10 % — 180 ml Give. Label: Take one table-spoon three times a day
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In case that single dose is tiny, we can use drops. Such types of solutions are prescribed from 5 ml to 20 ml. You should remember that 1 ml of water solution contains 20 drops, 1 ml of oily solution — 30 drops and 1 ml of spirituous solution — 60 drops.

Rp.:	Sol. Atropini sulfatis 0,1 % — 10 ml D.S. Закапывать по одной капле в оба глаза три раза в день	R.	Solution of Atropine sulfate 0.1 % — 10 ml Give. Label: Instill the one drop three times a day
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**Suspension** is a liquid medicinal formulation received from the mixture of insoluble solid compounds with different liquids. Suspensions can be prescribed for oral administration, in the form of ear drops, nasal drops or eye drops, for enteral and parenteral use intravenously/intramuscularly/subcutaneously.

There are two ways of writing out a prescription:

Expanded form:

Rp.:	Hydrocortisoni acetatis 0,05 Aquaе destillatae 10 ml M.f. suspensio D.S. Закапывать в оба глаза по две капли два раза в день. <u>Перед использованием взболтать</u>	R.	Hydrocortisone acetate 0,05 Distilled water 10 ml Mix to make suspension Give. Label: Instill in the eyes two drops two times a day. <u>Shake before use</u>
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Short form:

Rp.:	Suspensionis Hydrocortisoni acetatis 0,5 % — 10 ml D.S. Закапывать в оба глаза по две капли два раза в день. <u>Перед использованием взболтать</u>	R.	Suspension of Hydrocortisone acetate 0.05 — 10 ml Give. Label: Instill in the eyes two drops two times a day. <u>Shake before use</u>
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**Emulsion** is a liquid medicinal formulation received from the mixture of insoluble liquid compounds in liquids, so the active compound is in form of tiny drops.

There are emulsions for oral administration, for external use and for intramuscular injections. They can have oily and seed base.

All oily emulsions consists of water, oil and emulgator in the ratio of 17 parts of water, 2 parts of oil and 1 part of emulgator.

For the preparation of oily emulsion, different types of oils can be taken:

1. Castor oil — oleum Ricini
2. Almond oil — oleum Amygdalarum
3. Apricot kernel oil — oleum Persicorum
4. Liquid paraffin — oleum Vaselini

Rp.:	Emulsi olei Amygdalarum 200 ml D.S. Принимать внутрь по одной столовой ложке три раза в день	R.	Emulsion of Almond oil 200 ml Give. Label: Take orally one table-spoon three times a day
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If the methods of preparations, doses of active components and its concentrations are described in pharmacopoeia — such drugs are called **officinal**. When we are going to write out a prescription of officinal drug we just have to write the name and the quantity.

Rp.:	Solutionis Formaldehydi 200 ml D.S. Для хирургического отделения	R.	Solution of Formaldehyde 200 ml Give. Label: For department of surgery
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The following drug forms are available in ready-official formulations for oral administration:

**Draught** — liquid medicine, intended for a single oral administration.

**Liquors** — water and alcohol solutions of one or more drugs.

**Limonades** — sweet acidified liquid intakes. They are prepared by dissolving in water and hydrochloric simple syrup, citric, tartaric, phosphoric or lactic acid.

**Wines medical**. Pharmacopoeia of some countries provides medical drug wines as herb infusions prepared from grape wine or dissolving the drug in the wine.

**Magma** is water precipitates, similar large-particulate suspensions intended for oral administration.

**Gels** are semi-colloidal formulations, which can be regarded as a variety of suspensions. They are used inside and externally.

**Jellies** are homogeneous masses like gels.

**Lavations** are solutions for administration in the rectum as nutritional or therapeutic enema.

## LIQUID DOSAGE FORMS IS OBTAINED FROM HERBAL RAW MATERIALS

**Infusions and decoctions** are liquid medicinal forms preparing in a drugstore from the different types of herbs. They are water extracts from medical herbs. These medicinal formulations contain a lot of active compounds. The sources for infusions are leaves, flowers and herbs. All of them contain a lot of glycosides and ether oils.

For preparing the decoctions, we can use solid parts of plants: roots, rootstocks and cortex. Active compound can be extracted only under high temperature and prolonged heating.

Infusions and decoctions are usually administered orally and sometimes for gargling. For oral administration infusions are prescribed for 10–12 administrations because a ready form can be used only during 3–4 days.

### Infusions and decoctions

Medicinal formulation	Parts of plants	Extracting liquid	Heating time	Cooling time	How to use
Infusion	leaves, flowers, herbs	distilled water	15 min	45 min	cold
Decoction	cortex (bark), roots, rootstocks	distilled water	30 min	10 min	hot

Rp.:	Infusi herbae Thermopsidis 0,6 — 180 ml D.S. Принимать внутрь по одной столовой ложке 6 раз в день	R.	Infusion of Thermopsis herb 0.6 — 180 ml Give. Label: Take it orally one table-spoon 6 times a day
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Rp.:	Decocti corticis Quercus 200 ml D.S. Для полосканий горла	R.	Decoction of Oak bark 200 ml Give. Label: For gargling
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**Aromatic waters** are water extracts from plant material containing ester oil. They are transparent, slightly opalescent and have the smell of their constituent substances.

Aromatic water is generally used to correct the taste or odor of drugs. Some of them have an independent therapeutic effect, due to the presence of antiseptic properties and ability to increase locomotor activity and the suction capacity of the gastrointestinal tract.

Aromatic water is officinal non-dosed dosage form:

Rp.:	Aquae Foeniculi 100 ml D.S. Внутрь по одной чайной ложке три раза в день	R.	Fennel aromatic water 20 ml Give. Label: Take orally one tea-spoon 3 times a day
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**Medicinal pickings** are officinal non-dosed dosage forms. It is a mixture of milled parts of dried herbs sometimes mixed with ester oils and solid crystalline substances. Medicinal pickings are the oldest and simplest forms of use of medicinal plants. They are designed for making infusions or decoctions at home and are used orally or topically in the form of lotions, rinsing baths. There are medicinal herbal mixtures for smoking. Medicinal pickings are released in carton boxes or bags to 50.0; 150.0; 200.0. Since the drug charge dosing makes the patient him-self, the composition of medicinal pickings does not include toxic and potent plants. The signature must specify the method of preparation and usage of drugs.

Rp.:	Specierum polivitaminicarum 100,0 D.S. 1 столовую ложку заварить в одном стакане кипятка и принимать в охлажденном виде по 1/2 стакана 2 раза в день	R.	Multivitamin medicinal picking 100.0 Give. Label: 1 tablespoon brewed in one glass of boiled water and take in the chilled 1/2 cup 2 times a day
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**Galenic drugs** (in honor of ancient Roman scientist) are tinctures, extracts and spirituous. All the Galenic drugs are officinal. **Neo Galenic drugs** are like **Galenic** ones, but they are more purified due to modern manufacturing processes.

**Tincture** is a liquid medicinal form, spirituous infusion from the different parts of plans made with no heating. Tinctures are usually more concentrated than other types of solutions, that's why they are prescribed in bottles of 5–30 ml and are administered in drops.

Rp.:	Tincturae Valerianae 20 ml D.S. Принимать внутрь по 25 капель 3 раза в день	R.	Valerian tincture 20 ml Give. Label: Take orally 25 drops 3 times a day
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**Extract** is concentrated infusion of active components from different types of plants. The making process is the same as that in tinctures, but extract concentrate remains much more under high temperature. Extracts have liquid, thick and moisture-free forms depending on the technology.

Rp.:	Extracti Viburni fluidi 20 ml D.S. Принимать внутрь по 20 капель 3 раза в день	R.	Liquid extract of Viburnum 20 ml Give. Label: Take orally 20 drops 3 times per day
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**Syrup** is concentrated solution of sugar with addition of some active compounds.

Rp.:	Sirupi Sennae 150 ml D.S. Принимать внутрь по одной чайной ложке 3 раза в день	R.	Senna syrup 150 ml Give. Label: Take orally one tea-spoon 3 times a day
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**Spirituos** are alcohol or water-alcohol solutions of different ethers or other volatiles. Usually, they are prescribed for external applications, rarely as a component of injections. All the spirituous are officinal.

Rp.:	Spiritus camphorati 50 ml D.S. Для растирания суставов	R.	Camphor alcohol 50 ml Give. Label: For the massage of joints
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**Balsams** are liquids with an aromatic odor. A balsam is composed of essential oils, resins, aromatic compounds, esters. Balsams have antiseptic properties, eliminate odors, have anesthetic and expectorant activity, and increase urination.

**Elixirs** are tinctures, which contain essential oils and tar extracts.

**Drinks** are a liquid dosage form, which comprises an active substance, water and various syrups.

**Mucilage** is a thick viscous liquid obtained by dissolving in water gums, starch or treating plant material comprising mucous substances. Mucous substances are nitrogen-free organic compounds such as high polymer polysaccharides. The most important mucilages are those of acacia, Irish moss, starch, althaea root.

Mucilage has a shielding effect, reduces inflammation and irritation, makes difficult absorption of co-administered drugs, delay onset of effect and prolong their action. This makes it possible to achieve more uniform dosing suspension.

Mucilage drugs should not be prescribed together with alcohol, acids, alkalis, large amounts of electrolytes. This causes coagulation of proteins and damages the mucus. All mucilages are officinal. When prescribing them, the dosage form, the name of the medicinal plants and the total amount of mucus are indicated. Mucilage may be prescribed alone as a coating agent for acute gastritis, poisoning, but mostly it is a part of the medicines containing drugs with an irritating effect.

