

**MINISTRY OF HEALTH OF UKRAINE
ODESSA NATIONAL MEDICAL UNIVERSITY**

DEPARTMENT OF PHARMACOLOGY AND PHARMACOGNOSY

METHODICAL INSTRUCTIONS

**FOR THE PRACTICAL CLASSES
IN PHARMACOLOGY FOR THE THIRD YEAR
STUDENTS OF PHARMACEUTICAL FACULTY**

Odessa 2022

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Methodical instructions for the students of Medical faculty, who are learning pharmacology, contain the list of basic topics, questions and preparations, provided by the academic plan and program of Ministry of Health of Ukraine.

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INTRODUCTION

Methodical instructions for the students of Medical faculty, who are learning pharmacology, contain the list of basic topics, questions and preparations, provided by the academic plan and program of Ministry of Health of Ukraine. Every methodical unit to a certain topic consists of two parts: individual work outside of the class (home work) and original practical work in class. For each class a student should execute a home work in the form of: 1) study the material according given control questions; 2) write prescriptions for drugs with an indication of their specifics of medical using; 3) perform tasks for self-control (the answers to the test tasks are given at the end of this manual). The results of home and original work must be reflected in copybook for practical classes. The list of the basic literature is in the end of methodical instructions.

LIST OF ABBREVIATIONS

ABP	– arterial blood pressure		reuptake inhibitor
ACE	– angiotensin converting enzyme	Supp.	– suppository
Ampul. (amp.)	– ampoule	Syn.	– synonyms
AR/SE	– adverse reaction / side effect	Tab.	– tablet (s)
Bot.	– bottle	TCA	– tricyclic antidepressants
Caps.	– capsule	TS	– therapeutic systems
CCB	– calcium channel blockers	TTS	– transdermal therapeutic system
CNS	– central nervous system		
Comb.	– combined		
CU	– conventional units		
CU	– code units		
CWA	– chemical warfare agents		
DD	– daily dose		
f/inf.	– for infusions		
f/inj.	– for injections		
I.M. (i.m.)	– intramuscularly		
I.V. (i.v.)	– intravenously		
IACE	– inhibitors of ACE		
IHD	– ischemic heart disease		
IU	– international units		
MAO	– monoamine oxidase		
OPC	– organophosphorus compounds		
P.O. (p.o.)	– by mouth		
Powd.	– powder		
S.C. (s.c.)	– subcutaneously		
S.L. (s.l.)	– sublingually		
SD	– single dose		
Sol.	– solution		
SSRI	– selective serotonin		

CONTENT MODULE I. MEDICAL PRESCRIPTION. GENERAL PHARMACOLOGY

Actuality of the unit. Medical prescription is the unit of pharmacology, which learns the rules of prescription of drugs in different medicinal forms. Prescription is one of the types of medical documentation and represent written administration from doctor to the pharmacist about making, prescribing medical drug to the definite person at the definite dosage and volume with marking way of its usage. Prescriptions are prescribed on the special forms, regulated by the Ukrainian Ministry of Health. Prescription is not only an medical document, it's also an juridical one. Doctor takes all responsibility for its prescribing. That's why it is important to know not only the structure of the prescription, rules of its prescribing, classification of medicinal forms, but be able to adequately choose and write prescription for the medical drug at the definite medical form, considering condition of the patient, his age and weight.

Pharmacology is the fundamental medical science on complicated processes of interaction of organism and drugs in different conditions and it is the theoretical basis of pharmacotherapy. In common biological aspect, pharmacology is the science dealing with the cooperation of exogene chemical substances of biological and non – biological origin with living organisms. Studing of the pharmacology at the cell and subcell levels help to find new ways of cooperation between organism and medicines, and to get new information about pharmacology effects. That's why general pharmacology we can see as consisting from the 3 parts.

1) **Pharmacokinetics** – a part of pharmacology, describes the processes of drug absorption, distribution, metabolism and elimination from the organism.

2) **Pharmacodynamics** – another part of pharmacology describes the mechanisms of action and therapeutic effects of the drugs.

3) **Pharmacotoxicodynamics** – a part of pharmacology studies possible unpleasant action of the drug at the organism.

The training objectives. *To know:* medical formulation, calculation rules and prescribing in different dosage forms. the history of the subject, modern concepts, research methods in pharmacology; the main pharmacokinetic processes drugs; the main criteria for determining the pharmacodynamics, farmakotoksikodinamics, their importance for the effective and safe pharmacotherapy.

To be able to: prescribe any drugs, solve the test tasks, situational and pharmacotherapeutic targets for this section.

Intersubject integration. Mathematics, Physics, normal anatomy, histology, inorganic, organic chemistry, biochemistry, physiology of normal.

Unit 1. MEDICAL PRESCRIPTION. SOLID FORMS: POWDERS, TABLETS, PILLS, CAPSULES, POWDERS FOR EXTERNAL USE

I. Individual work

Control questions

1. Conception of medical and pharmaceutical prescription. Sources of drug substances. Galen's and new – Galen's preparations. Definition of conceptions: Medicinal raw materials, drug substance, drug form. Classification of drug forms.

2. The State Register of Medicinal Products and the State Pharmacopoeia of Ukraine. Their content and purpose. Medicines Lists A and B.

3. Pharmacy and its structure. Terms of storage products list A and B.

4. Current concepts of dosage forms. Classification of formulations intended (dosing), and manufacturing consistency. Traditional and new generation of dosage forms – therapeutic system

(TC): TC conductive, TC controlled release agents (oral, injectable, implantable, transdermal (TTS), and others.).

5. The recipe as medical, legal and financial documents. Order of the Ministry of Health of Ukraine № 360 from 19.07.2005 "On approval of writing prescriptions and requirements of orders for medicines and medical products in pharmacies and their structural subdivisions. "Types of prescription forms (Form 1 and 3), their purpose, use and storage.

6. The structure and content of the prescription of its individual parts. Mandatory rules of their registration, as well as in exceptional cases. Methods of prescription formulations: expanded and condensed.

7. Medical formulation dosage forms. The term "dose" of the drug dosage forms. The methods of calculation prescriptions for dosage forms. Features of the calculation of doses for children.

SOLID FORMS: POWDERS, TABLETS, PILLS, CAPSULES, POWDERS FOR EXTERNAL USE

1. Powders for oral administration. Their types (simple and complex). Massing and flavoring substances used for powders.
2. Discharging rules for main and officinal powders.
3. Capsules, tablets and dragees. Their characteristics and types (simple, complex and proprietary). Discharging rules.
4. Other solid dosage forms: granules, soluble tablets, candies, lozenges, glossety, pills, spansuly, Kakheti fees.
5. Solid non – dosed drug forms (powders). Rules of prescribing simple and complex powders. Constitutional substances for powders.
6. Other undosed dosage forms: mustard, pencils, tooth powders, poultices.
7. Medicinal fees. Regulations prescribing.

Calculation of doses of medication depending on the age

Age	of the adult dose
18 years	3/4
14 years	1/2
7 years	1/3
6 years	1/4
1 year	1/12
before 1 year	1/12 – 1/24

as well as by the formulas: $\text{Dose} = a \cdot b / 20$ or $\text{Dose} = a \cdot m / 70$, where a – an adult dose, b – the child's age, m – weight (kg).

List of practical works

- 1) Make a complete scheme of the recipe, indicating the sequence of its component parts.
- 2) Make a table of the most important prescription abbreviations.
- 3) Compile a table of noun endings in the most frequently used cases.
- 4) Calculate the dose of the drug for a 7-year-old child.

List of practical works. Write prescriptions:

- 1) 30 powders containing tetracycline hydrochloride (Tetracyclini hydrochloridum), SD - 0.25. On 1 powder 4 times a day.
- 2) 10 powders containing papaverine hydrochloride (Papaverini hydrochloridum), SD - 0.02. 1 powder 3 times a day.
- 3) 10 powders containing paracetamol (Paracetamolum) and acetylsalicylic acid (Acidum acetylsalicylicum) equally by SD - 0.24. 1 powder 3 times a day.

- 4) 20 capsules containing 0.25 (RD) oxacillin sodium salt (Oxacillinum-natrium). 2 capsules 4 times a day.
- 5) 40 nitroglycerin tablets (Nitroglycerinum), SD - 0.0005. 1 tablet under the tongue.
- 6) 50 tablets containing analgina (Analginum), SD - 0.25 dibazola (Dibazolum) and phenobarbital (Phenobarbitalum) equal to RD - 0.02. 1 tablet for the night.
- 7) 25 tsefalgina tablets (Cephalginum). 1 tablet 3 times daily.
- 8) 100.0 powder containing 2% amikazola (Amycazolum). Apply to the skin surface. Calculate the amount of (DM) amikazola.
- 9) 100.0 powders containing 10% of resorcinol (Resorcinum) and salicylic acid (Acidum salicylicum). Treat the affected surface.
- 10) 50.0 anti-asthmatic collection (Species antiasthmaticum). 1/2 teaspoon collection burn and inhale the smoke 2 times a day.
- 11) powders 10 "Fervex" («Fervex»). Take 1 pack-tick 3 times a day, previously dissolved in warm boiled water.

Tasks for self-control. Answer the following questions:

- 1) What is the difference from the pharmaceutical and medical formulation?
- 2) What is the meaning of "crude drug", "precursor", "drug substance", "drug form", "medicinal drug", "medicinal agent"?
- 3) What drugs are included to the list A and B? What features, storage and prescribing of narcotic (psychotropic) means?
- 4) How do we classified dosage forms as intended and physico – chemical properties?
- 5) Which drug forms do we called officinal and magisterial? What is the meaning of "therapeutic system" and "conducting therapeutic system"? What are the varieties of the traditional forms and their advantages?
- 6) What is the prescription? What forms of prescription do we have in Ukraine? What are the rules of their registration?
- 7) What are the components of the prescription (in Latin and native languages). What does show each part? Rules of registration.
- 8) What cases do we write prescriptions in full form and in which – shortened?
- 9) Which types of doses do we know?
- 10) What does it mean – "breadth of therapeutic action?" In that case, if the drug has a great breadth of therapeutic action, it is a high or low toxic drug?
- 11) What are the different ways to calculate the prescription to the dosage forms? What is their essence?
- 12) According to what rules are written magistral and the main officinal powders for oral?
- 13) What has been the dose solid and granular substances?
- 14) What rules are written officinal capsules, tablets and dragee?
- 15) What features of writing out complex and patented capsules, tablets and dragee?
- 16) What is the dose expressed in solid and granular substances?
- 17) According to what the rules are issued and trunk Officio-functional powders for oral?
- 18) What rules are issued officinal capsules, tablets, pills?
- 19) Features of prescribing complex and patented capsules, table-current pills.
- 20) What features of prescribing powders?
- 21) What means are used for shaping powders and-sypok?
- 22) Regulations prescribing powders in an abbreviated and expanded form.

II. Original practical work in class

1. To view the collection of drugs in solid dosage forms.
2. To write recipes:
 - 1) Iron sulfate (Ferri sulfas), SD - 0.5 in the powders.
 - 2) Ascorbic acid (Acidum ascorbinicum), SD - 0.05 powders, tablets, pills and capsules.

- 3) 20 powders containing pyridoxine hydrochloride (Pyridoxini hydrochloridum), SD - 0,002 and nicotinic acid (Acidum nicotinicum), SD - 0,025.
- 4) 30 capsules containing lipase (Lipasa), amylase (Amylase) equal to SD - 25000 IU, and the protease (Proteasa), SD - 1200 IU.
- 5) 100 pills Festal (Festal).
- 6) 50.0 powder containing 5.0 g streptocida (Streptocidum). Apply to the skin surface.
- 7) 50.0 powder containing 1% of salicylic acid (Acidum salicylicum), 3% boric acid (Acidum boricum) oxide and 15% (Zinci oxydum zinc). Apply to the skin surface.
- 8) 100.0 granules glycerophosphate (Glycerophosphatis).
- 9) 20 soluble tablets of Panadol (Panadol extra).
- 10) 20 tablets containing 100 mg of oxytetracycline hydrochloride (Oxytetracyclini hydrochloridum) and calcium diphosphate (Calcii diphosphoricum).
- 11) 20 tablets containing 300 mg sodium salicylate (Natrii salicylicum) and 30 mg of caffeine (Coffeinum).
- 12) 50 pills, each containing 4 mg of bromhexine (Bromhexinum).
- 13) 6 pancreatin powder (Pancreatinum) 600 mg.
- 14) 50 "lipostabil» («Lipostabil» capsules). Assign 2 capsules three times a day

Unit 2. SOFT MEDICINAL FORMS: SUPPOSITORIES, PATCHES, OINTMENTS, PASTES, AND LINIMENTS.

I. Individual work

Control questions

1. General characteristics of suppositories. Suppositories rectal and vaginal. Substances, used as basis for the suppositories preparation. Rules of main and officinal suppositories prescribing.
2. Transdermal dosage systems: patches, discs, pads. Prescribing rules.
3. General characteristics and rules of prescribing non – dosed drug forms: main and officinal ways.
4. Soft non – dosed drug forms (ointment, pastes). Types of ointments. Difference between ointments and pastes. Constitutional substances for ointments and pastes. Rules of prescribing. Non – dosed plasters. Kinds of them. Rules of prescribing.

List of practical works. Write prescriptions:

- 1) Write detailed and short forms of 20 rectal suppositories, containing Indometacinum. SD – 0,1 .One suppository before bedtime.
- 2) 20 patented suppositories ‘Bethiolum’. One suppository before bedtime.
- 3) 12 vaginal suppositories , containing Nystatinum 250000 each. One suppository before bedtime.
- 4) Transdermal plaster “Nitroderm” containing 50 mg of Nytroglycerinum. Put it as application at the skin of the right shoulder.
- 5) 100,0 ointment, paste, containing 2% Amycazolium.
- 6) 100,0 ointment, paste, containing 10% of both Resorcinum and Acidum salicylicum in equal share. Dub staggered surface
- 7) 50,0 of patened ointment ‘Flucinar’. Dub staggered surface.
- 8) 20,0 of 10% linimentum Synthomycinum. Dub staggered surface.
- 9) 20 Emplastrum Capsici, square 20x20. Put at the needed region of the skin.

Tasks for self-control. Answer the following questions:

- 1) What is a soft dosage forms?
- 2) What rules are written for officinal and magistral suppositories?
- 3) What means the TTC and what are the rules they written?
- 4) What do we refer to the non – dosage solid, liquid and soft medicinal forms?

- 5) According to what rules are written non – dosed officinal medical forms?
- 6) What constituents used to prepare the magistral ointments, liniments, pastes?
- 7) What are the features of their prescribing in detailed method ?

II. Original practical work in class

1. To view the collection of drugs.
2. Prescribe the prescriptions:
 - 1) Dimedrolum (*Diphenhydramine*), SD – 0,01 in rectal suppositories.
 - 2) 20 vaginal suppositories, containing Metronidazolium 0,5 each. One suppository before bedtime.
 - 3) 10 patented rectal suppositories ‘Anusolum’.
 - 4) Transdermal patch ‘Nitropercuten’, containig 25 mg of Nitroglycerin. Put it as application at the skin of the right shoulder.
 - 5) 50.0 ointment, liniment, pastes containing 5.0 Streptocidum.
 - 6) 10.0 ointment containing 1% Tetracyclini hydrochloridum. Lubricate the skin surface.
 - 7) 50.0 ointments, pastes containing 1% of salicylic acid (*Acidum salicylicum*), 3% boric acid (*Acidum boricum*) and 15% zinc oxide (*Zinci oxydum*).

Unit 3. LIQUID MEDICINAL FORMS: INFUSIONS, DECOCTIONS, MIXTURES, TINCTURES, LIQUID EXTRACTS, SYRUPS, MUCUS, AND DROPS FOR ORAL USAGE.

I. Individual work

Control questions

1. General characteristics of decoctions and infusions. Difference in preparation of these medicinal forms. Types of prescriptions. Information about medical species.
2. The general rules of prescription Galen’s forms (tinctures, liquid extracts).
3. General characteristic of tinctures. Difference from infusions. Simple and complex tinctures. Rules of prescription, a way of batching.
4. General characteristics of extracts. Kinds of extracts. Rules of prescription fluid extracts, way of dosage.
5. New Galen’s forms. Difference from the Galen’s forms.
6. Mixtures, their characteristics and contents. Syrups, aromatic waters and mucuses as ingredients of mixtures. Forms of mixtures prescribing, their dosing.
7. Sol.s for inner use. Rules of calculation and prescription main and officinal sol.s. Features of prescribing spirit and oil sol.s.
8. Concept about drops for inner use, as versions of sol.s for inner use. Officinal and main prescriptions. Rules of calculation.
9. Suspensions for inner use. The characteristic and differences from sol.s. Rules of prescription.
10. Mucus for inner use. Rules of prescription.
11. Non – dosed sol.s. Drops (eye, ear, dental and nasal), lotions, gargles, syringes. Rules of prescribing.
12. Suspensions, emulsions and aerosols for external use. Rules of prescribing.

List of practical works. Write prescriptions:

- 1) Infusion folium Menthae piperitae, SD – 0,05. For inner use, 1 table spoon 4 times a day, 3 days.
- 2) Decoction cortex Quercus, SD – 1,0 For inner use, 1 table spoon 4 times a day before meal, 3 days.
- 3) Tincture Hypericum 30 ml.
- 4) Compound of the tinctures Convallaria and Valeriana, SD – 10 drops each one.
- 5) Fluid extract of Frangula, SD – 30 drops
- 6) 15 ml. of Lantosidum.

- 7) Mixture from Natrii bromidum (*Sodium bromide*), SD – 0,1 and Coffeini – natrium benzoas (*Caffeine – sodium benzoate*), SD – 0,05. For inner use, 1 table spoon 4 times a day.
- 8) Mixture containing infusion of grass (herba) Adonis Vernalis, SD – 0,5; Natrii bromidum (*Sodium bromide*), SD – 0,5; Codeini phosphas (*Codeine phosphate*), SD – 0,015. For inner use, 1 table spoon 3 times a day.
- 9) Mixture from: infusion of Valerian's root (radix Valeriana), SD – 0,75; tincture of Convallaria, SD – 10 drops; Natrii bromidum (*Sodium bromide*), SD – 0,3. For inner use, 1 table spoon 3 times a day.
- 10) 100 ml starch mucilage (Mucilaginis Amily). For inner use, 1 table spoon 3 times a day.

Tasks for self-control. Answer the following questions:

- 1) What relates to liquid dosage forms?
- 2) What are the infusions and decoctions? How do they differ? Terms of preparation and dosing for adults and children.
- 3) How are written infusions and decoctions?
- 4) What do we refer to herbal medicines? How do they differ from the infusions and decoctions? What rules are written and how they are dispensed?
- 5) What is the difference New – Galen's herbal medications? According to what rules are written and how they are dispensed?
- 6) What means mixture? By what rules they are prescribed and dosed?

II. Original practical work in class

1. To view the collection of drugs in liquid dosage forms.
2. To write prescriptions:
 - 1) Infusion of folium Uvae ursi, SD – 0,8. For inner use, 1 table spoon 3 times a day.
 - 2) Decoction of radix Polygalae, SD – 1,5. For inner use, 1 table spoon 3 times a day.
 - 3) Tincture Belladonna, SD – 10 drops.
 - 4) 25 ml. of complex tincture, composed from the 1 part tincture Belladonna, 4 parts tincture Convallaria and tincture Valeriana equally.
 - 5) Fluid extract of Grataegus. 20 drops 3 times a day.
 - 6) 15 ml. of Adonisidum (*Adoniside*)
 - 7) Mixture, containing infusion of radicis Valerianae, SD – 0,5; Natrii bromidum (*Sodium bromide*), SD – 0,3. For inner use, 1 table spoon 3 times a day.
 - 8) Mixture, containing Pepsinum SD – 0,5 and Acidum hydrochloricum dilutum SD – 10 drops. 1 table spoon 3 times a day before meal.
 - 9) Mixture for adult and 6 years old kid, made on decoctum radix Althaeae SD – 0,5, containing Natrii hydrocarbonas SD – 0,3. 1 spoon 3 times a day
 - 10) Mixture 'Quatera' 200 ml. 1 table spoon 3 times a day.
 - 11) 200 ml mucus salep (Mucilaginis Salepy). For inner use, 1 table spoon 3 times a day.
 - 12) 200 ml. 10% of sol. Calcii chloridum (*Calcii chloride*). 1 table spoon 3 times a day. Calculate an SD for Calcii chloridum.
 - 13) Dioninum, drops for inner use. SD – 0,01 20 drops 3 times a day for 10 days. Write in developed and short form.

Unit 4. LIQUID MEDICINAL FORMS: FOR INJECTIONS, SOLUTIONS, SUSPENSIONS. AEROSOL FOR INHALATION AND FOR EXTERNAL USE.

I. Individual work

Control questions

1. General characteristic and the requirements showed to medicinal forms for injections. Forms of release (an ampoule, Bot., syringes – tubes), advantages and lacks. The solvents used for

preparation of sol.s for injections. Rules of prescribing officinal medicinal forms for injections (sol.s, suspensions, powders). Features of prescribing main forms for injections.

2. Features of prescribing of patented and New Galen's dosage sol.s.
3. Dosage and non dosed aerosols. Characteristic and rules of prescription.
4. Liquid form undosed. The concept of solutions for outdoor applications: drops (eye, ear, dental, nasal), lotions, rinses, irrigation. Regulations prescribing.
5. Suspensions, emulsions, aerosols for topical application. Regulations prescribing.

List of practical works. Write prescriptions:

- 1) 10 ampoules, containing 1 ml. 0,1% sol. Atropini sulfas, injection S.C. 1 ml., account SD.
- 2) 10 vials, containing 500.000 units of Streptomycini sulfas (*Streptomycin sulfate*). Powder for I.M. injections. 500000 units 2 times a day, dilute in 2 ml. 0,25% sol. Novocain.
- 3) 500 ml. of sterile isotonic 0,9% sol. Natrii chloridum (*Sodium chloride*). Prescribe 500 ml. I.V.
- 4) 10 ampoules, containing 1 ml. 1% oil sol. Progesteronum (*Progesterone*). I.M. injection, 1 ml.
- 5) 6 vials, containing 5 ml. 2,5% suspension Hydrocortisoni acetat (*Hydrocortisone acetate*). For injection in the cavity of affected joint; 3 ml. 1 time a week.
- 6) 10 ml. of 5% spirit sol. Iodum (Iodine). 5 drops at milk 2 times a day after meal for 30 days.
- 7) Suspension "Maalox", vial for 250 ml. 1 table spoon 4 times a day
- 8) Aerosol 'Berotek' 15 ml. One inhalation 3 times a day.

Tasks for self-control. Answer the following questions:

- 1) What refers to dosage forms for injection? What are the requirements to impose it? What are the rules for their prescribing?
- 2) What features prescribing dosage forms for injection in vials?
- 3) What are the features of prescribing organopreparations, dosage units of biological actions?
- 4) What are the main features of prescribing dosage forms for injection?
- 5) What are the rules for writing out the solutions and oral drops? Do we have features when prescribe oil, alcohol and patented solutions?
- 6) How to calculate the concentration of the sol. from a single dose of the drug in dry form, and conversely?
- 7) What are the features prescribing suspensions, emulsions for oral administration, aerosols for inhalation?

II. Original practical work in class

1. To view the collection of drugs in liquid dosage forms.

2. To write prescriptions:

- 1) 180 ml. 33% of sol. Magnesium sulfate. 1 table spoon 3 times a day
- 2) 10 ml. 1% spirit sol. Nitroglycerinum. Take 2 drops on sugar under the tongue.
- 3) 5 ml. 0,125 % oil sol. Ergocalciferolum. Prescribe 2 drops twice a day.
- 4) 30 ml. Corvalolum. 30 drops on take.
- 5) 250 ml. 5 % suspension Salazopyridazinum. Inject like enema by 20 ml. before night.
- 6) Aerosol 'Ipradol' 15 ml. Double inhalation 5 times a day.
- 7) 10 ampoules, containing 1 ml. of 24% sol. Euphyllinum (*Aminophylline*). Prescribe by 1 ml. intramuscular 2 times a day. Count number of dry substance, what is need for creating such concentration of sol.
- 8) 10 ampoules containing Heparinum by 5 ml. (1ml. – 5000ED). By 5000 ED S.C. 1 time a day.
- 9) 30 vials, containing powder for injection Benzylpenicillinum – natrium 1000.000 units. To dilute the contents of the vial in 2 ml. of 1% sol. Lidocainum before injection, inject I.M. 6 times a day.
- 10) 10 vials containing 0,1 g of Lydasum (*Hyaluronidasum*). Before use the contents of the vial should be diluted with 1 ml. 1% sol. of sterile Lidocainum. Inject S.C. in the region of scar.
- 11) 800 ml. 5% sterile sol. of Glucosum. For manipulations.
- 12) 10 patented ampoules containing 1 ml. suspension 'Zymosanum'. Inject I.M. every other day.

- 13) Platyphyllini hydrotartras, SD – 0,005 in powder; tablets, drops for inner use, in ampoules with 0,2 % sol., 1 ml. for S.C. injection.
- 14) 100 ml. 0,02% sol. of Furacilinum. For irrigating wound.
- 15) 100 ml. 10% oil sol. of Camphora (Camphor) for rubbing.
- 16) 10 ml. 0,1 % sol. Naphthysinum. For dropping in the nose.
- 17) Aerosol ‘Amprovisolum’ 50 ml. for external use. Place at the staggered surface for 5 sec.
- 18) 20 vials containing 1.0 Ceftriaxone (Cephtriaxonum). By 1 g I.M. 1 times a day for 5 days. Before injection dissolve contents of the vial in 2 ml. of 1% sol. of lidocaine.