**Resin** is a concentrated alcohol extract from plant material the preparation of which is followed by evaporation and precipitation of active substances in water.

**Oleoresins** — liquid extracts containing volatile oils or resins.

**Fluid glycerin** is a liquid preparation obtained by extraction of plant material with a mixture of glycerol and water.

**Mixture** is a blend of different medicinal formulations one of which is liquid. We can mix some solid active components with the liquid ones. Mixtures are usually prescribed for oral administration, rarely for external use.

Rp.:	Codeini phosphatis 0,1 Barbitali-natrii 2,0 Sirupi simplicis 15 ml Aquaе destillatae ad 150 ml M.D.S. Принимать внутрь по одной столовой ложке три раза в день	R.	Codeine phosphate 0.1 Barbital-sodium 2.0 Sugar syrup 15 ml Distilled water 150 ml Mix. Give. Label: Take orally one table- spoon three times a day
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#### Names of the liquid drug forms

Russian	Latin	English
аппликация	applicatio	application
ароматная вода	aqua aromatica	aromatic water
бальзам	balsamum	balsam
вино медицинское	vinum medicinale	vine medicinal
гель	gelum	gel
глазные капли	oculoguttae	eye drops
глазные примочки	collyria	eye- wash, eye lotion
глицерин	glycerinum	glycerin
глоток	haustus	draught

<b>Russian</b>	<b>Latin</b>	<b>English</b>
души (промывания)	perlutiones	douche
жидкость, ликер	liquor	liquor
капли	guttae	drops
капли для носа	naristillae	nasal drops
клизма	enema	lavage, lavation, lavement
коллодий	collodium	collodion
краска	pigmentum	paint
лимонад	limonatum	limonade
линимент	linimentum	liniment
линктус	linctus	linctus
лосьон	lotio	lotion
магма	magma	magma
масло	oleum	oil
микстура	mixtura	mixture
мыло	sapo	soap
напиток	potio	potion
настой	infusum	infusion
настойка	tinctura	tincture
обмывание	irrigatio	irrigation
олеат	oleatum	oleate
орошение	nebula	spray
отвар	decoctum	decoction
полоскание для горла	gargarisma	gargle
полоскание для рта	collutorium	mouth- wash
раствор	solutio	solution
сироп	sirupus	syrup
слизь	mucilago	mucilage
смола	resina	resin
спирт	spiritus	spirit
студень	gelatum	jelly
суспензия	suspensio	suspension
ушные капли	auristillae	ear-drop
шампунь	champoo	sampoo
экстракт	extractum	extract
эликсир	elixir	elixir
эмульсия	emulsum	emulsion

## MEDICINAL FORMS FOR INJECTION

**Injections** are groups of drug in different sterile medicinal formulations (solutions, powders, suspensions, emulsions) aseptically packed and used for parenteral infusions.

Drugs for injections can be in ampules or bottles made of special glass in aseptic environment. Drugs for injections usually are prescribed for intravenous, intramuscular or subcutaneous injections, etc. Usually drugs for one injection are administered in ampules, for several injections — in bottles. Nowadays we also can use unit-dose syringe.

Almost all medicinal formulations for injections are officinal. As solvents we can take special water for injections (lat. Aqua pro injectionibus), 5 % glucose solution, 0.9 % Sodium-Chloride solution, 33 % ethyl alcohol, etc.

Advantages of injections are the following:

1. Rapid onset
2. Precise dosing
3. No effects of the enzymes of GI tract on the drug

Rp.:	Solutionis Atropini sulfatis 0,1 % — 1 ml D.t.d. N 10 in ampullis S. Подкожно 0,5 мл 2 раза в день	R.	Solution of Atropine sulfate 0.1 % — 1 ml Send 10 ampoules Give. Label: Subcutaneously 0.5 ml 2 times a day
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Rp.:	Suspensionis Hydrocortisoni acetatis 2,5 % — 5 ml D.t.d. N 10 in ampullis S. Вводить в полость сустава по 5 мл один раз в неделю	R.	Suspension of Hydrocortisone acetate 2.5 % — 5 ml Send 10 ampoules Give. Label: Inject in joint cavity 5 ml one time per week
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Rp.:	Streptoliasi 250 000 ED D.t.d. N 6 in ampullis S. Растворить содержимое ампулы в 100 мл 5 % раствора глюкозы, вводить внутривенно капельно	R.	Streptoliase 250 000 UA Send 10 ampoules Give. Label: Dissolve contents of ampule in 100 ml of 5 % glucose solution, inject it intravenously, by drop infusion
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If we prescribe some drug in powder in bottles we do not write the word “bottle” in our prescription.

Rp.:	Benzympenicillini-natrii 500 000 ED D.t.d N 6 S. Содержимое флакона растворить в 2 мл воды для инъекций, вводить внутримышечно, медленно шесть раз в день	R.	Benzympenicillinum-sodium 500 000 UA Give such a dose in the amount 6 Give. Label: Dissolve contents of bottle in 2 ml of water for injection, give it intramuscular six times per day
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## SOFT DRUG FORMS

Soft forms are pastes, ointments, suppositories, plasters, creams etc. They are united within one group. As a basis, they include greases and substances like grease. These substances shouldn't take any harmful effect on the skin, react to the medicinal matters and change during the storage. They must have a capacity of easy joining with drugs, of greasing as well as of melting by the body's temperature. Bases are to be accessible. Depending on the ointment description, some bases have to be well adsorbed by skin, the other by contrast have to remain on the skin like a thin cover. Very important are ointments' abilities of no spoiling clothes, not to leave spots and to be lightly washed off if necessary with the help of soap or without it.

**Ointments** are drug forms for external use. A soft consistence is their typical feature. Ointments consist of a base and of medical matters which are divided within and belong to undivided drug forms. They are prescribed in a recipe with a common amount. Ophthalmic ointments are prescribed in amount of 5.0–10.0. Ointments for treating affected parts of skin are prescribed from 20.0 to 100.0 and more. An ointment consisting of one medical matter and one base is called a simple one. Such an ointment can be prescribed by two ways: 1) by a developed way and 2) by a shorted one:

Rp.:	Anaesthesini 2,0 Vaselini ad 20,0 M.f. unguentum D.S. Для нанесения на пораженный участок кожи	R.	Anaesthesin 2,0 Vaseline to 20,0 Mix to make ointment Give. Label: For putting on the affected part of skin
Rp.:	Ung. Anaesthesini 10 % — 20,0 D.S. Для нанесения на пораженный участок кожи	R.	Ointment of Anaesthesin 10 % — 20.0 Give. Label: For putting on the affected part of skin

Complex ointments include more than one ingredient. Such ointments are prescribed by a developed way:

Rp.:	Acidi borici 2,0 Prednisoloni 0,4 Vaselini Lanolini aa ad 20,0 M.f. unguentum D.S. Смазывать пораженный участок	R.	Boric acid 2.0 Prednisolone 0.4 Vaseline Lanolin of each 20.0 Mix to make an ointment Give. Label: Put on the affected part
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Rp.:	Ichthyolammonii 10,0 Lanolini 45,0 Paraffini flavi mollis 5,0 Misce fiat unguentum Da. Signa: Прикладывать дважды в день к пораженной коже	R.	Ichthammol 10.0 Lanolin 45.0 Yellow Soft Paraffin 5.0 Mix to make ointment Give. Label: Apply twice a day to affected part of skin
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Officinal ointments are prescribed according Pharmacopoeia name without indication of component parts:

Rp.:	Oculenti Hydrocortisoni 5,0 D.S. Глазная мазь	R.	Hydrocortison oculent 5.0 Give. Label: Ophthalmic ointment
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Rp.:	Unguenti Ichthyoli 50,0 D.S. Прикладывать дважды в день к пораженному месту	R.	Ointment of Ichthammol 50.0 Give. Label: Apply twice a day to affected part of skin
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**Pastes** are thick ointments containing 25 % and more (60 %) of powdery substances. When putting on skin, pasts act longer, they have distinctly expressed abilities of adsorbing and drying to some extent. If powdery substances are at the amount of less than 23 %, indifferent powders are added for receiving a paste (talc, zinc oxide, starch).

Many pasts are officinal and are demitted at chemist' shop in ready-made form for use. These pasts are to be prescribed in a shortened way:

Rp.:	Pastae Zinci 25,0 D.S. Наносить на пораженные участки кожи	R.	Zinc paste 25.0 Give. Label: Put on affected parts of skin
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**Suppositories** are divided drug forms which are solid under room temperature and melting under body temperature. One may distinguish rectal suppositories, vaginal suppositories and small stick-bougies. Suppositories include medical substances as well as a base (mostly cocoa oil or its substitute). Medical matters are used in the suppositories for taking a local and resorption effect. Maintenance of a strict dose measuring by prescribing drastic and virulent matters is highly necessary. Vaginal suppositories can be of different forms: globuli, ovules, pessaries. If the suppositories mass has not been indicated by the physician, the rectal suppositories are made up with a mass of 3 grams, the vaginal ones — with a mass of not less than 4 grams. Suppositories are

prescribed by two ways. In the first case, single doses of all ingredients included into a composition are indicated. In the second case, doses are indicated for all the amounts of prescribed suppositories:

Rp.	Chloramphenicoli 0,3 Olei Cacao 3, 0 M.f. supp. rectale D.t.d. N 10 S. По 1 суппозиторию в прямую кишку 2 раза в день	R.	Chloramphenicol 0.3 Cocoa oil 3.0 Mix to make a rectal suppository Give such a dose in the amount 10 Label: One suppository into rectum twice a day
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Official suppositories are prescribed in a shorted form:

Rp.	Supp. "Anusolum" N 6 D.S. По 1 суппозиторию в прямую кишку 2 раза в день	R.	Suppositories of Anusol in amount 6 Give. Label: One suppository into rectum twice a day
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**Plasters** are drug forms for external use. There are two kinds of plasters: 1) solid plasters, which are tight by the room temperature and are getting soft by the body temperature 2) liquid or skin plasters. The second sort of plasters is a fluid which retains a film on the skin after a dissolving agent has been evaporated.