Unit 5. CHECKING OF PRACTICAL SKILLS ON “MEDICAL PRESCRIPTION”

Unit 6-7. GENERAL PHARMACOLOGY. PHARMACOKINETICS

I. Individual work

Control questions

1. The human body and the drug. The drug and the poison.
2. Pharmacology in system of medical and biological sciences. Its tasks and the basic directions (theoretical, experimental, clinical). Separate directions of development: pediatric, geriatric, radiating, immunopharmacology, psychopharmacology, pharmacogenetics, chronopharmacology
3. History of pharmacology. A role of native and foreign scientist in becoming and development pharmacologists, as sciences (N.V.Lazarev, M.P.Nikolaev, M.P.Kravkov, A.I.Cherkes, S.V.Anichkov, V.V.Zakusov, A.V.Valdman, Z.V.Ermoljeva, G.E.Batrak, J.B.Maksimovich, etc.). Modern development of pharmacology in Ukraine.
4. Modern methods of researches in pharmacology. Ways of search, creation and development new medical products. Before clinical and clinical researches (phase I – IV). Concept about world standards showed to creation and tests of medicines – GLP(Good preclinical test) , GCP(Good clinical test), GMP (Good manufacture production). Functions of State pharmacological center MH of Ukraine.
5. The definitions of the terms pharmacokinetics, pharmacodynamics, and pharmacotoxicodynamics. The nomenclature and principles of classification of medical products. Kinds of pharmacotherapy.
6. PHARMACOKINETICS of the drugs:
 1. Routes of drug administration. Their advantages and disadvantages.
 2. Absorption of drugs. Factors influencing the absorption; active and passive transmembrane transport; Concepts about bioavailability and bioequivalence of medicines. Value of linkage of medicinal substances with fibers of blood, a gastroenteric path, purulent releasing and so forth.
 3. Drug distribution. Factors influencing drug distribution. Penetration through histo-hematic barriers: placenta, blood – brain, etc. Deposition of medicines.
 4. Biotransformation of the drugs at the organism. Drug metabolism; its possible pathways. The meaning of the liver microsomal enzymes;
 5. The concept of elimination and excretion of drugs. Ways excretion of drugs from the body. Factors determining excretion.
 6. The concepts of basic pharmacokinetic parameters (adsorption rate constant, half – period of adsorption, the time to reach maximum concentration, half – life of medi, steady – state concentration, total and renal clearance, the elimination rate constant and excretion). Age features of pharmacokinetics (the children of the first years of life, the elderly).

Tasks for self-control. Choose the correct answers.

1. Part of the dose that reaches the systemic blood circulation in an unchanged form, called:
 - A. Therapeutic dose;
 - B. The maximum concentration;
 - C. The optimal dose;
 - D. Bioavailability;
 - E. Clearance;
2. Which of these routes of drug administration aren't enteral?
 - A. Vaginal;
 - B. Rectal;
 - C. Sublingual;
 - D. Transbuccal;
 - E. Transdermal;
3. Which of these options is a prerequisite for the rapid penetration of the drug through the blood – brain barrier?
 - A. The long half – life period;
 - B. High hydrophilicity;
 - C. Persistent protein binding;
 - D. Ionized state;
 - E. High lipophilicity;
4. What shows drug clearance (Cl)?
 - A. Conventional blood plasma volume, which is released from the drug per unit time;
 - B. The period of time over which the drug concentration in plasma decreased by 50%;
 - C. The complete elimination of the drug from the body;
 - D. The rate of disappearance of the drug from the body through biotransformation and excretion;
 - E. The time of arrival of the drug from the site of administration into the systemic circulation in the extravascular administration;
5. What does indicate the half – life period of the drug ($T_{1/2}$)?
 - A. The time necessary for the absorption half dose from the injection site into the bloodstream;
 - B. The time at which the concentration of drug in blood plasma decreased by 50%;
 - C. The complete elimination of the drug from the body;
 - D. The relationship between the rate of excretion of the drug, and its concentration in blood plasma;
 - E. The rate of excretion of the drug through the kidneys;

II. Original practical work in class

1. To analyze the material and work with the tests (Krok-1).
2. Solve situational problems.
 - 1) patients receiving cytotoxic drugs, while taking small doses of alcohol came pathological intoxication. Explain features of metabolism of drugs when co-administered inhibitor of microsomal liver enzymes.
 - 2) time steps, which of the two drugs will be more, if it is known that one of them binds to blood protein in a greater degree?
 - 3) The two patients have entered the same amount of drug. It is known that a history of hepatitis are transferred. The organization of the patient and why after 2 hours the concentration of the drug will be higher?
 - 4) When digitoxin pharmacokinetic studies revealed that it is slowly eliminated from the body after completion of the blood is determined etsya treatment for 14 days. What do you call this phenomenon?
 - 5) The drug is practically insoluble in water and soluble in lipid. What predpochtitel route of administration of the drug, based on the pharmacokinetic properties?
 - 6) Barbiturates induce microsomal liver enzymes. What tactics dosing must be selected for the antibiotic, which is used in conjunction with barbiturates?
 - 7) Which of the two substances quickly enters the body, it is known that:
 $t_{1/2a} = 0.5$ and $t_{1/2a} = 2$ hours;
 $k_{01} = 9,2 \text{ h}^{-1}$ and $k_{01} = 0,2 \text{ h}^{-1}$;

8) Which of the two substances quickly excreted from the body, if it is known that:

$t_{1/2} = 4$ hours, and $t_{1/2} = 8$ h;

$k_{el} = 0.5 \text{ h}^{-1}$ and $k_{el} = 3 \text{ h}^{-1}$;

9) Which of the two substances is best captured by the tissues from the blood plasma, it is known that:

1.2 $V_d = V_d = 1$ and 8 l ;

10) The bioavailability of two substances above, if you know that:

$F = 87\%$ and $F = 27\%$;

11) Which of the two substances quickly excreted from the body, if it is known that:

$Cl = 2.64 \text{ ml / h}$ and $Cl = 8 \text{ ml / hr}$;

12) Do any of the patients most likely to cause toxic effect of chlorpromazine in the event of an overdose, it is known that renal clearance is:

$Cl = 50 \text{ ml / h}$ and $Cl = 25 \text{ ml / hr}$;

13) Which of the substances long-term stays in the body, if it is known that

$MRT = 8 \text{ h}$; $MRT = 2 \text{ hours}$; $MRT = 81 \text{ h}$; $MRT = 13 \text{ h}$; $MRT = 68 \text{ h}$.

Unit 8-9. GENERAL PHARMACOLOGY. PHARMACODYNAMICS

I. Individual work

Control questions

1. PHARMACODYNAMICS of the drugs:

- Types of drug action: local and resorptive; direct and indirect; specific and nonspecific; reversible and irreversible; non – selective and selective; basic and side; desirable and adverse.
- The types of mechanisms of action of drugs: interactions with different biological substrates. Effect on the receptors. The concept of affinity, intrinsic activity complementarity, agonist, antagonist, agonist – antagonist. The effect on ion channels, activity of enzymes, transport systems, membrane permeability, protein synthesis, genes, etc.
- Dependency of the pharmacological effect of drugs on the properties (chemical structure, the degree of dissociation, polarity, dosage, quality). Types doses. The breadth of the therapeutic effects of drugs. The concept of biological standardization. Value based "concentration (dose) – effect."
- The effect of the body's condition (age, sex, pregnancy, lactation, the severity of the main and concomitant diseases, allergic status, bad habits) to the action of drugs. The role of genetic factors in the development of pharmacological effect. The concept of *pharmacogenetics*. Pharmacogenetic approaches to predict therapeutic efficacy and toxicity of drugs.
- The dependence of pharmacological effects from external factors. Influence of environment (climate, environment, working conditions), and biological rhythms. The concept of *chronopharmacology*. The impact of subjectivity in the appointment of pharmacotherapy. The concept of *clinical pharmacology*. Requirements to modern medicines.
- The effect of drugs in their re – introduction and cancellation – sensitization; accumulation and its species; tolerance (addiction), tachyphylaxis; drug dependence (addiction) and its phase (mental, physical) and abstinence syndrome. Medical and social aspects of the fight against drug addiction. The concept of the syndrome of "cancellation" and "return" ("bounce").
- Drugs interaction: addition, potentiation, antagonism and its types. Information about polypragmasy;
- Incompatibility of drugs: physical, chemical, pharmacological. Use in medical practice.

2. PHARMACOTOXICODYNAMICS (see methodical work № 44)

- Conception about safety, undesirable (side) action, reaction, phenomenon.
- Undesirable action of drugs – organotoxicity, allergic reactions, idiosyncrasy, mutagenity, teratogenity, embryotoxicity, fetotoxicity, carcinogenicity. Overdosing absolute and relative (toxic effects).

3) The concept of pharmacological control.

Tasks for self-control. Choose the correct answers.

1. *Drugs interacting with receptors form reversible intermolecular bonds to which relate?*
 - A. Van der Waals
 - B. Covalent
 - C. Ionic
 - D. Hydrogen
 - E. Dipole
2. *Desensitization of receptors leads to development:*
 - A. Tolerance
 - B. Dependence
 - C. Synergism
 - D. Rebound syndrom
 - E. Incompatibility
3. *Surgery used a combination of narcosis. Thus the final effect is the arithmetic sum of the effects of these drugs. What type of drug interactions?*
 - A. Potentiation
 - B. Cumulation
 - C. Antagonism
 - D. Addition
 - E. Sensitization
4. *How do we call the rapid development of the weakening of the pharmacological effect of the drug with repeated administration?*
 - A. Cumulation
 - B. Sensitization
 - C. Tolerance
 - D. Idiosyncrasy
 - E. Tachyphylaxis
5. *Pregnant woman during the month take tranquilizers, which showed weakening sucking reflex in infants. What action was realized at that time?*
 - A. Teratogenic
 - B. Allergic
 - C. Carcinogenic
 - D. Embryotoxic
 - E. Fetotoxic

II. Original practical work in class

1. Work with the tests (Krok-1).
 2. Solving of situational tasks.
- 1) To create an effective drug concentration in the body is necessary to introduce a therapeutic dose at defined intervals. Specify the pharmacokinetic criteria that should be considered when appointing the interval of administration of drugs.
 - 2) An ambulance bring to the hospital a man, who took a large dose of hypnotic drugs from derivatives of barbituric acid (phenobarbital). Among a set of measures and medicines the doctor has prescribed intravenous administration of sodium bicarbonate. What justified the decision of the doctor?
 - 3) When combined NSAID (Butadion) and oral anticoagulant (Warfarin) there will be an increase unrelated to blood albumin (free) fraction of warfarin. That in this case there will be with a patient? Name this type of interaction.
 - 4) After two weeks of taking the drug is an inducer of hepatic microsomal oxidation, there was a significant reduction of its pharmacological effect. What is the phenomenon took place?
 - 5) It is known that patients with genetically determined deficiency of glucose-6-phosphate dehydrogenase to the appointment of some antimalarial drugs can develop hemolysis. How do we call this atypical reactions to drugs?

- 6) Patient with heart failure has been assigned a cardiac glycoside Digoxin, which circulates in the blood for a long time. First, his condition improves, but over time, appeared signs of glycoside intoxication. How can this be explained?
- 7) Patient before tooth extraction was conducted novocain block anesthesia, after what at the injection site appeared edema and hyperemia, itching, weakness, hypotension, motor excitation. What is the name of complications?
- 8) Patients with essential hypertension was appointed β -blocker (Metoprolol). After six months of his admission the patient begin to notice the feeling of breathlessness, coughing. The patient stopped to use this drug. However, the state of the patient has deteriorated sharply: the blood pressure become unstable, often hypertensive crises. How do we call this phenomenon?
- 9) Patient with rheumatoid arthritis for a long time taking glucocorticoid drugs (Prednisone). While improving the health of patients, without first talking to your doctor, abruptly stop taking the drug. As a result, the patient showed signs of acute adrenal insufficiency (severe weakness, hyperpigmentation, nausea, sudden drop in blood pressure, etc.). What is the name of complications? As in such cases (task 8 and 9) must be done to remove the drug?
- 10) In the postoperative period the patient for a long time administered narcotic analgesics Promedol. After cancellation the drug in the patient appears severe mental and somatic disorders. How do we call this phenomenon?

CONTENT MODULE 2. DRUGS THAT AFFECT AFFERENT AND EFFERENT INNERVATION

Actuality of the unit. Synapse – highly specialized morfofunctional system located at the contact of the neuron to other neurons or effector cells of organs. Conducting of nerve impulses are doing by mediators which formed in presynaptic membrane and are deposited in the synaptic vesicles of the labile and stable fractions. Depending on the nature of the mediator divided into cholinergic synapses (acetylcholine), adrenergic (norepinephrine), dopaminergic (dopamine), serotonergic (serotonin), histaminergic (histamine) GABAergic (GABA) and others. Drugs to interfere with the speed of the nerve impulse are called synaptic or neurotransmitter substances. They either facilitate (act like – mimetics, agonists) or difficult (break, block – blockers, litics or antagonists) functioning synapses. By adjusting the speed of synaptic conduction, mediators change the status of the peripheral and central nervous system.