Plasters are commonly distinguished as medicinal and non-medicinal ones. Non-medicinal plasters are used for skin protecting against external influence, for fixing a bandage **ect**.

Medicinal plasters contain pharmacologically active matters. Such plasters are used with the aim of therapeutic influence on skin. Plasters are prescribed according to the rules of the official drug forms.

**Creams** are ready-made drug forms that are less sticky by their consistence than ointments. Cream composition contains medical matters and a basis as well. Creams are used for the treatment of skin diseases.

### Names of the soft drug forms

Russian	Latin	English
крем	cremor	cream
мазь	unguentum	ointment
паста	pasta	paste
пастырь	emplastrum	plaster
суппозиторий	suppositorium	suppository

### Samples of the soft drug forms prescription

Rp.:	Cremoris "Locacorten" 15,0 D.S. Смазывать 2-3 раза в день	R.	Locacorten cream 15 g Give. Label: Apply two or three times daily
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Rp.:	Pastae Xylocaini 15,0 D.S. Для анестезии поверхности слизистой оболочки	R.	Xylocaine Paste 15 g Give. Label: For surface anesthesia of mucosa
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Rp.:	Tubam unguenti "Capsolinum" D.S. Нанести плотным слоем на пораженный участок и растирать	R.	One tube of Capsolin Give. Label: Rub tightly on affected area
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Rp.:	Supp. "Cortisolum" N 10 D.S. Принимать три раза в день	R.	Cortisol suppositories in amount 10 Give. Label: Take three times a day
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## MEDICINAL AEROSOLS

Medicinal aerosols include inhalations, properly aerosols, vapors, vitrellas.

**Inhalations** are drug forms which are intended for introduction of a drug in the form of the finest drops (not more than a few microns) into inferior parts of respiratory ways. The active matters take hereby a local effect and can be adsorbed from the lungs into the blood and manifest resorption effect.

Nowadays, the officinal inhalations are used in medicine and are prescribed in accordance with officinal drug form prescriptions. However, magistery mixtures or solutions can be used, too.

Rp.:	Inhalationis Salbutamoli 10 ml D.S. Для ингаляций	R.	Salbutamol inhalations 10 ml Give. Label: For inhalations
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**Aerosols** are minute particles of liquid and solid matters which are thinly atomized in a gas or in a gas mixture. Dimensions of aerosol particles are several microns, and when the extent of dispersion is increasing, the drug activity rises as well. Aerosols are used for drug introduction into the alveolar system of lungs or for external use.

Aerosols are prescribed in accordance with the rules of ready drug form prescriptions.

**Vapors** are officinal drug forms which have solid or liquid consistence under room temperature and begin vaporizing by a small heating. Vapor formed in process of this vaporization is inhaled for receiving a local effect on the respiratory ways. Some preparations are already able to form vapors under room temperature, that's why they are given out in inhalants.

**Vitrellas** are ampoules of a thin glass which are inserted into a soft tissue and contain volatile matters (liquids). When crushing an ampoule, the liquid impregnates the tissue and is evaporated. A medical effect develops very quickly by inhaling these vapors through the nose. Vitrellas are prescribed in accordance with the rules of prescribing the officinal drug forms.

### Names of drug forms which are similar to aerosols

Russian	Latin	English
аэрозоли	aërosola	aerosols
витрелли	vitrellae	vitrellas
ингаляции	inhalationes	inhalations
пары	vapores	vapors

**BRIEF REFERENCE INFORMATION ON THE MAIN DRUGS  
OF VARIOUS PHARMATHERAPEUTIC GROUPS**

Drug name	Medicinal forms	Average therapeutic doses and the routes of administration
ACICLOVIR	Bottles 0.25; tablets 0.2	Adults and children over 12 yrs.: 5 mg/kg i/v every 8 hrs. (to be injected slowly). Children 3 mo–12 yrs.: 5 mg/kg; the contents of bottle to be dissolved in 10 ml of 0.9 % NaCl solution. <i>Herpes simplex</i> — Adults: orally 200 mg 5 times a day; prophylaxis: 1 tab 4 times a day. <i>Herpes zoster</i> — 800 mg 5 times a day
ALENDRONIC ACID	Tablets 0.01	Orally 10 mg once a day 30 min before meals
ALFACALCIDOL	Tablets and capsules 0.25, 0.5 and 1 mcg; 0.0009 % oil solution in bottles 5 and 10 ml for oral use; 0.0002 % 20 ml solution in bottles for oral use and for injections in vials 0.5 and 1 ml	Orally 1 times a day (in the morning): adults with osteoporosis 0.0005–0.001 mg, with rickets and osteomalacia 0.001–0.003 mg, with osteodystrophia 0.002 mg per day
ALLOPURINOL	Tablets 0.1	Orally 100–300 mg as a single dose pc with plenty of water daily; if necessary up to 400–600 mg a day in 2–4 doses
ALPRAZOLAM	Tablets 0.00025, 0.0005	Orally 0.25–0.5 mg 3 times a day
ALTEPLASE	50.0 mg powder in bottles	The contents of the vial dissolve in 50 ml of of saline solution. Introduce 15 ml i/v with jet, in a subsequent i/v with drip
AMANTADINE	Tablets 0.1	Orally (after meal), start with 0.05–0.1 g, first 2 doses 3–4 times a day; daily dose 0.2–0.4 g
AMIKACIN	0.1, 0.25, 0.5 bottles. 5 %, 12.5 % and 25 % solution in ampoules 2 ml. 5 % gel in 30.0 tubes	I/m or i/v 500 mg 3 times a day (the contents of the bottle to be dissolved in 2–3 ml of water for injections)
AMINOPHYLLINE	Tablets 0.15; 24 % sol. in amp. 1 ml for i/m injections and 2.4 % sol. in amp. 5 and 10 ml for i/v injections	Orally 1 tablet 3 times a day (after eating); i/v 10–20 ml of 2.4 % solution; i/m 1 ml of 24 % solution
AMIODARONE	Tablets 0.2; 5 % solution in 3 ml ampoules	Orally 200 mg 2–3 times a day; i/v 5 mg/kg (slowly in 250 ml of 5 % glucose solution)
AMITRIPTYLINE	Tablets 0.025; 1 % solution in 2 ml ampoules	Orally 15–25 mg a day, i/v or i/m in 3–4 doses (injections)
AMLODIPINE	Tablets 0.005	Orally 5 or 10 mg once a day
AMOXICILLIN	Tablets 0.5, 0.75, 1.0; soluble tablets 0.125, 0.25, 0.5; capsules 0.25, 0.5; 1.0 g/1 ml solution (per os); 0.125 g/, 0.25 g/5 ml suspension (per os)	Adults: orally 500 mg 3 times a day; children under 2 yrs.: orally 20 mg/kg 3 times a day; children 2–5 yrs.: orally 125 mg 3 times a day; children 5–10 yrs.: orally 250 mg 3 times a day
AMPHOTERICIN B	Powder 50 000 IU in bottles: a) for i/v injection; b) for inhalations; 30 000 IU/1.0 g ointment in tubes 15.0 and 30.0	I/v, by drop infusion; the contents of the bottle dissolve in 10 ml of water for injections, then in 450 ml of 5 % glucose solution (122 IU/1 ml) during 4–6 hrs. (250 IU/kg). 50 000 IU/10 ml inhalations 1–2 times a day. A thin layer of the ointment to be applied 1–2 times a day on the affected area of the skin
APREPITANT	Capsules 80 and 125 mg	Orally in the first day 125 mg; in the 2nd and 3rd day at the morning — 80 mg
ARTHROTEC	Tablets	Orally, 1 tablet 2–3 times a day (last tablet — before going to bed)

Drug name	Medicinal forms	Average therapeutic doses and the routes of administration
ARTICAINE	Solution 1 % and 2 % in ampoules 5 and 20 ml	Routes of administration dependent on the type of anesthesia: infiltrative, conductive (spinal, epidural) by 1–15 ml of 1 % or 2 % sol.
ATENOLOL	Tablets 0.025, 0.05, 0.1	Orally 0.05–0.1 g 1–2 times a day
ATORVASTATIN	Tablets 0.01, 0.02	Orally 10–40 mg once a day
ATROPINE	Powder, tablets 0.0005; 0.05 % — 0.1 % solution in 1 ml ampoules; 1 % eye ointment	Orally, s/c, i/v or i/m 0.25–1.0 mg, or 1–2 drops of 0.5–1 % solution (eye drops) instilled into conjunctival sac; 1 % eye ointment; maximal single dose 1 mg; maximal daily dose 3 mg
AZITHROMYCIN	Tablets 0.125, 0.5; capsules 0.25; syrup in bottles (0.1 g, 0.2 g/5 ml)	Orally once a day. Adults: 500 mg; children: 10 mg/kg
BENZATINE BENZYL PENICILLIN	Bottles 300 000 IU, 600 000 IU, 1200 000 IU, 2 400 000 IU	I/m 300 000–600 000 IU i/m once a week, or 1 200 000–2 400 000 IU (in 2–3 ml of water for injections) once per 2 weeks
BENZYL PENICILLIN	Bottles 250 000 IU, 500 000 IU, 1000 000 IU	I/m 250 000–500 000 IU 4–6 times a day; by slow i/v injection 1–2 million IU in 5–10 ml; i/v 2–5 million IU in 100–200 ml of NaCl isotonic solution; (1000 IU/1 ml) once a day
BENZYL PENICILLIN PROCAINE	Bottles 300 000 IU, 600 000 IU, 1200 000 IU, 3000 000 IU and 4000 000 IU	I/m 300 000–500 000 IU 2 times a day; contents of the bottle is diluted in 2.4 ml of water for injection
BERODUAL	Aerosol with a metering valve, 15 ml (300 doses). Each dose contains 0.05 mg of fenoterol hydrobromide and 0.02 mg of ipratropium bromide	For inhalation of 1–2 doses three times a day
BETAXOLOL	Tablets 0.01 and 0.02; 0.25–0.5 % solution in 2.5 ml, 5 ml, 10 ml, 15 ml bottles	Orally 10–20 mg once a day; 1 drop of 0.25–0.5 % solution instilled into conjunctival sac 2 times a day
BISOPROLOL	Tablets 0.005 and 0.01	Orally 1–2 tablets a day
BRUSTAN	Tablets	Orally 1 tablet 3 times a day
CALCITONIN	Solution for injection in 1 ml ampoules (100 IU); nasal spray in 2 ml aerosol bottles (200 IU) with pump-sprayer	I/m 100 IU every other day (if there are severe pains in the bones every day), intranasal 200 IU daily
CANDESARTAN	Tablets 0.008, 0.016	Orally 8–16 mg once a day
CARBAMAZEPINE	Tablets 0.2	Orally 100–200 mg 2–4 times a day
CARVEDILOL	Tablets 0.00625, 0.0125 and 0.025	Orally 0.0125 once a day
CEFACLOX	Capsules 0.25; 0.5; granulated material to prepare oral suspension (0.025 g/0.05 g/1 ml); oral suspension (0.125 g/0.25 g/5 ml); dry substance to prepare suspension 1.5 g (0.125 g/5 ml) and 3.0 g (0.5 g/5 ml)	Orally 250 mg 3 times in 24 hours; children 10 mg/kg per dose
CEFEPIM	Bottles 0.5; 1.0; 2.0	I/m, i/v 500–1000 mg every 12 hours
CEFOTAXIME	Bottles 0.25, 0.5, 1.0 and 2.0	I/m, i/v for adults and children over 12 years 1 g every 8 hours. For i/m injections and i/v the introduction through the jet dissolve with water for injection (0.5 g in 2 ml), for i/v drip dissolve with isotonic sol. NaCl
CEFTAZIDIME	Bottles 0.25; 0.5; 1.0 and 2.0	I/m, i/v 1000 mg every 8 hours or 2000 mg every 12 hours
CEFUROXIME	Powder for injections in bottles, 0.25, 0.75 and 1.5	I/m, i/v 0.5–1.5 g 3 times a day. For children daily dose — 30–100 mg/kg in 3–4 injections
CEPHALEXIN	Capsules and tablets 0.25, 0.5, 1.0. 2.5 % and 5 % suspension for oral use in 60 ml bottles	Orally 0.25–0.5 g 4 times a day. For children daily dose — 25–50 mg/kg



Drug name	Medicinal forms	Average therapeutic doses and the routes of administration
CEFAZOLIN	Bottles 0.125, 0.25, 0.5, 1.0 and 2.0	I/v, i/m 0.25–0.5 3 times a day. Dissolve in isotonic NaCl
CHLORAMPHENICOL	Tablets 0.25; 0.5; coated tablets 0.25; capsules 0.1; 0.25; 0.5; 0.25 % eye drops in 10 ml bottles	Orally 250–500 mg 3–4 times in 24 hours; eye drops: 1 drop 3 times in 24 hours
CHLOROCHINE	Tablets 0.25; 5 % solution in 5 ml ampoules	Orally (after meal) 200–250 mg per one course of treatment, the 1st intake 100 mg, in 6–8 hrs. 500 mg, for 2nd or 3rd day 500 mg; i/m 500 mg every 6–8 hrs.; i/v slowly 500 mg, dissolved in 10–20 ml of 0.9 % NaCl solution
CHLORPROMAZINE	Dragees 0.025; 0.05 and 0.1; coated tablets 0.01 for children; 2.5 % solution in 1; 2; 5 and 10 ml ampoules	Orally (1 dragees 3 times a day); i/m up to 0.6 g a day; i/v 0.025–0.05 g (no more than 0.1 g) in 24 hours. Children depending on their age 0.04–0.075 g in 24 hours
CHLORTHALIDONE	Tablets 50 and 100 mg	Orally 25–100 mg once at the morning
CIPROFLOXACIN	Coated tablets 0.25; 0.5; 0.75; 0.2 % solution in 50 and 100 ml bottles; 1 % solution in 10 ml ampoules	Orally 125–500 mg 2 times a day; i/v 100–200 mg 2 times a day
CLARITHROMYCIN	Tablets 0.25, retard-tablet 0.5, powder for suspension (1.5 and 2.5); bottles 0.5	Orally 0.5–1.0 every day. I/v slowly 1.0 per day (in 2 receiving)
CLENBUTEROL	Tablets 0.02 mg; syrup 0.0001 % and 0.0002 % — 100 ml	Orally ½–1 tablet 2 times a day; 5–10 ml syrup 2 times a day, for children from 2.5 to 10 ml
CLINDAMYCIN	Capsules 0.15; 0.075 (for children); 15 % solution in 2, 4, 6 ml ampoules; syrup in 80 ml bottles (75 mg/5 ml)	Orally, adults: 150 mg every 6 hours; children: 10–20 mg/kg in 3–4 doses; i/m and i/v (driply): adults: 600 mg 2–4 times a day; children: 1–30 mg/kg a day in 2–4 doses
CLONIDINE	Tablets 0.000075 and 0.00015; 0.01 % solution in 1 ml ampoules; 0.125 %; 0.25 % and 0.5 % solution (eye drops) in 1.5 ml tube-droppers	Orally 0.075 mg 2–4 times a day; i/v or s/c 0.5–1.5 ml of 0.01 % solution; i/v dissolved by 0.5–1.5 of 0.01 % solution in 10–20 isotonic solution NaCl and infused slowly during 3–5 min. Instillations in conjunctival sac 0.25–0.5 % solution 1 drop 2–4 times a day
CLOPIDOGREL	Coated tablets 0.075	Orally 1 tablet once a day without regard to food
CLOZAPINE	Tablets 0.025 and 0.1	Orally 1–2 tablets once a day
CODEINE	Powders and tablets 0.015	Orally, adults: 10–20 mg; children: over 2 years 1–7.5 mg once a day depending on the age (under 2 years are not administered); maximal single dose for adults orally 50 mg; maximal daily dose 200 mg
COLISTIN	Pwder for injections and inhalations 2'000'000 IU	I/v 2'000'000 IU in 200 ml isotonic NaCl. 1 inhalation 2 times a day
CO-TRIMOXAZOLE	For adults: tablets sulphametoxazole 0.4 and trimetoprim 0.08; for children 0.1/0.02; oral suspension (0.2/0.04/5 ml) 480 ml; 3 ml ampoules (0.08/0.015/1 ml)	Orally 2 tablets 2 times a day; suspension 5 ml 2 times a day; i/m for adult and child under 12 years 3 ml 2 times a day
CYPROTERONE ACETATE	Tablets 0.01 and 0.05; 10 % oil solution in ampoules 3 ml	Orally 0.05 2 times a day; i/m 3 ml every 10–14 days
DABIGATRAN	Capsules 75, 110, 150 mg	Orally 110–300 mg 1–2 times a day
DARIFENACINE	Coated tablets 7.5 mg	Orally 1 tablet once a day
DARUNAVIR	Coated tablets 0.4 and 0.6	Orally 1 tablet at the morning
DEXAMETHASONE	Tablets 0.0005	Orally 0.5–1 mg once a day
DIAZEPAM	For children: tablets 0.001, 0.002; 0.005, 0.01; 0.5 % solution in 2 ml ampoules	Orally 5–10 mg 1–2 times a day; children (depending on age): daily dose 2–10 mg. I/m or i/v 10 mg 3 times a day