Using drugs that do mimic or block effects of mediators we can selectively modified many body functions, including autonomic system, regulating activity of cardiac muscle, smooth muscle, blood vessels, glands, presynaptic terminals. Thus, these compounds are employed in many diseases in clinical practice. Substances that affect synaptic transmission and penetrate the blood – brain barrier, are neurotropic and are discussed in the relevant section.

Actuality of the topic. This group of drugs either stimulate (irritating) peripheral receptors, enhances the function of an organ, system, or vice versa, decreases the sensitivity of nerve endings of afferent excitation and prevents them (protective effect). These drugs have a wide and varied use in everyday medical practice.

Classification of drugs affecting the afferent innervation

1) Irritating receptors:

- annoying distractions action;
- expectorants;
- bitterness;
- vomiting;
- laxatives;
- cholagogue.

2)Protects the receptors:

- local anesthetic;
- astigent;
- coating drugs;
- antacids;
- absorbent, etc.

The training objectives. *To know* : the pharmacology of drugs that affect on the efferent part of the nervous system, the pharmacology of agents affecting the receptors of the skin and mucous membranes

To be able: to write and justify the choice of drugs of this section in a different forms, to solve the test tasks, situational and pharmacological tasks, prescribe and analyze prescriptions on preparations in this section.

Intersubject integration. Normal and pathological anatomy and physiology, histology, biochemistry.

Unit 10. CHOLINOMIMETICS

Actuality of theme. Cholinotropic drugs have an active ting agent (cholinomimetics) or inhibitory (cholinoblockers) impact on the transmission of impulses in the cholinergic synapses in skeletal muscle, autonomic ganglia (sympathetic and parasympathetic), in the endings of postganglionic parasympathetic fibers of the internal organs. Consequently, cholinomimetic drugs low

blood pressure, heart rate, intraocular pressure, increases peristalsis of intestine and urinary tract, improve the tone of the uterus, the function of the excretory glands, accelerate neuromuscular transmission and reflex activity of skeletal muscle.

These and other effects make this group irreplaceable for the treatment of glaucoma, atony of intestine and urinary tract diseases, myasthenia gravis, paresis and paralysis after a stroke, poliomyelitis and others.

I. Individual work

Control questions

1. The efferent innervation: modern representations about its neurotransmitter systems and functionality.
2. Synaptic transmission as an object of the pharmacologic effects. Structure and function of synapses. The concept of agonist (mimetic) and antagonistic (blocking or political) substances. Typical mechanisms of direct and indirect action.
3. Cholinergic mediation. M – and N – cholinergic receptors, localization, and their subtypes function. Mechanisms cholinomimetic (direct and indirect) and anticholinergic action.
4. Classification of CHOLINERGIC AGONISTS:
 - *M – cholinergic agonists* – Pilocarpine, Aceclidine;
 - *N – cholinergic agonists* – Nicorette, Lobeline, Cyciton;
 - *M – ,N – cholinergic agonists:*
 - *direct – acting* – Carbachol;
 - *Indirect – acting (anticholinesterases):*
 - *Reversible* – quaternary amines (Neostigmine, Pyridostigmine); tertiary amines, alkaloids (Physostigmine, Galanthamine);
 - *Irreversible** – Armine¹
5. M – CHOLINOMIMETICS. Pharmacodynamics. Undesirable effects. Indications and contraindications. Acute poisoning by muscarine. Assistance measures, antidote therapy.
6. N – CHOLINOMIMETICS. Pharmacodynamics. Indications for use. Undesirable effects. Toxic effects of nicotine. The negative effects of smoking.
7. M, N – CHOLINOMIMETICS direct and indirect (anticholinesterase substance) action. Mechanisms of action. Pharmacological effects. Pharmacokinetics. Comparative characteristics of preparations. Indications for use. Undesirable effects.
8. Pharmacological safety and interchangeability medicines.
9. Poisonings with OPS. First Aid (reaktivator cholinesterase: Dipiroksim, Alloksim, Izonitrozin).

List of practical works. Prescribe drugs with their application (*separately from the prescription!*):

№	Name of the drug	Drug form
1.	Pilocarpine (<i>Pilocarpini hydrochloridum</i>)	Vial 5 ml. 1 % sol., eye drops
2.	Neostigmine (<i>Proserinum</i>)	Tab. 0,015; amp. 0,05 % sol. 1 ml.
3.	Cyciton (<i>Cytitonum</i>)	Amp. 1 ml.
4.	Galanthamine (<i>Galanthamini hydrobromidum</i>)	Amp. 1 % sol. 1 ml.
5.	Pyridostigmine (<i>Pyridostigmini bromidum</i>)	Tab. and dragee 0,06; amp. 0,5 % sol. 1 ml.
6.	Alloksim (<i>Alloximum</i>)	Amp. 0,075 lyophilic powder

Tasks for self-control. Choose the correct answers.

1. What effects cause M – cholinomimetics?

¹ By anticholinesterases irreversible actions are phosphororganic compounds (OPC), chemical warfare agents (CWA), insecticides and other poisons.

- A. Increase the heart rate
 - B. Increases the secretion of exocrine glands
 - C. Relaxes the smooth muscles of internal organs
 - D. Causes mydriasis
 - E. Reduces intraocular pressure
2. *Select groups of drugs used in cases of poisoning by anticholinesteras organophosphate substances :*
- A. N – holinomimetics
 - B. Adrenomimetics
 - C. Ganglionic blockers
 - D. Reaktivator cholinesterase
 - E. Adrenoblockers
3. *Tell the symptoms of poisoning mushrooms containing muscarine:*
- A. Bronchospasm
 - B. Tachycardia
 - C. Increase sweating
 - D. Hypertension
 - E. Diarrhea
4. *Name the conditions when we prescribe the anticholinesterase drugs:*
- A. Atony of intestine
 - B. Consequences of poliomyelitis
 - C. Convulsions
 - D. Glaucoma
 - E. Bronchial asthma
5. *The effects of Cytitonum :*
- A. Inhibits vasomotor center
 - B. It is a reflex excitation of the respiratory center
 - C. Inhibits sympathetic ganglia of blood pressure
 - D. Increases intestinal motility
 - E. Causes miosis

II. Original practical work in class

1. To view the collection of drugs.
2. Work with the tests (Krok-1).
3. Prescribe and ground the choice of drug:
 - 1) drug of choice for the emergency in glaucoma crisis, not influencing the neuro – muscular transmission and autonomic ganglia;
 - 2) drug for the treatment of glaucoma crisis, improving neuro – muscular transmission and activating ganglia;
 - 3) newborn asphyxia;
 - 4) for treatment of myasthenia gravis;
 - 5) for treating paralytic intestinal obstruction ;
 - 6) in the regenerative period poliomyelitis;
 - 7) at poisoning with OPS;
 - 8) a drug that causes bronchospasm and increased tone of skeletal muscles;
 - 9) preparation of forming reversible complexes with ACE and prevents inactivation of ACh;
 - 10) replacement drug pilocarpine;
 - 11) the drug is contraindicated in gastric ulcer.

Unit 11. CHOLINERGIC ANTAGONISTS (CHOLINERGIC BLOCKERS)

Actuality of theme. Cholinergic antagonists are divided into two main groups: M – and N – cholinergic blockers. M – cholinoblockers because of their pharmacological effects (bronchodilation, relaxing the bile, urinary tract, the uterus, causing tachycardia, reduced function of the excretory

glands, etc.) are the drugs for the treatment of bronchial asthma, bradyarrhythmias, relief of renal, intestinal, biliary colic, necessary for sedation of patients before surgery and others. N – cholinoblockers divided into 2 groups: drugs that block N – cholinergic receptors of autonomic ganglia – ganglionic blockers, and drugs that block N – cholinergic receptors of skeletal muscle – muscle relaxants. Application of ganglionic blockers today is limited because they do a lot of adverse effects (orthostatic collapse, etc.). They are now used mainly in urgent help to hypertensive crisis, controlled hypotension, pulmonary edema. Myorelaxants – substances relaxing skeletal muscles, are the central and peripheral actions. Central muscle relaxants (tranquilizers and others.) used for the treatment of convulsions and are treated in the "Agents acting on the central nervous system." Now it is unthinkable without peripheral muscle relaxants modern surgery, traumatology and others fields of medicine.

I. Individual work

Control questions

1. Classification of CHOLINERGIC ANTAGONISTS:

1) M – holinegic blockers – atropine, belladonna preparations, scopolamine, homatropine, platifillin, metacin, ipratropium, gastrotsepin etc. ;

2) N – holinegic blockers :

– ganglionic blockers – gigrony, pentamin, benzogeksony, pahikarpin, pyrylium;

– myorelaxants – tubocurarine, diplatsin, pipekuroniyu, vecuronium, atracurium, dithylin;

3) M, N – holinegic blockers(central) – cyclodol, aprofen, amizil, tropacin.

2. M – cholinergic blockers (atropinsimilar). History of creation. General characteristics. Classification:

a) *plant origin* (alkaloids, tertiary amines) – atropine and drugs of belladonna, scopolamine, platifillin;

b) *synthetic* – quaternary (metacin, ipratropium, tiotropium bromide, etc.), tertiary amines (pirenzepine).

Pharmacokinetics. Pharmacodynamics. Features of action in individual drugs. Indications and contraindications. Acute poisoning of plants containing atropine: the clinical picture, how to treat

3. N – cholinergic blockers – GANGLIONIC BLOCKERS. Classification by duration of action:

a) short – acting (15 – 20 minutes) – Hygronium;

b) intermediate – acting (1 – 6 hours) – Benzohexonium, Pentaminum, Pachicarpinum;

c) long – acting (6 – 12 hours) – Pirilenum.

Pharmacokinetics. Pharmacodynamics. Indications and contraindications. Undesirable effects. Clinic of overdose.

4. N – cholinergic blockers (MYORELAXANTS). Classification:

a) non – depolarizing drugs, curare – like agents – Tubocurarine, Diplacinum, Pipecuronium, Vecuronium, Atracurium;

b) depolarizing – Dithylinum (*Succinylcholine*);

c) mixed – Dioxonium.

Pharmacokinetics. Pharmacodynamics. Differences of individual groups. Therapeutic use. Undesirable effects. Treatment in cases of overdose.

Classification of muscle relaxants by duration of action:

1) Long-acting muscle relaxants (more than 50 min): arduan

2) Muscle relaxants of medium duration of action (20-50 min): esmeron, nimbex, trarium

3) Short-acting muscle relaxants (15-20 min): mivacron

4) Ultra-short-acting muscle relaxants (less than 10 minutes): listenone

5. M – and N – CHOLINERGIC BLOCKERS (central) – Cyclodolum, Amizilum, Aprofen and others. Mechanism of action. Indications and contraindications. Adverse effects.

List of practical works. Prescribe drugs with their application (*separately from the prescription!*):

№	Name of the drug	Drug form
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1	2	3
1.	Atropine (<i>Atropini sulfas</i>)	Amp. 0,1 % sol., 1 ml.; eye drops – vial 1 % sol. 5 ml.
2.	Platifilline (<i>Platyphyllini hydrotartras</i>)	Amp. 0,2 % with 0,2 % sol. 1 ml.
3.	Scopolamine (<i>Scopolamini hydrobromidum</i>)	Amp. with 0,05 % sol. 1 ml.
4.	Metacin (<i>Methacinum</i>)	Tab. 0,002; amp. 0,1 % sol. 1ml.
5.	Homatropine hydrobromide (<i>Homatropini hydrobromidum</i>)	Vial of 0,25 % sol., eye drops, 5 ml.
6.	Ipratropium (<i>Ipratropium bromidum</i>) syn.: Atrovent	Aer. f/ing (1 dose – 0,00004), 15 ml. (200 doses); amp. by 1, 2 ml. sol. f/inh. (1 ml. – 0,00025)
7.	Pirenzepine (<i>Pirenzepi</i>) syn.: Gastrozepin	Tab. by 0,025; 0,05
8.	Cyclodol (<i>Cyclodolum</i>)	Tab. by 0,002
9.	Pachicarpin (<i>Pachycarpini hydroiodidum</i>)	Amp. 3 % sol. 2 ml.
10.	Pentaminum (<i>Pentaminum</i>)	Amp. 5 % sol. 1; 2 ml.
11.	Tubocurarine (<i>Tubocurarinum chloridum</i>)	Amp. by 1,5 ml. (1 ml. — 0,01)
12.	Dithylinum (<i>Dithylinum</i>)	Amp. 2 % sol. 5 , 10 ml.

Tasks for self-control. Choose the correct answers.