Drug name	Medicinal forms	Average therapeutic doses and the routes of administration
DIGOXIN	Tablets 0.00025, 0.0001; 0.025 % solution in 1 ml ampoules	Orally, the 1st day 0.25 mg 4–5 times a day, later 0.25 mg 3–1 times a day. I/v slowly 0.25–0.5 mg in 10 ml of 5 % or 20 % glucose solution 1–2 times a day
DILTIAZEM	Coated tablets 90 and 180 mg	Orally 1 tablet 2 times a day
DIPHENHYDRAMINE	Powder; tablets 0.02, 0.03, 0.05; suppositories 0.005, 0.001, 0.015, 0.02; 1 % solution in 1 ml ampoules	Orally 30–50 mg 1–3 times a day; i/m 10–50 mg; i/v 20–50 mg in 75–100 ml of 0.9 % NaCl solution
DOBUTAMINE	0.5 % solution in ampoules 50 ml, and 1.25 % — 20 ml	I/v 2.5–10 mcg/kg*min. Speed & duration of injection is adjusted depending on the effect
DOPAMINE	0.5 & 1 % solution in ampoules 2 ml; 2 % — 10 ml, 4 % — 5 ml. Dissolve in 5 % glucose or isotonic NaCl	I/v drip: the initial rate of introduction 1–5 mcg/kg*min; if necessary, increased to 10–25 mcg/kg*min; daily dose 400–800 mg
DORIPENEM	Powder for injections 0.5	I/v 500 mg 3 times a day
DORNASE ALFA	Solution for nebulizer 2.5 ml 1000 U (1 mg)/ml	For inhalations 2500 U (2.5 mg) once a day
DOXAPRAM	2 % solution in 5 ml ampoules	I/v slowly at postoperative respiratory depression
DOXAZOSIN	Tablets 0.001	Prostate hyperplasia — orally 1–16 mg once a day; Hypertension — orally 1–8 mg once a day
DOXYCYCLINE	Capsules 0.05, 0.1; coated tablets 0.1; ampoules 0.1 (to be dissolved in 0.9 % NaCl solution mg/ml)	Orally and i/v 100–200 mg once a day
ENALAPRIL	Tablets 0.005; 0.01; 0.02	Orally 10–20 mg once a day
ENFUVIRTIDE	Bottles 0.09 complete with a solvent	Subcutaneously 90 mg 2 times a day
ENOXAPARIN	10 % solution for subcutaneous injections in syringes 0.2, 0.4, 0.6, 0.8 and 1.0 ml (10'000 IU/ml)	Subcutaneously 150 IU/kg (1.5 mg/kg) once a day
ENTACAPONE	Coated tablets 200 mg	Orally 200 mg together with levodopa and dopa-decarboxylase inhibitor
EPLERENONE	Coated tablets 0.025	Orally 1 tablet once a day
ERGOTAMINE	0.05 % solution in 1 ml ampoules; 0.1 % solution in 10 ml bottles; tablets (dragées) 0.001	Orally 1 mg 1–3 times a day; s/c and i/m 0.25–0.5 mg; i/v slowly 0.5 ml of 0.05 % solution
ERYTHROPOIETINS BETA	Bottles 1000, 2000, 3000, 4000 and 5000 U complete with a solvent	Subcutaneously 20 U/kg 3 times a week; 10 U/kg 7 times a week. I/v 40–80 U/kg 3 times a week
ESOMEPRAZOLE	Coated tablets and capsules 0.02 and 0.04	Orally 20–40 mg once a day
ETHAMBUTOL	Tablets 0.1, 0.2 and 0.4. Capsules 0.25	Orally adults 15–30 mg/kg 3 times a week. Children 15–25 mg/kg per day but no more than 1.0
ESTRADIOL	Tablets 0.002	Orally 0.5–1 tablet once a day
ETHOSUXIMIDE	Capsules 0.25; 100 ml bottles of solution for oral administration (contains 5 g of the preparation)	Orally 250 mg 15 drops 1–4 times a day; maintaining dose 250 mg a day
ETHYL ALCOHOL	40 %, 70 % and 95 %	Apply for medical reasons
EZETIMIBE	Tablets 0.01	Orally 1 tablet once a day
FLECAINIDE	Tablets 50, 100, 150 and 200 mg	Orally 50–150 mg 2 times a day
FLUDROCORTISONE	Tablets 0.0001; 0.1 % ophthalmic ointment	Orally 1–3 tablets 1 times a day. Ophthalmic ointment applied 1–3 times a day, no longer than 2 weeks
FLUOXETINE	Capsules 0.02	Orally 20 mg once a day.

Drug name	Medicinal forms	Average therapeutic doses and the routes of administration
FLUPENTIXOL	Tablets (dragee) 0.5 & 1 mg. 2 % and 10 % oil solution in ampoules 2 ml	I/m 0.05–0.2 once every 2–4 weeks
FOLIC ACID	Tablets 1 mg	Orally 1 tablet once a day
FORMOTEROL	Powder for inhalation in capsules 0.00012	0.012–0.024 mg 2–4 times in 24 hours. The medicine is used with the help of the special device «Airolaser»
FOSINOPRIL	Tablets 0.01 and 0.02	Orally 1 tablet once a day
FUROSEMIDE	Tablets 0.04; 1 % solution in 2 ml ampoules	Orally 40 mg once a day (in the morning); In case of insufficient effect the dose should be increased up to 80–120 mg (up to 160 mg) a day in 2–3 doses with 6 hrs. interval). I/m or i/v slowly by stream infusion 20–60 mg 1–2 times in 24 hours
GALANTAMINE	Tablets 5 and 10 mg	Orally 5–10 mg 3 times a day
GENTAMYCIN	Powder in 0.08 g bottles; 4 % solution in 1 ml, 2 ml ampoules; 0.1 % ointment in 10.0, 15.0 tubes; 0.3 % eye drops in tube instillator	I/m or i/v 0.4 mg/kg 2–3 times a day Ointment for external application 2–3 times a day. Eye drops: 1 drop instilled 3–4 times a day
GLIBENCLAMIDE	Tablets 0.005	Orally after meals 1–2 times a day, initially 2.5–5–10 mg
GRISEOFULVIN	Tablets 0.125; 10 % suspension in 100 ml bottles; 2.5 % liniment in 30.0 g tubes	Orally 8 tablets once a day during meals (to be mixed with 1 teaspoonful of vegetable oil); children: 21–22 mg/kg a day. A thin layer of 30 000 mg of the liniment to be applied over the affected area daily
HALOPERIDOL	Tablets 0.5, 1, 1.5, 2, 5 and 10 mg. 0.5 % solution in ampoules 1 ml	Orally 1.5–2 mg once a day. I/m 1 ml once a day
HEPARIN	Bottles 5 and 10 ml, ampoules 1, 2, 3, 5 ml (5000 U in 1 ml)	I/v 60–70 U/kg*hour (up to 5000 U), then drip 12–15 U/kg*hour (up to 1000 U), further infusions controlled by INR
HEXAMETHONIUM	2.5 % solution in ampoules 1 ml	I/m 0.5–1 ml for cupping of a hypertensive crisis
HYDROCHLOROTHIAZIDE	Tablets 0.025, 0.1	Orally 25–50 mg once a day, up to 200 mg a day. As a single dose (in the morning) or divided into two doses (before noon)
HYOSCINE HYDROBROMIDE	Film-coated tablets 0.01; 2 % solution in 1 ml ampoules; rectal suppositories 0.01, 0.0075	Orally 10–20 mg, or 1–2 rectal suppositories 3–5 times a day (adults and children > 6 yrs.). Children 1–6 yrs.: orally 5–1 mg of suspension, or 1 rectal suppository (7.5 mg) 3–5 times a day. Adults: 1–2 ml s/c, i/m or i/v, children: 0.25–0.5 ml s/c, i/m or i/v 3 times a day
IMIPENEM	Imipenem bottles 0.25 and cilastatin bottles 0.5	I/v 250–500 mg of imipenem every 6 hrs. The contents of the bottle to be dissolved in 10 ml of solvent and then to be diluted in 100 ml of 0.9 % NaCl solution
INDAPAMIDE	Coated tablets, capsules 0.0025	Orally 2.5 mg once a day, in the morning and before meals
IPRATROPIUM BROMIDE	Aerosol containers 15 ml (300 unit doses)	Administered in 2 breaths (2 times × 20 mcg) 3–4 times a day
ISONIAZID	Tablets 0.1, 0.2, 0.3; 10 % solution in 5 ml ampoules	Orally 5–15 mg/kg 1–3 times a day, i/m 5–12 mg/kg once a day
ISOSORBIDE DINITRATE	Tablets 0.005, 0.01, 0.02, 0.04, 0.08	Sublingually 5–10 mg; orally 20–120 mg/day, divided into 2–3 doses
ISOSORBIDE MONONITRATE	Tablets 0.02, 0.04	Orally, initial dose 20 mg 2–3 times a day or 40 mg 2 times a day (up to 120 mg/day) with the interval not less than 6 hrs
ITRACONAZOLE	Capsules 0.1; 1 % solution in vials 150 ml	Orally 0.1–0.2 once a day

Drug name	Medicinal forms	Average therapeutic doses and the routes of administration
IVABRADINE	Coated tablets 5 mg, 7.5 mg	Orally 1 tablet 2 times a day
KETOTIFEN	Capsules and tablets 0.001; syrup (0.0002 g in 1 ml, 0.02 g in 100 ml)	Orally, adults: 1–2 mg 2 times a day (during meals); children: depending on age and body mass 1/3–1/2–1 tablet 2 times a day
LAMOTRIGINE	Tablets 0.025, 0.05 and 0.1. Chewable tablets 0.005, 0.025, 0.1 g	Orally 0.1 g 2 times a day
LEVOFLOXACIN	Tablets 0.25 and 0.5. 0.5 % solution in bottles 100 ml	Orally or i/v drip 0.25–0.5 g 1–2 times a day
LEVOSIMENDAN	Concentrated solution in vials 10 ml (2.5 mg/ml)	I/v drip, dissolve in 5 % glucose
LEVOTHYROXINE SODIUM	Tablets 0.000025; 0.00005; 0.000015; 0.000175; 0.00025	Orally 0.025 mg once a day 20–30 min before a meal
LIDOCAINE	Solutions in ampoules; 1 % 10 ml; 2 % 2 and 10 ml; 10 % 2 ml	For anesthesia: infiltrative 0.25–0.5 %; conductive 0.5–2 %; terminal 1–5 % solution; i/m 200–400 mg; i/v 50–100 mg, then drip at the rate of 2 mg/min
LITHIUM CARBONATE	Coated tablets 0.3	Orally 300–600 mg 2–3 times a day
LIZINOPRIL	Tablets 0.0025, 0.005, 0.01 and 0.02	Orally 2.5–25 mg once a day
LOSARTAN	Tablets 0.05	Orally 50 mg once a day
MANNITOL	15 % solution in bottles 200 and 400 ml; 20 % — 500 ml	I/v drip 0.5 g/kg (prophylactically), for therapeutic purposes 0.25–1.5 g/kg. Ddaily dose 140–180 g
MEDAZEPAM	Tablets 0.01	An average single dose 10–20 mg; an average daily dose 3–40 mg
MEFLOQUINE	Tablets 0.25	Orally for prophylaxis 250 mg once a week then again 4 weeks once a week, for medical purposes 15 mg/kg as a single dose
MESOCARB	Tablets 0.005; 0.01; 0.025	Orally 5–25 mg 2 times a day
METFORMIN	Tablets 0.25; 0.5 and 0.85	Orally 500 mg (during meals, swallow it whole) 2–3 times a day. Maximum daily dose 2500 mg
METHOTREXATE	Coated tablets 0.0025	Orally 5–7.5–5 mg once a week
METHYLPHENIDATE	Tablets 0.005 and 0.01	Orally 1 tablet once a day
METHYLPREDNISOLONE	Tablets 0.004 and 0.016	Orally 2–20 mg once a day
METOCLOPRAMIDE	Tablets 0.01; 0.5 % solution in 2 ml ampoules	Orally 10 mg 3 times a day (before meals); i/m (or i/v) 2 ml (10 mg/2 ml)
METRONIDAZOL	Tablets 0.25, 0.5; vaginal suppositories 0.5; 0.5 % solution in 100 ml bottles	Orally 250–500 mg 2 times a day; i/v (driply) 500 mg; suppositories 2 times a day
MISOPROSTOL	Tablets 0.2 mg	Orally 1 tablet 3–4 times a day
MONTELUKAST	Tablets 0.01; chewable tablets 0.005	Orally 1 tablet once a day. For Kids of 6–15 years: 1 chewable tablet 1 time per day (in the evening)
MOXIFLOXACIN	Tablets 0.4	Orally 400 mg once a day
MOXONIDINE	Tablets 0.2, 0.3 and 0.4 mg	Orally 0.2–0.4 mg once a day
NAKOM	Tablets containing levodopa 0.25 and carbidopa 0.025	Orally 1–2 tablets 2–3 times a day
NADOLOL	Tablets 0.02, 0.04, 0.08, 0.12 and 0.16	Orally 40 mg (initial dose) once a day. Maximal daily dose — 240 mg
NADROPARIN	Solution in disposable syringes 0.3; 0.6, 0.8 and 1 ml (9500 U/ml)	Subcutaneosly 0.2–0.9 ml 1–2 times a day
NANDROLONE	5 % oily solution in 1 ml ampoules.	I/m 25–50 mg once in 2–3 weeks
NEBIVOLOL	Tablets 5 mg	Orally (to swallow during or after a meal) 1 tablet once a day
NATRII VALPROAS	Tablets 0.15, 0.2, 0.3	Adults: daily dose of 300–600 mg at the beginning of the treatment, later up to 900–1500 mg
NEOSTIGMINE	Powder; tables 0.015; 0.05 % solution in 1 ml ampoules	Orally 10 mg 2–3 times a day; s/c 0.5 mg 1–2 times a day; 1–2 drops 0.5 % solution in conjunctive cavity 1–4 times a day

Drug name	Medicinal forms	Average therapeutic doses and the routes of administration
NEVIRAPINE	Tablets 0.2. 1 % suspension in bottles 240 ml	Orally 0.2 g per day for 2 weeks. Then the same dose every 12 hr
NICORANDIL	Tablets 0.01	Orally 1–2 tablets 2 times a day
NIMODIPINE	Tablets 0.03. 0.02 % solution for infusion in bottles 50 ml	Orally 1 tablet 3 times a day. I/v slowly 0.001 g/hour (5 ml of 0.02 % in isotonic NaCl)
NITRAZEPAM	Tablets 0.005	Orally as sleeping pills 30 min before sleep. Single dose 5–10 mg
NITROFURANTOINUM	Tablets 0.03; 0.05; 0.1	Orally, adults: 100–150 mg 3–4 times a day; children: 5–8 mg/kg daily in 3–4 doses
NITROGLYCERIN	0.1 % solution for injections 5, 10 and 25 ml. Tablets 0.5 mg	I/v drip, before using dissolve with isotonic NaCl to obtain 0.005 % or 0.01 % solution. The introduction rate is controlled under the supervision of BP. Sublingual 1 or 2 tablets (at onset of angina pectoris)
NITROXOLINE	Tablets 0.05	Orally 100 mg 4 times a day
NORETHISTERONE	Tablets 0.35, 5 and 10 mg	Orally 1 tablet 1–3 times a day
NYSTATIN	Tablets 500 000 U. Vaginal tablets 100 000 U. Suppositories 125 000 U (vaginal) and 500 000 U (rectal)	Orally 1–2 tablets 3–4 times a day. Insert suppositories 1–2 times a day
OCTREOTIDE	0.005 %, 0.01 % and 0.05 % solutions for injections in ampoules 1 ml	Subcutaneously 1 ml 3 times a day. I/v drip 25 mcg/hr during 5 days to stop bleeding from esophageal varices
OFLOXACIN	Tablets 0.2. Ophthalmic ointment 0.3 % — 3.0	Orally 200 mg 2 times a day
ONDANSETRON	Tablets 0.004; 0.008; suppositories 0.0016; 0.08 % syrup in 50 ml bottles (2.5 and 5 ml measure spoons); 0.2 % solution in 2 ml ampoules	Orally, in rectum, i/v or i/m 8–32 mg a day
OXPRENOLOL	Tablets 0.02 and 0.08	Orally 0.02 g 3 times a day
PARICALCITOL	Sol. 5 mcg/ml in amp. 1 and 2 ml	I/v, maximal initiate dose 40 mcg
PENICILLAMINE	Capsules 0.15	Orally 150–300 mg once a day
PERINDOPRIL	Tablets 0.002 and 0.004	Orally 1 tablet once a day
PHENAZEPAM	Tablets 0.0005; 0.001 and 0.0025	Orally 0.25–0.5 mg 2–3 times a day
PHENOXYMETHYL PENICILLIN	Coated tablets 0.25	Orally 250 mg 4–6 times a day
PHENYLEPHRINE	1 % solution in ampoules 1 ml	I/v, i/m, subcutaneously 0.3–1 ml
PHENYTOIN	Tablets in 20 tablets pack	Orally 1/2–1 tablet 2–3 times a day
PHYTOMENADIONE	Capsules 0.01 (0.1 ml of 10 % sol.)	Orally 10–20 mg 3–4 times a day
PILOCARPINE	Powder; 1 % and 2 % solution in 5 and 10 ml bottles; 1 % and 2 % eye ointment; eye covers 0.0027	In conjunctive cavity per 1–2 drops of 1–2 % solution; ointment should be put under eyelid before bedtime
PINDOLOL	Tablets 0.005; 0.01, 0.015; delayed-action tablets 0.02; 0.5 % solution for oral administration (0.005 g/1 ml); 0.02 % solution in 2 ml ampoules	Orally 5–10 mg 1–3 times a day, 30 minutes after meal; i/v slowly 0.4 mg during 5 min (2 ml of 0.02 % solution)
PIPEMIDIC ACID	Capsules 0.2; 0.4; tablets 0.4; vaginal suppositories 0.2; suspension for children in 100 ml bottl (0.1 g/5 ml)	Orally, adults: 400 mg 2 times a day. Vaginally 1 suppository a day. Children: from 1 to 15 yrs. 15 mg/kg in 2 doses
PIPERACILLIN	Bottles 1.0; 2.0	I/v (by stream infusion slowly or dripily) or i/m 1000–2000 mg in 8–12 hrs
PIRENZEPINE	Tablets 0.025 and 0.05; 0.5 % solution in 1 ml ampoules	Orally 0.050 g 3 times a day 30 min before meals; i/v or i/m per 5 mg every 12 hours