1. Plants containing M-holinergic blockers:

- A. Datura
- B. Adonis
- C. Belen
- D. Hawthorn
- E. Brier

2. Therapeutic use of Atropine:

- A. Bronchospasm
- B. To narrow pupil
- C. Hepatic colic
- D. Diarrhea
- E. Hyperthermia

3. What M – holinergic blockers well absorbed in the gastrointestinal tract?

- A. Metacin
- B. Atropine
- C. Scopolamine
- D. Pirenzepine
- E. Ipratropium bromide

4. The main adverse effects of ganglionic blockers:

- A. Orthostatic collapse
- B. Bradycardia
- C. Constipation
- D. Improved tone of the uterus during pregnancy
- E. Atony of the bladder and difficulty urination

5. What are the adverse effects of depolarizing myorelaxants:

- A. Bronchodilation
- B. Muscle pain in the postoperative period
- C. Arrhythmias
- D. Hypokalemia
- E. Increase intraocular pressure

II. Original practical work in class

1. To view the collection of drugs.
2. Work with the tests (Krok-1).

3. Prescribe and ground the choice of drug:

- 1) Selective M – cholinergic blockers for treatment of asthma;
- 2) Selective M – cholinergic blocker used for treatment of ulcer disease;
- 3) Spasmolytic for removing of liver and kidney colica
- 4) Poisoning of fly – agaric mushroom
- 5) For treatment of hypertensive disease;
- 6) Drug in case of Parkinson's disease;
- 7) N – cholinergic blocker in obstetrics
- 8) In orthopedic practice for a relaxation of muscles;
- 9) For a controlled hypotonia;
- 10) Myorelaxant which action is weakened anticholinesterase preparations. What preparations strengthen effect of such type of myorelaxant?
- 11) Myorelaxant, to reduce the effects of which we need to do blood transfusion.
- 12) The drug that causes orthostatic collapse;
- 13) The drug replacing of Metatsinum;
- 14) The drug, causing respiratory arrest in overdose.

Unit 12. ADRENOMIMETICS

Actuality of theme. Adrenergic agents influence on the adrenergic synapses, where catecholamines (dopamine, norepinephrine, epinephrine) are mediators. That impact can be activating (agonists) and the brake (antiadrenergic). In the peripheral nervous system, adrenergic synapses are located mainly in the endings of postganglionic fibers of the internal organs, cardiovascular system.

Adrenomimetics are the drugs of choice in the collapse, shock, bronchial asthma, bradyarrhythmias, hypoglycemic coma, and others.²

I. Individual work

Control questions.

1. Adrenergic mediation. α - and β – adrenergic receptors: their types, localization in organism, the main effects.

2. Substances adreno – positive (adrenergic agonists, adrenomimetics, sympathomimetics) and adreno – negative or antiadrenergic (adreno – antagonists). Selective and non – selective adrenergic drugs. The feasibility of the creation of selective drugs. The mechanisms of direct and indirect action.

3. Classification of ADRENERGIC AGONISTS:

1) α - and β – adrenergic agonists:

- *direct* – Epinephrine (Adrenaline) tartrate and hydrochloride;
- *indirect* – Dopamine*, Ephedrine;

2) α -adrenergic agonists – Noradrenaline, Mesatonum, Naphthyzinum, Halazolinum (Xelomethazoline)

Central α_2 -adrenomimetics Clophelinum (Clonidine), Methyldopa, Guanfacine**;

3) β – adrenergic agonists:

- Non – selective ($\beta_1 + \beta_2$) – Isadrinum, Alupent (Orciprenalinum)***;
- Cardioselective (β_1) – Dobutamine;
- β_2 -selective:

- – *short-acting* (3-8h)

Salbutamol, Fenoterol (Partusisten), Hexoprenaline (Ipradol, Gynipral), Terbutaline;

- – *long – acting* (10 – 12 h) – Formoterol, Salmeterol, Clenbuterol;

² *To adrenomimetics with indirect action are also included stimulants (amphetamines, cocaine), antidepressants (see. "Drugs affecting the central nervous system").

**Central α_2 -adrenoceptor agonists are discussed in topic № 25

*** Orciprenaline stimulates predominantly β_2 -adrenergic receptors.

4. The ALPHA and BETA-ADRENOMIMETICS with direct action. Pharmacokinetic and pharmacodynamics of Epinephrine (Adrenaline). The concept of *pacemakers*. Indications and contraindications for use. Adverse effects.
5. Pharmacology of indirect adrenomimetics.
6. The ALPHA – ADRENOMIMETICS. General characteristics. Pharmacokinetics and pharmacodynamics. Adverse effects. Indications and contraindications to application. Concept about *anticongestants*.
7. The BETA – ADRENOMIMETICS. General characteristics. Classification by selectivity of action. Pharmacokinetics and pharmacodynamics non – selective beta – adrenomimetics. Indications. The concept of *cardiotonics, bronchodilators and tocolytics*. Adverse effects and contraindications to application.

List of practical works. Prescribe drugs with their application (*separately from the prescription!*):

№	Name of the drug	Drug form
1.	Adrenaline hydrochloride (<i>Adrenalini hydrochloridum</i>)	Amp. 0,1 % sol., 1 ml.
2.	Dopamine (<i>Dofaminum</i>)	Amp. 4 % sol., 5 ml.
3.	Ephedrine (<i>Ephedrini hydrochloridum</i>)	Amp. 5 % sol., 1 ml.; tab. 0,025
4.	Noradrenaline (<i>Noradrenalini hydrotartras</i>)	Amp. 0,2 % sol., 1 ml.
5.	Mesatonum (<i>Mesatonum</i>)	Amp. 1 % sol. 1 мл, tab. 0,01
6.	Halazolinum (<i>Halazolinum</i>) syn.: Xelomethazoline	VIAL 0,05 and 0,1 % sol., nasal drops
7.	Isadrinum (<i>Isadrinum</i>) syn.: Novodrin	Tab. by 0,005; vial 0,5 % sol. f/inh. by 25, 100 ml.
8.	Dobutamine (<i>Dobutaminum</i>)	Amp. 5 % sol., 5 ml.
9.	Salbutamol (<i>Salbutamolum</i>) syn.: Ventolin	Aer. f/inh. 0,1 mg/dose, balloon 10 ml.; tab. 0,002, 0,004
10.	Fenoterol (<i>Fenoterolum</i>) syn.: Berotec, Partusisten	Aerosol f/inh. 0,2 mg/dose, 15 ml.; tab. 0,005; (<i>Partusisten</i>) – vial sol. f/inh. (1 ml. – 0,005) by 10 ml.

Tasks for self-control. Choose the correct answers.

1. What are the effects of the β -adrenomimetics on the heart?:
 - A. Positive chronotropic
 - B. Positive inotropic
 - C. Negative inotropic
 - D. Positive dromotropic
 - E. They reduce myocardial requirement in oxygen
2. Specify the effects of adrenaline:
 - A. Decrease systolic blood pressure
 - B. Relaxes the bronchs, the uterus
 - C. Increases the motility of the gastrointestinal tract
 - D. Causes hyperglycemia
 - E. Decrease intraocular pressure
3. What drug will lead to tachyphylaxis in readmission
 - A. Adrenaline
 - B. Mesatonum
 - C. Ephedrine
 - D. Isadrinum
 - E. Dobutamine
4. Indications for adrenaline are
 - A. Stoppage of heart

- B. Hypertensive crisis
 - C. For prolongation of action local anaesthetics
 - D. Hyperglycemic coma
 - E. Anaphylactic shock
5. *What are the adverse effects when using agonists*
- A. Collapse
 - B. Arrhythmia
 - C. Dry in the nasopharynx
 - D. Bronchospasm
 - E. Desensitization of receptors

II. Original practical work in class

1. To view the collection of drugs.
2. Work with the tests (Krok-1).
3. Prescribe and ground the choice of drug:
 - 1) In case of collapse;
 - 2) In case of anaphylactic shock;
 - 3) Adrenomimetic drug used in case of bronchial asthma;
 - 4) Adrenomimetic drug (“nasal decongestant”) used in case of vasomotor rhinitis;
 - 5) Adrenomimetic drug used in case of bradyarrhythmia;
 - 6) Adrenomimetic drug used in case of hypoglycemic coma;
 - 7) Preparation, which way of introduction extremely intravenous owing to necrotic actions;
 - 8) In the hypertonus of the uteri;
 - 9) For prolongation of action local anaesthetics;
 - 10) In case of ganglionic blocker overdosing;
 - 11) Adrenergic agonist, that may cause insomnia;
 - 12) The drug, causing tachycardia;
 - 13) The drug from the group of selective β -agonists;
 - 14) Selective α_2 -adrenomimetic short-acting;
 - 15) The drug salbutamol replacing;
 - 16) The drug norepinephrine replacing;
 - 17) The drug that causes mydriasis.

Unit 13. ADRENERGIC ANTAGONISTS. SYMPATHOLYTICS.

Actuality of the unit. This group of drugs is divided into drugs acting on receptors (blockers) and reducing the content of catecholamines in the synapse (sympatholytic). Adrenolytics are the leading drugs in the treatment of the most common diseases of the cardiovascular system: hypertension, tachyarrhythmias, ischemic heart disease (angina, myocardial infarction, atherosclerosis), etc. The knowledge of this group of drugs is necessary for the doctor of any specialty.

I. Individual work

Control questions

1. Classification of ANTIADRENERGIC drugs:
 - 1) α -, β – adrenergic antagonists – Labetalol, Proxodolol, Carvedilol;
 - 2) α -adrenergic antagonists:
 - Nonselective (α_{1+2}) – Dihydroergotamine, Nicergolinum (Sermionum), Phentolamine, Tropicafen, Aminazinum, Pyroxanum;
 - Selective (α_1) – Prazosin, Doxazosin, Terazosin
 - 3) β – adrenergic antagonists:
 - Nonselective (β_{1+2}) – Propranolol (Anaprilinum), Oxprenolol*, Pindolol*, Timolol
 - Selective (β_1) – Atenolol, Metoprolol, Bisoprolol, Betaxolol, Acebutolol*, Celiprolol*
 - 4) Sympatholytics – Reserpine, Octadinum

2. ALPHA – ADRENOBLOCKERS. General characteristics. Pharmacodynamics and pharmacokinetics. Distinctive features of preparations. Adverse effects. Indications and contraindications to application of selective and not – selective preparations.

adrenergic antagonists are classified into the following groups:

1. Alpha-blockers: Alpha-1-blockers (alfuzosin, doxazosin, prazosin, silodosin, tamsulosin, terazosin, urapidil);
2. Alpha 2-blockers (yohimbine);
3. Alpha-1,2-blockers (nicergoline, phentolamine, propoxan, dihydroergotamine, dihydroergocristine, alpha-dihydroergocriptine, dihydroergotoxin).

3. BETA – ADRENOBLOCKERS. General characteristics. History of creation. Classification on selectivity of action. Pharmacodynamics. The benefits of selective drugs. Features of drugs with intrinsic sympathomimetic activity.

Pharmacokinetics. Classification *on duration of action*:

- a) Long acting ($T_{1/2} - 6 - 24$ h): Nadolol, Timolol, Atenolol, Bisoprolol, Betaxolol;
- b) Intermediate duration of action ($T_{1/2} - 3 - 6$ h): Propranolol (Anaprilinum), Pindolol, Metoprolol, Celiprolol;
- c) Short acting ($T_{1/2} - 1 - 4$ h): Oxprenolol, Acebutolol.

Indications and adverse effects.

4. ALPHA, BETA – ADRENOBLOCKERS. Pharmacodynamic. Indications and contraindications to assignment.

5. SYMPATHOLYTIC drugs. Pharmacodynamic. Indications and contraindications for use. Adverse effects.

6. Safety of pharmacology and interchangeability medicines.

List of practical works. Prescribe drugs with their application (*separately from the prescription!*):

№	Name of the drug	Drug form
1.	Dihydroergotamine (<i>Dihydroergotaminum</i>)	Amp. 0,1 % sol. 1 ml., tab. 0,0025
2.	Phentolamine (<i>Phentolamini hydrochloridum</i>)	Tab. 0,025
3.	Prazosin (<i>Prazosinum</i>) syn.: Minipress	Tab. 0,001, 0,005
4.	Doxazosin (<i>Doxazosinum</i>)	Tab. 0,002, 0,004
5.	Anaprilinum (<i>Anaprilinum</i>) syn.: propranolol, inderal, obzidan	Tab. 0,01 and 0,04
6.	Pindolol (<i>Pindololum</i>)	Tab. 0,005; ampl. 0,02 % sol. 5 ml.
7.	Timolol (<i>Timololum</i>)	Tab. 0,005, 0,01; vial 0,25; 0,5 % sol. 5 ml. (eye drops).
8.	Metoprolol (<i>Metoprololum</i>) syn.: spesicor, lopresol	Tab. 0,05 and 0,1; amp. 1 % by 5 ml.
9.	Atenolol (<i>Atenololum</i>)	Tab. 0,05, 0,025 и 0,1
10.	Carvedilol (<i>Carvedilolum</i>)	Tab. 0,0625, 0,0125, 0,025
11.	Reserpine (<i>Reserpinum</i>)	Tab. 0,0001, 0,00025

Tasks for self-control. Choose the correct answers.