Drug name	Medicinal forms	Average therapeutic doses and the routes of administration
PLATYPHYLLINUM	Tablets 0.005; 0.2 % solution in ampoules 1 ml; rectal suppositories 0.01	Orally 1 tablet 2–3 times a day. Subcutaneously 1–2 ml once. Per rectum 1 supp. 2 times a day
POLYMYXIN B	Bottles 0.025 and 0.05	I/v drip 1 mg/kg 2 times a day. (maximal daily dose 0.15)
PREDNISOLONE	Tablets 0.001, 0.005; 0.5 % ointment in of 10.0 g and 20.0 g tubes	Orally 5–10 mg; apply ointment to the affected parts of the body
PROCAINAMIDE	Tablets 0.25 and 0.5; 10 % solution in 10 ml bottles and 10 % solution in 5 ml ampoules	Orally 1 tablet 6 times a day; i/m 5–10 ml (up to 20–30 ml/in 24 hours); i/v of ampoules dissolve in 15 ml of 5 % solution of glucose or isotonic solution, introduce at 2 ml/min
PROCAINE	Powder; 0.25 % and 0.5 % solution in 1; 2; 5; 10 and 20 ml ampoules; 1 % and 2 % solution of 1; 2; 5 and 10 ml; 0.25 % and 0.5 % sterile solution in 200 and 400 ml bottles; 5 % and 10 % ointment; 0.1 suppository	For in-filter anesthesia 0.25 of 0.5 % sol.; for conduction aesthesia 1–2 % sol.; for peridural anesthesia 2 % sol.; for spino-cerebral anesthesia 5 % sol.; for thermal anesthesia 10–20 % sol.; orally 30–40 ml of 0.25–0.5 % sol.; i/v slowly 5–15 ml of 0.25–0.5 % sol.
PROGESTERONE	1 % and 2.5 % oil solution in 1 ml amp.	I/m 5–15 mg once a day
PROMETHAZINE	Coated tablets 0.005; 0.01; 0.025; 0.05, dragees 0.25 and 0.05; 2.5 % solution in 2 ml ampoules	Orally after meal, adults 12.5–25 mg 3–4 times a day; i/m 1–2 ml 2.5 % solution once a day; i/v per 2 ml of 2.5 % sol. once a day
PROPRANOLOL	Tablets 0.01 and 0.04; 0.25 % solution in 1 ml ampoules	Orally 10–40 mg 3–4 times a day; i/v slowly 1 mg
PYRIDOSTIGMINE BROMIDE	Tablets or dragee 0.06; 0.5 % solution in 1 ml ampoules	Orally 60 mg 1–3 times a day; s/c or i/m 0.4–1 ml of 0.5 % solution
QUETIAPINE	Tablets 0.025, 0.1 and 0.2 g	Orally 100 mg 3 times a day
RALTEGRAVIR	Tablets 0.4	Orally 1 tablet 2 times a day (to swallow)
RAMIPRIL	Tablets, capsules 1.25, 2.5 and 5 mg	Orally 1 tablet/capsule 2 times a day
RETINOL	Dragee 3300 U	Orally 1–2 dragee every day
RIBOMUNYL	Tablets 0.25 and 0.75 mg of ribosomal fractions	Orally 3 tablets 0.25 mg or 1 tablet 0.75 mg in the morning fasting 4 days a week during a month
RIFABUTIN	Capsules 0.15	Orally 1–2 capsules once a day
RIFAMPICIN	Capsules 0.05 and 0.15; ampoules 0.15	Orally 450 mg once a day; i/v in drops (150 mg dissolve in 2.5 ml of water for injection, after that shake and further dissolve 125 ml in 5 % solution of glucose)
RIMANTADINE	Tablets 0.05 and 0.1	Orally 1 tablet 2 times a day
RIVAROXABAN	Coated tablets 10, 15 and 20 mg	Orally 10–30 mg once a day
ROPIVACAINE	Solution 0.2 %, 0.75 % and 1 % in 10 and 20 ml bottles	For in-filter, conduction and peridural anesthesia
SERTRALINE	Tablets 0.05 and 0.1	Orally 50–200 mg once a day
SOMATROPIN	Powder for injections 4, 4.86, 8, 10, 12, 12.96, 16 and 24 U	Subcutaneously or i/m 3, 6 or 7 times a week: 0.125–1 U/kg per week
SOTALOL	Coated tablets 0.08; 0.12; 0.16; 0.24	Orally 80–200 mg 4–2 times a day
SPIRONOLACTONE	Tablets 0.025	Orally, a daily dose may range from 50 mg to 300 mg, usually 100–200 mg (in 2–4 doses)
STREPTOMYCIN	Bottles 0.25; 0.5; 1.0	I/m 500 mg 2 times a day (in 5 ml of isotonic solution NaCl)
STROPHANTHIN	Solution 0.025 % and 0.05 % in ampoules 1 ml	I/v slowly 1 ml (0.025 %), or 0.3–0.5 ml (0.05 %)
SULFACETAMIDE	30 % solution in 5 ml ampoules and 5 and 10 ml bottles; 20 % eye drops solution in 1.5 ml drip-tube; 30 % ointment 10.0	I/v slowly 3–5 ml of 30 % solution 2 times a day; eye drops: 1–2 drops 3 times a day; eye ointment is put under inferior eyelid 3 times a day

Drug name	Medicinal forms	Average therapeutic doses and the routes of administration
SULFINPYRAZONE	Tablets 0.1 and 0.2	Orally 1–2 tablets 2 times a day
SUMATRIPTAN	0.5 ml ampoules (6 mg of the preparation); coated tablets 0.05 and 0.1	S/c 6.0 mg; orally 50–100 mg during the migraine attack. The maximum daily dose is 300 mg
TAMSULOSIN	Coated tablets and capsules 0.4 mg	Orally 0.4 mg once a day
TENOFOVIR	Coated tablets 300 mg	Orally 300 mg once a day
TERBINAFINE	Tablets 0.125; 0.25; 1 % ointment in tubes, cream, gel 15.0 and 30.0	Orally 125 mg 2 times a day or 250 mg once a day. Ointment is applied to the affected parts of the body 1–2 times a day until absorbed
TERBUTALINE	Tablets 0.0025; 0.05 % solution in 1 ml ampoules; 0.0005 powder capsules for inhalation	Orally, adults: 5 mg every 6 hrs.; children: above 12 yrs. — 2.5 mg 3 times a day. S/c 0.25 mg, the following application should be not earlier than in 4 hours. Inhale dualfold (interval 60 sec) every 4–6 hrs
TESTOSTERONE	1 % or 5 % oil solution in 1 ml ampoules	I/m 10–25 mg once a day
TETRACYCLINE	Coated tablets 0.05; 0.1; 0.25; 1 % eye ointment 3.0; 7.0; 10.0; 3 % ointment 5.0; 10.0; 30.0; 50.0	Orally 200–250 mg 3–4 times a day; eye ointment: is put under inferior eyelid 3–5 times; ointment is applied to the affected parts of the body 1–2 times a day
THIAMAZOLE	Tablets 0.005	Orally 5–10 mg after meal 3–4 times a day
THIAMINE	Tablets 0.002, 0.005, 0.01 and 0.1. 2.5 % and 5 % solutions in 1 and 2 ml ampoules	Orally 10 mg 1–3 times a day. I/m 0.025–0.05 g once a day
THYMOGEN	0.01 % solution in 1 ml ampoules	I/m 50–100 mcg once a day
TIANEPTINE	Tablets 0.0125.	Orally (before meal) 12.5 mg 3 times a day
TICLOPIDINE	Coated tablets 0.25	Orally 250 mg once a day, during or immediately after meal
TILORONE	Tablets 0.125; 0.25	Orally 125–250 mg once a day.
TINIDAZOLE	Tablets 0.15; 0.5	Orally 150–500 mg 2–3 times a day
TOLPERISONE	Dragees 0.05	Orally 50–100 mg 2–3 times a day
TOLTERODINE	Tablets 0.001 and 0.002	Orally 1 tablet 2 times a day
TOPIRAMATE	Capsules 15 and 25 mg; tablets 25, 50 and 100 mg	Initial dose 25–50 mg/day orally. Max daily dose — 500 mg
TRAMADOL	Capsules 0.05; drops (0.1 g/1 ml) in bottles; ampoules 1 ml and 2 ml (0.05 g/1 ml); rectal suppositories 0.1	I/v (slowly in drops) 50–100 mg up to 400 mg. The same dose is injected i/m or s/c. Orally in capsules up to 400 mg a day or in drops 20 drops (50 mg) per dose up to 8 times in 24 hours
TRANEXAMIC ACID	Tablets 0.25 g; 5 % solution in 5 ml ampoules	Orally 250–500 mg 3–4 times a day; i/v, slowly 10–15 ml. The maximum daily doze is 200 mg
TRIAZOLAM	Tablets 0.00025 of blue color and 0.0005 of white color	Orally 0.25–0.5 mg 30 min. before bedtime
TRIHENYDROXYMETHYL	Tablets 0.001; 0.002; 0.005	Orally 0.5–1 mg 1–5 times a day
VALSARTAN	Capsules 0.08 and 0.16	Orally 1 capsule once a day
VANCOMYCIN	Capsules 0.125, 0.25; bottles 0.5, 1.0, 5.0	Orally 125–500 mg 4 times a day; i/v 500 mg every 6 hrs. or 100 mg every 12 hrs. Preparation: basic solution of 500 mg/10 ml further to be dissolved in 200 ml of 0.9 % NaCl solution
VERAPAMIL	Tablets, dragees or capsules 0.04, 0.08, 0.12; 0.25 % solution in 2 ml ampoules	Orally 40–80 mg 3–4 times a day; i/v 5–10 mg
VILDAGLIPTIN	Tablets 50 mg	Orally 1–2 tablets once a day
WARFARIN	Tablets 0.0025	Orally 1–3 tablets 1–2 times a day
ZIDOVUDINE	Capsules 0.1, 0.25	Orally 200–250 mg 5–6 times a day
ZOLPIDEM	Tablets 0.01	Orally 10 mg before bedtime