1. Pharmacokinetic effects of α -blockers are:

- A. Reducing the motility of the gastrointestinal tract
- B. Acute hypotension
- C. Mydriasis
- D. Reflex bradycardia
- E. Improving intraorganic circulation

2. Beta-blockers cause:

- A. «-» chronotropic effect

- B. "+" inotropic effect
 - C. "-" dromotropic
 - D. Increased myocardial oxygen demand
 - E. Cardioprotective effect
3. *Specify features of β -blockers with intrinsic sympathomimetic activity from other members of this group:*
- A. Mildly reduced blood pressure
 - B. Has more pronounced effect in decreasing HR
 - C. Has a powerful "-" inotropic effect
 - D. Practically hasn't an atherogenic effect
 - E. Less cause "rebound" syndrome
4. *Indications for β -blockers:*
- A. Bradyarrhythmia
 - B. Arterial hypertension
 - C. Angina pectoris
 - D. Bronchial asthma
 - E. Atherosclerosis
5. *Adverse effects of β -blockers*
- A. Peripheral vasoconstriction
 - B. Hyperglycemia
 - C. Bronchospasm
 - D. Increased production of triiodothyronine
 - E. Desensitization of receptors

II. Original practical work in class

1. To view the collection of drugs.
2. Work with the tests (Krok-1).
3. Prescribe and ground the choice of drug:
 - 1) for diagnostics pheochromocytoma;
 - 2) for treatment of benign prostatic hyperplasia;
 - 3) for treatment obliterating endoarteritis;
 - 4) antianginal, requiring careful use in hypothyroidism, diabetes, etc.;
 - 5) for treatment of glaucoma;
 - 6) selective β -blocker is not recommended during pregnancy;
 - 7) for treatment of hypertonic disease with the expressed displays of an atherosclerosis;
 - 8) the preparation, which effect develops after 7 – 14 days of reception.
 - 9) when tachyarrhythmia;
 - 10) From the group of selective β -blockers;
 - 11) From the group of selective α -blockers;
 - 12) The drug atenolol replacing;
 - 13) The drug prazosin replacing;
 - 14) The drug, causing bronchospasm.

Unit 14. PREPARATIONS IRRITATING THE PERIPHERAL RECEPTORS OF SKIN AND MUCOUS MEMBRANES

Actuality of the unit. Expectorant, laxative, choleric and other means of irritants are often used for the treatment of diseases of the respiratory and digestive system; They are an important part of the complex therapy of acute and chronic diseases.

I. Individual work

Control questions

IRRITATING agents of diverting action

- *Plant origin* – menthol and drugs based on it (validol, ointment "Menovazin", "Efkamion"), mustard seeds (mustard), oil of turpentine refined (turpentine), and others.
- *Synthetic* – ammonia sol. finalgon, methyl salicylate and others.

Mechanism of action. Application

EXPECTORANTS. Classification.

- a) *secretomotor* (stimulants of expectoration) – reflex action – grass of Thermopsisidis, root of istoda, mukaltin, Pertussin, Terpin hydrate; direct action – herb thyme, marshmallow root, rhizome cyanosis, plantain leaves, potassium iodide;
- b) *mucoytics* (bronchosecretolytics) – Acetylcysteine, Bromhexine, Ambroxole (Lasolvan).

Mechanisms of action. Indications and contraindications. Side effects. The concept of pulmonary surfactant (Curosurf, Exosurf, beraktant).

BITTERS.

- 1) *Real bitters* – dandelion root, grass centaury
- 2) *Aromatic bitters* (species, juice of Goose – grass leaves, Tea appetitiful, Plantaglucide).

Mechanisms of action. Usage.

EMETIC drugs. Classification:

- 1) *Central action* – apomorphine;
- 2) *reflex* – Thermopsis preparations, ipecac, copper sulfate, hypertonic sodium chloride sol.

Mechanisms of action. Indications for use. Side effects.

LAXATIVES. Classification according to localization of their effect in defined parts of intestine:

- a) drugs, accelerating motor function through *whole intestine*
 - osmotic laxatives – Sodium sulfate, Magnesium sulfate;
 - polyatomic alcohols – Xylitol, Lactulose, Mannitol;
 - drugs, that increase volume of intestine content (bulging agents) – Agar, Methylcellulose, Psyllium seeds, bran;
 - stool softeners – plant and mineral oils, Glycerin suppositories;
- b) drugs, accelerating mostly the motor function of *small intestines* – Castor oil;
- c) drugs, accelerating mostly the function of *large intestine*:
 - preparations of plant origin, containing antraglycosides – bark of Frangula; leaves of Senna, Senade, Regulax;
 - synthetic – Phenolphthalein, Isaphenin, Bisacodyl, Guttalax.

Mechanisms of action. Side effects. Indications and contraindications.

The *modern anatomical and therapeutic classification identifies 6 groups* of drugs with a laxative effect:

1. Emollients
2. Contact laxatives
3. Bulking Laxatives
4. Osmotic laxatives
5. Laxatives in enemas
6. Other laxatives

BILE EXPELLING preparations. Classification:

1. drugs, stimulating the bile production (choleretics);
 - a) preparations, containing bile acids and bile – Cholenzym, Allohol;
 - b) preparations of the plant origin – fetus of Hips (Cholosas), flowers of Immortelle, Flacumin, Legalon, Cholagol;
 - c) synthetic drugs – Oxaphenamide, Cycvalonum, Nicodin, Ursofalk;
2. drugs, promoting the expelling of bile from gall-bladder into intestine (cholekinetics):
 - a) cholecystokinetics – Magnesium sulfate, Sorbite, Xylitol, olive oil, Pituitrinum, etc.;
 - b) spasmolytics – Atropine, Papaverine, No – Spa and others.

Mechanisms of action, indications and contraindications for use.

List of practical works. Prescribe drugs with their application (*separately from the prescription!*):

№	Name of the drug	Drug form
1.	Bitter tincture (<i>Tinctura Amara</i>)	Vial 25 ml.
2.	Patented medicinal forms, containing Menthol: ointment “ Menovazine ”, “ Efcamone ”, tabl. “ Pectusinum ”, aerosolum “ Camfomen ” etc.	
3.	Acetylcysteine (<i>Acetylcysteinum</i>)	Powder by 0,1, 0,2; amp. 20 % sol. 5 ml. for inhalations; amp. 10 % sol. 2 ml. for injections
4.	Mixture containing infusion of Thermopsis grass (herba <i>Thermopsisidis</i>), SD – 0,05 and Ammonia anise drops (<i>Liquorum ammonii anisatus</i>), SD – 10 drops	
1)	Mucaltin (<i>Mucaltinum</i>)	Tab. 0,05
2)	Ambroxole (<i>Ambroxolum</i>) syn.: Lasolvan	Tab. 0,03; amp. 0,015 % sol. 2 ml. for injections; vial. 0,75 % sol. 100 ml. for peroral intake and inhalations
3)	Castor oil (<i>Oleum Ricini</i>)	Vial 30 ml., caps. 0,5 and 1,0.
5.	Bark of Frangula (<i>cortex Frangulae</i>), SD – 2,5	
4)	Bisacodyl (<i>Bisacodylum</i>)	Dragee 0,005; suppositories 0,01
5)	Magnesium sulfate (<i>Magnesii sulfas</i>)	SD – 25,0.
6)	Allohol (<i>Allocholium</i>)	Patented tab.

Tasks for self-control. Choose the correct answers.

1. Specify the secretory motor expectorant reflex action:

- A. Potassium iodide
- B. Thermopsis Grass
- C. Ambroxol
- D. Terpene
- E. Acetylcysteine

2. Specify mucolytics, who stimulate the production of pulmonary surfactant:

- A. Bromhexine
- B. Acetylcysteine
- C. Mucaltin
- D. Terpene
- E. Ambroxol

3. Specify laxatives that increase the motility of the whole intestine:

- A. Bisacodyl
- B. Forlaks
- C. Castor oil
- D. Magnesium sulphate
- E. Xylitol

4. The man with the aim of a suicide has taken a large number of sleeping pills from the group of barbiturate. What is the laxative used in this case?

- A. Regulaks
- B. Izafenin
- C. Magnesium sulfate
- D. Senade
- E. Castor oil

5. Specify cholagogue holetsistokinetikov from the group:

- A. Atropine
- B. Allohol
- C. Xylitol

- D. Magnesium sulphate
E. No-spa

II. Original practical work in class

1. To view the collection of drugs.
2. Work with the tests (Krok-1).
3. Prescribe and ground the choice of drug:
 - 1) Expectorant drug in the form of infusion;
 - 2) Mucolytic having detoxication properties;
 - 3) Secretomotor expectorant plant origin in tablets;
 - 4) Laxative in the decoction form;
 - 5) Synthetic laxative, causing chemical irritation of the intestinal mucous membrane receptors;
 - 6) Laxative for chronic constipation, acting mainly in the small intestine;
 - 7) Drug, stimulating bile secretion;
 - 8) Choleric comprising a bile acid;
 - 9) Bile expelling preparations from spasmolytic group
 - 10) Drug in case of myositis;
 - 11) To increase your appetite;
 - 12) Synthetic laxative enhancing motor function primarily of the large intestine;
 - 13) The drug bromhexine replacing;
 - 14) Holetsistokinetik.

Unit 15. PREPARATIONS PROTECTING THE RECEPTORS OF SKIN AND MUCOUS MEMBRANES.

Actuality of the unit. This group is designed to protect skin cells and receptors, mucous membranes from the damaging effects of chemical factors. Particularly important are local anesthetics, interrupting the flow of pain impulses in the central nervous system and are an integral part of the major and minor surgery, dentistry. Cementing, enveloping, antacids regularly used in the treatment of gastric ulcers and 12 duodenal ulcer, hyperacidity gastritis, dermatology and others.

I. Individual work

Control questions

LOCAL ANESTHETICS:

1. Conception of local anesthesia and its variants. Desirable properties of local anaesthetics. Historical review.
2. Classification according to by the *chemical structure*;
 - a) complex ethers – Procaine (Novocain®), Tetracaine (Dicain), Benzocaine (Anaesthesin), Cocaine*;
 - b) amides – Trimekain, Lidocaine, Articaine (Ultracaine), Etidocaine, Prilocaine, Ropivacaine, Bupivacaine;
 - c) from different groups – Pramoxine, Phenacaine.
3. Classification according to the *duration of anesthesia*:
 - short acting (to 30 – 50 min) – Procaine;
 - intermediate acting (to 45 – 50 min) – Lidocaine, Articaine, Trimekain;
 - long acting (> 90 min) – Etidocaine, Bupivacaine, Dicain

Classification of local anesthetics:

 1. Means used for surface anesthesia: dicain, anestezin, promecain
 2. Means used for infiltration anesthesia: novocaine, trimecaine, bupivacaine
 3. Means used for all types of anesthesia: cocaine, ultracaine, lidocaine
4. Chemical structure and physico – chemical properties.

5. Pharmacodynamics of local anaesthetics. Mechanism of action.

6. Factors affecting the development of the activity and the effect of local anesthetics Advantages and disadvantages of every mentioned group.

7. Pharmacokinetics of local anaesthetics.

8. Indications for usage. Features of destination for various types of local anesthesia. Combination with adrenomimetics.

9. Undesirable reactions, preventing and treating. Interactions with another drugs (anticholinesterase, sulfonamides, etc.).

ASTRINGENTS: Classification:

– organic – oak's bark, Tannin, blueberry, sage, knotweed, celandine, walnut fruit;

– inorganic – salts of heavy metals (Zn, Fe, Ag);

Mechanisms of action. Conditions, defining the character of heavy metals salts action (grade of dissociation, solving ability, tissue type, pH of the surrounding). Indications for usage.

COATING DEMULCENTS. (Starch, root of Althea, Aluminium salts and others) Mechanism of action. Indications for use.

ADSORBENTS (Activated carbon, Kaolin, Carbolong, enterosorbets – Polysorbate, Enterodesum, Enterosgelum). Mechanisms of action, indications for use.

. ANTACIDS. Classification:

– *absorbable*: Sodium hydrocarbonate, Calcium carbonate;

– *non – absorbable*: on the base of Al and Mg – Al hydroxide, “Maalox”, “Phosphalugel”, “Almagel” (aluminum hydroxide, magnesium oxide +), Aluminium phosphate gel (aluminum phosphate + pectin + agar), gastal (+ aluminum hydroxide, magnesium carbonate) sucralfate / Venter / sodium aluminum hydroxycarbonate / alyugastrin.

– *combined*: Vikalin, Vicair.

Mechanisms of action. Indications for usage. Undesirable effects

THE FILM-FORMING AGENT – medical glue, oblekol, furaplast, Lifuzol. Mechanism of action. Indications for use.

3

List of practical works. Prescribe drugs with their application (*separately from the prescription!*):

№	Name of the drug	Drug form
1.	Anaesthesia (<i>Anaesthesinum</i>)	Tab. 0,3; 5 % ointment
2.	Patented preparations on the basis of Anaesthesinum: Bellasthesinum ”, Pavesthesinum ”, suppositories Anaesthesolum, ointment Menovazinum, Sledianum	
3.	Novocain (<i>Novocainum</i>) syn.: Procaine	Amp. 0,25% sol. (for infiltration anesthesia); 1 – 2 % sol. (for conductive anesthesia) 10 ml.
4.	Lidocaine (<i>Lidocainum</i>)	Amp. 1 % sol. 10 and 20 ml.; 10 % 2 ml.; 2 % 2 and 10 ml.
5.	Trimekain (<i>Tetracainum</i>) syn.: Dicain	Amp. 0,5 %; 1 %, 2 % and 3 % sol.s 5 ml.
6.	Ultrakain (<i>Ultracainum</i>)	Amp. 1 % and 2 % sol. 1 ml.
7.	Zinc sulfate (<i>Zinci sulfas</i>)	Eye drops 0,1 %, 0,25 %, 0,5 % sol. 10 ml.
8.	Maalox (<i>Maalox</i>)	Patented tab., suspension in vial 250 ml.
9.	Enterogel (<i>Enterogelum</i>)	Pack with gel by 45, 135, 225, 450, 650 and 900 g.

^{3*} Currently cocaine not used in medical practice

Tasks for self-control. Choose the correct answers.

1. *Indications for the use of novocain are:*
 - A. Infiltration anesthesia (2%)
 - B. Conduction anesthesia (0,25%)
 - C. Conduction anesthesia (1-2%)
 - D. Infiltration anesthesia (0,25%)
 - E. As a vasoconstrictor
2. *What drugs can prolong the action of local anesthetics?*
 - A. Epinephrine hydrochloride
 - B. Atropine
 - C. Mezaton
 - D. Anaprilin
 - E. Neostigmine
3. *Specify the adverse effects of lidocaine:*
 - A. Violation of the heart rate
 - B. CNS stimulation
 - C. Lowering blood pressure
 - D. Increased blood pressure
 - E. The pain in the epigastric
4. *What plants have astringent action?*
 - A. The leaves of mint
 - B. St. John's wort grass
 - C. Valerian root
 - D. Oak bark
 - E. The leaves of sage
5. *The main indications for the use of absorbent are:*
 - A. Calculous cholecystitis
 - B. Acute poisoning
 - C. Flatulence
 - D. Intestinal obstruction
 - E. Diarrhea

II. Original practical work in class

1. To view the collection of drugs.
2. Work with the tests (Krok-1).
3. Prescribe and ground the choice of drug:
 - 1) short-acting local anaesthetic for infiltration anaesthesia;
 - 2) local anaesthetic used in ophthalmology;
 - 3) local anaesthetic for conductive anaesthesia;
 - 4) local anaesthetic in suppositories;
 - 5) local anaesthetic as antiarrhythmic;
 - 6) astringent in eye drops;
 - 7) prevents the absorption of poison in case of poisonings;
 - 8) for treatment of peptic ulcer. 9) for the treatment of gingivitis;
 - 9) for the treatment of hemorrhoids
 - 10) local anesthetics of amide groups;
 - 11) organic astringent;
 - 12) mepivacaine replacing drug;
 - 13) preparation of activated carbon replacing;
 - 14) symptomatic treatment for heartburn

Unit 16. CHECKING OF PRACTICAL SKILLS ON “DRUGS INFLUENCING ON EFFERENT AND AFFERENTE NERVOUS INNERVATION”

CONTENT MODULE 3. DRUGS THAT AFFECT THE FUNCTIONS OF THE CENTRAL NERVOUS SYSTEM

Classification of drugs affecting the central nervous system

1) DEPRESSING FUNCTIONS OF CENTRAL NERVOUS SYSTEM (CNS depressants):

- General anaesthetics;
- hypnotics;
- anticonvulsants;
- non – narcotic analgesics;
- psychotropic substances (narcotic analgesics, psychodysleptics, neuroleptics, tranquilizers, psychosedative);

2) STIMULATING FUNCTIONS OF THE CENTRAL NERVOUS SYSTEM:

- psychotropic (psychostimulants, antidepressants);
- analeptics;
- nootropes, adaptogens

Actuality of the unit. To Know the pharmacology of drugs with depressing and stimulating effects on the central nervous system.

Be able: to solve the test tasks, situational and pharmacotherapeutic problems, prescribe and analyze prescriptions on preparations in this section

Intersubject integration. Physiology, pathological physiology, biochemistry of the central nervous system.

Unit 17. GENERAL ANAESTHETICS. ALCOHOLS

Actuality of the unit. Agents for anesthesia commonly used in surgical practice. Substances of this group, when introduced into the body in different ways cause the reversible loss of consciousness, the loss of all kinds of sensitivity, reduce muscle tone and reflex activity while maintaining vital body functions. Requirements to the general anaesthetics: high analgesic activity, wide spectrum of therapeutic action, good ability of anaesthesia management (introduction and removal of the anesthesia), absence of the excitation stage, low toxic effects on the body. Unfortunately, none of the known general anaesthetics not fully meet the above requirements.

Ethyl alcohol (ethanol) has found a wide use in pharmaceutical industry and in medical practice (antiseptic, disinfective, irritation etc.) Comprehension in the toxicology of ethyl alcohol (and other alcohols as well) is essential for its presence in beverages and for alcohol intoxication.

I. Individual work

Control questions

GENERAL ANESTHETICS

1. General characteristics. Classification:

a) For *inhalation narcosis*:

- fluid volatile substances – Ether⁴, Halothane(Ftorotan), Enflurane, Isoflurane;
- gases – Nitrous oxide;

b) For *noninhalation narcosis*:

- barbiturates – Thiopental, Hexenal ;

– non – barbiturates – Ketamine (Kalipsol), Propanidid (Sombrevin), Midazolam, Sodium hydroxybutyrate, etc;

2. Stages of anesthesia. Requirements to anesthetics.

⁴ Currently is not used practically.

3. Pharmacodynamics and pharmacokinetics of inhalation and noninhalation narcosis.
Advantages and disadvantages groups
4. Complications of anesthesia.
5. Elements of modern anesthesia. Conceptions of preanesthetic medication, the opening and the base, combined and mixed anesthesia, neuroleptanesthesia. Induction, maintenance and recovery.

ALCOHOLS

- 1) Pharmacokinetics and pharmacotoxicodynamics.
- 2) Usage in medical practice.
- 3) Acute poisoning, treatment. Chronic poisoning. Medical and social aspects of alcoholism treatment. Disulfiram (teturam) and drugs with disulfiram-like effect (apomorphine, metronidazole, sulfonamides, nitrofurans, etc.).
- 4) Methanol poisoning. The clinical picture of poisoning. First aid and antidotes.

List of practical works. Prescribe drugs with their application (*separately from the prescription!*):

№	Name of the drug	Drug form
1.	Propophol (<i>Propofolum</i>) syn.: Diprivan	Amp. 1 % emulsion by 20 ml.
2.	Propanidid (<i>Propanididum</i>) syn.: Sombrevin	Amp. 5 % sol. 10 ml.
3.	Ketamine hydrochloride (<i>Ketamini hydrochloridum</i>) syn.: Kalipsol, Ketalar, Ketanest	Vial 1 % sol. 20 ml. and 5 % sol. 10 ml.
4.	Thiopental-sodium (<i>Thiopenthalum-natrium</i>)	Vial 0,5 и 1,0
5.	Sodium oxybutyrate (<i>Natrii oxybutyras</i>)	Amp. 20 % sol. 10 ml.
6.	Ethanol (<i>Spiritus aethylicus</i>)	40 %, 70 %, 95 % sol.
7.	Teturam (<i>Teturamum</i>) syn.: Disulfiram	Tab. 0,15 and 0,25

Tasks for self-control. Choose the correct answers.

1. What preparation is most often causes damage to the liver:
 - A. Nitrous oxide
 - B. Halothane
 - C. Geksenal
 - D. Propanidid
 - E. Sodium hydroxybutyrate
2. Specify the anesthetic drug – acting:
 - A. Propanidid
 - B. Halothane
 - C. Thiopental
 - D. Isoflurane
 - E. Ketamine
3. The advantages of noninhalation narcosis are:
 - A. Easy handling anesthesia
 - B. Lack of excitation stage
 - C. Did the introduction is operating
 - D. Most of the breadth of therapeutic action
 - E. Low anesthetic activity
4. Disadvantages of inhalation narcosis are:
 - A. Explosiveness, flammability
 - B. Low breadth of therapeutic action
 - C. Inability to anesthesia management

D. Cause bronchospasm, bronhoreya

E. Application only in operation

5. *Specify the effect of alcohol on thermoregulation:*

A. increases heat production

B. Reduce heat production

C. Increases heat

D. Reduce heat

E. Does not affect heat transfer and heat production

II. Original practical work in class

1. To view the collection of drugs.

2. Work with the tests (Krok-1).

3. Prescribe and ground the choice of drug:

- 1) inhalation anesthetic drug, which is characterized by prolonged excitation stage
- 2) preparation for anesthesia (volatile liquid) without a stage of excitation, which has arrhythmogenic;
- 3) preparation for anesthesia, with the reintroduction of which may develop liver toxicity;
- 4) noninhalation anesthetic drug – a derivative of barbituric acid;
- 5) drug for anesthesia with sedative, hypnotic, anti – hypoxic, muscle relaxant effects;
- 6) the drug for preanesthetic medication to prevent hypersalivation
- 7) the drug, while taking use of alcoholic beverages which can cause nausea, vomiting, tachycardia, hypertension, shortness of breath, fear of death
- 8) To the hospital delivered a patient with complaints of vomiting, headache, severe pain in the stomach and in the calf muscles, flickering flies in front of the eyes. He drank alcohol on the eve. What caused the poisoning? What is the antidote?

Unit 18. HYPNOTIC AND ANTICONVULSIVE DRUGS

Actuality of the unit. Hypnotic drugs are pharmacological substances, contributing to the coming of sleep at the defined conditions. Insomnia is one of the most serious problems of medicine. It is now known a large number of drugs with hypnotic effect, but none of them meet the requirements of an ideal sleeping pills. The most important lack of practically all hypnotic drugs is the inability to produce the physiologic (normal) sleep. Besides, a big part of hypnotic drugs has serious adverse effects, which can be observed at the next morning after administration of drug. The choice of the optimal sleeping pills to treat insomnia of various origins is solved on the basis of the analysis of the nature of sleep disorders (phases and stages) and taking into account the profile of each individual pharmacological hypnotic drug.

Anticonvulsants decrease the function of motor centers and are used for treatment of convulsive syndrome of different nature, spastic syndrome and parkinsonism. Drugs used for removing of convulsions – is the task of emergency treatment, which should be the most successfully dealt with the doctor of any specialty. So, while studying this unit, the basic attention must be dedicated to the symptomatic anticonvulsive drugs.

I. Individual work

Control questions

HYPNOTICS

1. Definition of the group, history of use.
2. Structure of the physiological sleep. Kinds of hyposomnia.
3. Classification of hypnotic drugs:
 - 1) Derivatives of *Benzodiazepines* (tranquilizers) Nitrazepam, Phenazepam, Flunitrazepam, Alprazolam, Triazolam;
 - 2) Derivatives of *Barbital acid* (barbiturates): Phenobarbital, Reladorm (Cyclobarbital + Diazepam);
 - 3) Hypnotics of different chemical groups:

- Cyclopyrrolons – zopiclone (imovan);
- Imidazopyridines – zolpidem;
- Pyrazolopyrimidine – zaleplon (Andante);
- Ethanolamines – doxylamine (donormil);
- Thiazoles – clomethiazole (geminevrin);
- Aliphatic – chloral hydrate, bromisoval

Note: It is necessary to account that regulatory influence on the sleep is characteristic for some psychosedative drugs (bromides, Valerian), small doses of neuroleptics (Aminazinum, Chlorprothixene), some antidepressants (Amitriptyline, Azaphenum, Pyrasidolum), agonists of melatonin receptors (melatonin), a combination of drugs (Andipal, Bellataminalum, Palufinum, Gluferalum, Pagluferalum) and others. Sedative – hypnotic effects have all CNS depressant substances with an additional blocking action on the central M – choline and H1 – histaminoreceptors (clonidine, diphenhydramine, and others.), But they are not used like hypnotics.

4. Correlation “dose – effect” for hypnotics and sedatives. The difference between physiological and artificial (drug) sleep. Demands to so called “ideal hypnotic drug”.
5. Benzodiazepines. Pharmacokinetics, pharmacodynamics, adverse effects, use. Advantages and disadvantages of benzodiazepines. Therapeutic use.
6. Barbiturates. Pharmacokinetics. Pharmacodynamics. Adverse effects, interaction with other drugs. Acute and chronic poisoning with barbiturates, treatment.
7. General characteristics of hypnotics of different chemical groups.
8. Common principles of insomnia treatment. Comparative characteristics of the main groups of hypnotic drugs. Contraindications.

ANTICONVULSANTS.