## EXAMPLES OF WRITING OUT PRESCRIPTIONS FOR VARIOUS MEDICINAL FORMS

### SOLID MEDICINAL FORMS

#### Tablets

*Rp.: Tab. Atenololi 0,05 N. 20*  
*D.S. Orally 1 tablet once a day.*

*Rp.: Atenololi 0,05*  
*D.t.d. N. 20 in tab. (obductis*  
*(retardis)*  
*(vaginalis)*  
*(buccalis)*  
*(masticalis)*  
*S. Orally 1 tablet once a day.*

*Rp.: Tab. «Co-trimoxazolum» N. 20*  
*D.S. Orally 1 tablet 2 times a day.*

*Rp.: Tab. «Artrotec» N. 20*  
*D.S. Orally 1 tablet 2 times a day.*

*Rp.: Tab. «Sustac-mite» N. 30*  
*D.S. Orally 1 tablet 2 times a day.*

*Rp.: Tab. «Sustac-forte» N. 30*  
*D.S. Orally 1 tablet 2 times a day.*

*Rp.: Tab. «Amoxiclav 0.875 / 0.125» N. 20*  
*D.S. Orally 1 tablet 3 times a day.*

#### Dragées

*Rp.: Dragee Ibuprofeni 0,2*  
*D.t.d. N. 100*  
*S. Orally 1 tablet 4 times a day.*

#### Powders

##### *Simple, undivided into dosages*

*Rp.: Magnesii oxydi 30,0*  
*D.S. Take ¼ tablespoonful 2 hours after meals.*

##### *Simple, divided into dosages*

*Rp.: Colestyramini 3,0*  
*D.t.d. N. 24*  
*S. Orally (during meals) as a suspension (the content*  
*of 1 package should be dissolved in 80 ml of water)*  
*3 times a day.*

##### *Compound, divided into dosages*

*Rp.: Riboflavini 0,01*  
*Thiamini bromidi 0,02*  
*Sacchari 0,3*  
*M.f. pulvis*  
*D.t.d. N. 30*  
*S. 1 powder 3 times a day.*



<b>Capsules</b>	<p><i>Rp.: Omeprazoli 0,02</i>  <i>D.t.d. N. 14 in caps.</i>  <i>S. 1 capsule once a day.</i></p>
<b>Caramel</b>	<p><i>Rp.: Caramelis Dequalinii chloridi 0,00015</i>  <i>D.t.d. N. 30</i>  <i>S. One caramel per cheek or under the tongue every 4 hours. Keep until completely resorbed.</i></p>
<b>Granule</b>	<p><i>Rp.: Granulorum Acidi Aminosalicilici 100,0</i>  <i>D.S. One teaspoon of granules 3 times per day one hour after a meal (dissolve in ½ glasses and drink immediately).</i></p> <p><i>Rp.: Granulorum Ketoprofeni 0,08</i>  <i>D.t.d. N. 20</i>  <i>S. Inside the contents of one sachet in ½ cup of water 2 times a day.</i></p>
<b>Film</b>	<p><i>Rp.: Membranulam ophthalmicam cum Pilocarpini hydrochlorido 0,0027</i>  <i>D.t.d. N. 30</i>  <i>S. Place the film with eye tweezers behind the lower eyelid once a day.</i></p>
<b>Lamell</b>	<p><i>Rp.: Lamellam cum Trinitrolongo 0,001</i>  <i>D.t.d. N. 10</i>  <i>S. Fix the plate to the upper gum above the fangs until resorption.</i></p>
<b>Pastille</b>	<p><i>Rp.: Trochiscos «Septolete» N. 30</i>  <i>D.S. Keep in mouth until completely resorbed every 3 hours after eating.</i></p>

## LIQUID MEDICINAL FORMS

### Solutions

<b>Concentration of the solution in percent</b>	<p><i>Rp.: Sol. Nitrofurali 0.02 % — 500 ml</i>  <i>D.S. Gargle the throat 4 times a day.</i></p>
<b>Concentration of the solution in proportions</b>	<p><i>Rp.: Sol. Nitrofurali 1 : 5000 — 500 ml</i>  <i>D.S. Gargle the throat 4 times a day.</i></p>
<b>Concentration of the solution in the mass- and volume ratio</b>	<p><i>Rp.: Sol. Nitrofurali 0.1 — 500 ml</i>  <i>D.S. Gargle the throat 4 times a day.</i></p>
<b>Spirituos (alcoholic) solution</b>	<p><i>Rp.: Sol. Acidi borici spirituosae 1 % — 10 ml</i>  <i>D.S. 3 drops into the ear 2 times a day.</i></p>
<b>Detailed prescription</b> (in cases when a certain oil or alcohol of a certain concentration is required)	<p><i>Rp.: Mentholi 0,1</i>  <i>Olei Vaselini ad 10 ml</i>  <i>M.D.S. 5 drops into the nose.</i></p>

<b>Suspensions</b>	<i>Rp.: Susp. Hydrocortisoni acetatis 0.5 % — 10 ml</i> <i>D.S. Drop 2 drops into each eye 4 times a day. Shake before using.</i>
<b>Emulsions</b>	<i>Rp.: Emulsi olei Ricini 20 ml — 100 ml</i> <i>D.S. For 1 administration.</i>
<b>Broths and teas</b>	<i>Rp.: Inf. herbae Thermopsidis 0.5 — 200 ml</i> <i>D.S. 1 tablespoonful 4 times a day.</i>
<b>Galenic drugs</b>	
<i>Tinctures</i>	<i>Rp.: Tinct. Valerianae 25 ml</i> <i>D.S. 25 drops 3 times a day.</i>
<i>Extracts</i>	<i>Rp.: Extr. Frangulae fluidi 25 ml</i> <i>D.S. 25 drops before bedtime.</i>
<b>Neogalenic drugs</b>	<i>Rp.: Adonisidi 15 ml</i> <i>D.S. 15 drops 3 times a day.</i>
<b>Mixtures</b>	<i>Rp.: Sol. Natrii bromidi 2 % — 180 ml</i> <i>Coffeini-natrii benzoatis 0,6</i> <i>M.D.S. 1 tablespoonful 3 times a day.</i>
<b>SOFT MEDICINAL FORMS</b>	
<b>Liniments</b>	
<i>Manufactured</i>	<i>Rp.: Lin. Synthomycini 5 % — 25 ml</i> <i>D.S. Apply on the wound 2 times a day.</i>
<i>Prepared at the pharmacy</i>	<i>Rp.: Chloroformii 20 ml</i> <i>Olei Hyoscyami 40 ml</i> <i>M.f. linimentum</i> <i>D.S. Rub into the joint.</i>
<b>Ointments</b>	
<i>Short prescription</i>	<i>Rp.: Ung. Acicloviri 5 % — 5.0</i> <i>D.S. Apply to the affected skin areas 5 times a day.</i>
<i>Detailed prescription</i>	<i>Rp.: Benzocaini 0.25</i> <i>Mentholi 0.1</i> <i>Vaselini ad 20.0</i> <i>M.f. unguentum</i> <i>D.S. Smear the nasal mucosa 6 times a day.</i>
<b>Pastes</b>	
<i>Manufactured</i>	<i>Rp.: Pastae Zinci oxydi 40.0</i> <i>D.S. Apply to the affected surface of the skin.</i>

**Prepared at the pharmacy**

*Rp.: Benzocaini 2.5  
Zinci oxydi 20.0  
Vaselini ad 50.0  
M.f. pasta  
D.S. Apply to the affected surface of the skin.*

**Suppositories  
Manufactured**

*Rp.: Supp. cum Metronidazolo 0.5  
D.t.d. N. 10  
S. 1 suppository before bedtime.*

*Rp.: Supp. «Bethiolum» N. 10  
D.S. 1 suppository 2 times a day.*

**Prepared at the pharmacy**

*Rp.: Aminophyllini 0.36  
Olei Cacao q.s.  
ut f. supp. rectale  
D.t.d. N. 12  
S. 1 suppository 3 times a day.*

**Systema therapeuticum  
transcutaneum (STT)**

*Rp.: STT «Durogesic» 0,00005/h  
D.t.d. N. 5 (five).  
S: To apply in the form of applications on an intact skin  
surface one patch for 3 days.*

**MEDICINAL FORMS FOR INJECTIONS**

**Solutions in ampules**

*Rp.: Sol. Diphenhydramini 1 % — 1 ml  
D.t.d. N. 10 in amp.  
S. 1 ml subcutaneously.*

**Oil solution**

*Rp.: Sol. Oestradioli dipropionatis oleosae  
0.1 % — 1 ml  
D.t.d. N. 6 in amp.  
S. 1 ml intramuscularly once a day.*

**Bottled drug**

*Rp.: Benzylpenicillini 300 000 EД  
D.t.d. N. 12  
S. 300000 units in 2 ml of 0.5 % procaine solution  
4 times a day.*

**Prepared at the pharmacy**

*Rp.: Sol. Glucosi 5 % — 500 ml  
Sterilisetur!  
D.S. Intravenously drip-feed.*

**AEROSOLS**

*Rp.: Aerosolum «Camphomenum» N. 1  
D.S. For inhalations 3 times a day.*

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# **ФАРМАКОЛОГИЯ**

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На английском языке

*10-е издание*

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