1. Classification:

A. Drugs used **for removing of convulsions** (really anticonvulsants) – benzodiazepines (Diazepam), barbiturates (Hexenal, Thiopental, Phenobarbital etc.), Chloral hydrate, Nitrous oxide, Sodium oxybutyrate, Lidocaine, Magnesia sulfate, peripheral muscle relaxants.

B. Antiepileptic drugs

- Barbiturates and derivatives – phenobarbital, benzobarbital (benzonal), hexamidine (primidone);
- Benzodiazepines – clonazepam, diazepam etc .;
- Hydantoin derivatives – phenytoin (Diphenin), etc .;
- Fatty acid derivatives – valproate (Depakine) and sodium valproate, gamma – aminobutyric acid (sodium oxibutirate, Aminimalon), etc .;
- Derivatives of succinimides – ethosuximide, etc .;
- Other – carbamazepine, lamotrigine, topiramate, vigabatrin, gabapentin, levetiracetam.

C. Antiparkinsonian drugs:

1) Dopaminomimetics:

- Indirect action – precursor of dopamine (levodopa, NAC), which increase dopamine content and opposing its capture (midantan), MAO – B inhibitors (selegiline), etc .;
- Direct action – dopamine receptor agonists (bromokriptin, pramipexole);

2) The central M, N – holinoblockers – cyclodolum, narokin, tropacinum, etc.

D. Drugs for treatment of **spastic syndrome** – benzodiazepines (Diazepam, Phenazepam), GABA – ergic drugs (Phenibutum, Baclofen), Dantrolene, Midocalm, Tizanidine.

2. Comparative characteristics of selective representatives used for treatment of convulsions. Mechanism of action, special features of pharmacokinetics, rational use in case of convulsive syndrome.

3. Pharmacology of basic antiepileptic agents. Mechanism of action, pharmacokinetics and efficacy in different form of epilepsy (partial and generalized, status epilepticus). Adverse effects. Interaction with other drugs.

4. General characteristics of antiparkinsonian drugs. Pathogenetic principles of pharmacological correction of mediator dysfunction in the brain’s basal ganglia system (extrapyramidal system) in case

of Parkinson's disease. Drug's parkinsonism, causes and treatment.

1. Diazepam or clonazepam - intravenously

2. Tiopental sodium or geksenal - intravenously

3. Narcosis nitrous oxide or predion intravenously

4. Maintaining effect of previous agents: Magnesium sulfate - / m, rectally chloral hydrate, sodium hydroxybutyrate / o or w / w.

5. Muscle relaxants with anesthesia and mechanical ventilation (with failure of others. Events)

Classification of anticonvulsants on the mechanism of action:

1) Means, blocking the generation of discharges in neurons of the hearth (which increase the critical level of depolarization): barbiturates, succinimides, other (beclamide, noksiron).

2) Means, eliminating post-tetanic potentiation (promoting hyperpolarization PSM) hydantoin derivatives, iminostilbeny.

3) Means of activating the brake system of the brain: valproate, benzodiazepines, serotonin agonists brake unit - iminostilbeny.

4) Medications reduce alkalosis, brain hydration and secretion of liquor: acetazolamide (diakarb), Soutl.

5) Combined preparations: glyuferal (fenobarbi-tal + bromisoval + caffeine-benz.Na + Ca gluconate) panglyufe-Ral (the same + papaverine hydrochloride) falilepsin (phenobarbital + psevdonorefedrina - like ephedrine, mildly stimulates the central nervous system), barbeksaklon (phenobarbital + Benzedreks - cyclohexyl analogue of ephedrine).

List of practical works. Prescribe drugs with their application (*separately from the prescription!*):

№	Name of the drug	Drug form
1)	Phenobarbital (<i>Phenobarbitalum</i>)	Tab. 0,05 ;0,1 and 0,005 for children
2)	Nitrazepam (<i>Nitrazepamum</i>) syn.: Radedorm	Tab. 0,005 and 0,01
3)	Doxylamine (<i>Doxylamine</i>) syn.: Donormilum	Tab. 0,015
4)	Zopiclone syn.: Imovan	Tab. 0,0075
5)	Zolpidem	Tab. 0,01
6)	Zaleplon	Tab. 0,005 and 0,01
7)	Diphenin (<i>Dipheninum</i>) syn.: Phenytoin	Patented tab.
8)	Depakene (<i>Depakinum</i>) syn.: Sodium valproate, Konvulex	Tab. 0,3; syrup in vial 150 ml.; amp. 0,4 f/inj.
9)	Carbamazepine (<i>Carbamazepinum</i>) syn.: Finlepsin, Tegretol	Tab. 0,1; 0,2 и 0,4
10)	Ethosuximide (<i>Ethosuximidum</i>) syn.: Suksilep	Caps. by 0,25
11)	Levodopa (<i>Levodopa</i>)	Caps. and tab. 0,25 and 0,5
12)	Nacom	Patented tab. (Levodopa 0,25+ Carbidopa 0,025)

Tasks for self-control. Choose the correct answers.

1. How most of hypnotics change sleep structure?

- A. Prolong the process of falling asleep
- B. Increase the total duration of sleep
- C. Increase the phase of "slow" sleep
- D. Increase the phase of "rapid" sleep
- E. Do not affect on the sleep structure

2. Identify the main features of barbiturate poisoning:

- A. Excitation

- B. Coma
 - C. Hypothermia
 - D. Respiratory depression
 - E. Reduction of blood pressure
3. *Specify the pharmacodynamic effects of benzodiazepines*
- A. Anxiolytic
 - B. Hyperthermic
 - C. Vegetostabilize
 - D. Spastic
 - E. Sedative
4. *Specify the undesirable effects of barbiturates*
- A. Drug hangover
 - B. Slow metabolism of other drugs
 - C. Tolerance
 - D. «Cancel» syndrome
 - E. Neurological disorders
5. *What drugs are used to relief from convulsive states?*
- A. Magnesium sulfate
 - B. Bromisoval
 - C. Sodium Valproate
 - D. Diazepam
 - E. Thiopental

II. Original practical work in class

1. To view the collection of drugs.
2. Work with the tests (Krok-1).
3. Prescribe and ground the choice of drug:
 - 1) for warming compresses;
 - 2) hypnotic in case of difficulty of falling asleep;
 - 3) for "emotional" form of insomnia;
 - 4) hypnotic – inducer of liver microsomal oxidation;
 - 5) hypnotic, almost not causing apnea during sleep;
 - 6) with the expressed phenomenon "after – action";
 - 7) hypnotic don't do anxiolytic, anticonvulsant and muscle relaxant effects;
 - 8) for symptomatic elimination of seizures;
 - 9) for prevention of short epilepsy attacks;
 - 10) for prevention of long epilepsy attacks;
 - 11) in status epilepticus;
 - 12) dopaminergic antiparkinsonian agent;
 - 13) cholinergic drug for treatment Parkinson's syndrome.

Unit 19. NON-NARCOTIC ANALGESICS – ANTIPYRETICS. NON- STEROIDAL ANTIINFLAMMATORY DRUGS (NSAIDS)

Actuality of the unit. Non – narcotic analgetic drugs are synthetic substances, characterized by the analgesic, anti – inflammatory and antipyretic effects. Non – narcotic analgesic drugs bring moderate analgesic effect, mostly on pathogenetic level, by blocking the synthesis and excretion of inflammation mediators (prostaglandins, prostacyclins, bradykinin, histamine, serotonin, and others). A central component of the analgesic effect is less pronounced than peripheral. Unlike narcotic analgesics, these drugs do not provoke euphoria or addiction status. In recent years, widespread preparations possess pronounced anti – inflammatory activity approaching that to glucocorticoids. Since they do not have a steroid structure, referred to call as non – steroidal anti – inflammatory drugs (NSAIDs). They are widely used on an outpatient basis and as a means of "home remedies". However,

this is far from unsafe drugs. When they have the irrational use of serious undesirable – governmental actions (ulcerogenic, nephrotoxicity and hepatotoxicity, agranulocytosis, etc.). Inhibition of prostaglandin, namely cyclooxygenase (COX), is one of the leading mechanisms not only therapeutic, but also a negative effect (such as ulcerogenic). So today promising is the creation of the selective NSAIDs COX – 2 inhibitors (the enzyme is not responsible for the synthesis of pro – prostaglandin – gastroprotectives). Thus, the doctor of any profile must know the pharmacological characterization and assignment's rules of this group.

I. Individual work

Control questions

1. General characteristics of non-narcotic analgesics. The main types of potential pharmacological activity. History of creation.
2. Classification:
 - 1) Salicylic acid derivatives: Acetylsalicylic acid (Aspirin), Methylsalicylate. Acetylsalicylate lysin;
 - 2) Pyrazolone derivatives: Analginum (Methamizole), Butadion;
 - 3) Aniline derivatives: Acetaminophen (Paracetamol, Panadol);
 - 4) Acids derivatives:
 - propionic – Brufen (ibuprofen), ketoprofen (ketonal, full face – tum), fenoprofen, naproxen;
 - phenylacetic – Diclofenac sodium (Voltaren, Ortophenum);
 - indoleacetic – Indomethacin, Clinoril (sulindac), etodolac;
 - anthranilic – Mefenamic acid, etc.;
 - 5) The oxicams – piroxicam, tenoxicam, meloxicam;
 - 6) Coxibs – celecoxib
 - 7) Derivatives of different *chemical classes*: Ketorolac (ketanov, ketorol, ketalgin), nimesulide, dimexide bishofite etc.;
 - 8) Combined preparations: Arthrotec® (Diclofenac + Misoprostol), Dolaren (Diclofenac + Paracetamol), Coldreks (Paracetamol + Phenylephrine + Ascorbic acid + Terpin hydrate + Caffeine), Solpadeine (Paracetamol + Codeine + Caffeine), Pentalginum (Amidopyrine + Analginum + Codeine + Caffeine + Phenobarbital), Alka – Seltzer (Ascorbic acid + Acetylsalicylic acid) etc.

Note: The analgesic action of the component have drugs of different pharmacological groups – clonidine, some antidepressants (amitriptyline, imipramine), means for anesthesia (ketamine, nitrous oxide), antiepileptics (valproate, carbamazepine), H1 – histamine blockers (diphenhydramine, Promethazine) etc.

3. Mechanism of analgesic, antipyretic and anti – inflammatory effect of non – narcotic analgesic drugs.
4. Comparative characteristics of different group.
5. Selective COX-inhibitors. Advantages and prospects of using. Classification.

Inhibitors of COX-1 and COX-2	Selective COX-1 inhibitors	Selective COX-2 inhibitors	High-active COX-2 inhibitors
Majority of modern NSAIDs	Acetylsalicylic acid	Meloxicam	Celecoxib

6. Additional pharmacological effects of NSAIDs. Mechanism of action. Application.
7. Patented products, created on the base of this group of drugs. Advantages and disadvantages.
8. The pharmacokinetics of NSAIDs.
9. Indications for usage. Terms of dosing and destination
10. Adverse effects. Contraindications. Acute and chronic poisoning with salicylates. Treatment.

List of practical works. Prescribe drugs with their application (*separately from the prescription!*):

№	Name of the drug	Drug form
1	2	3
1.	Acetylsalicylic acid (<i>Acidum acetylsalicyllicum</i>) syn.: Aspirin, Aspirin-cardio	Tab. 0,1; 0,25; 0,325; 0,5
2.	Analgin (<i>Analginum</i>) syn.: Methamizole	Tab. 0,5; amp. 25 and 50 % sol. 1 and 2 ml.
3.	Paracetamol (<i>Paracetamolum</i>) syn.: Acetaminophen, panadol, Taleinol, Efferalgan	Tab. 0,2; 0,5; sol. for inner use 2,4 % by 100 ml.; sirup 5 % sol. 100 ml.; supp. rect. 0,1; 0,25 and 0,5
4.	Ibuprofen (<i>Ibuprofenum</i>) syn.: Brufen	Tab. 0,2; 0,4 и 0,6; syrup 2 % sol. 100 ml.; ointment 5 %; gel 10 % by 30,0
5.	Diclophenac-sodium (<i>Diclophenac-natrium</i>) syn.: Ortophen, Voltaren	Tab. 0,025; supp. rect. 0,05; amp. 2,5 % sol. 3 ml.; ointment 2 % by 30.
6.	Indomethacin (<i>Indometacinum</i>) syn.: Metyldole	Tab. 0,025, 0,0075, 0,01, 0,1; supp. rect. 0,05; ointment 10 % 40,0.
7.	Piroxicam (<i>Pyroxicamum</i>) syn.: Roxik	Tab. 0,01 и 0,02; supp. rect. 0,01 and 0,02; amp. 2 % sol. 1 ml.; gel 0,5% by 50,0
8.	Naproxen (<i>Naproxenum</i>) syn.: Bonifen	Tab. 0,25 and 0,5; supp. rect. by 0,25 and 0,5
9.	Meloxicam (<i>Meloxicamum</i>) syn.: Movalis	Tab. 0,0075 and 0,015; rectal supp. by 0,015
10.	Nimesulide (<i>Nimesulide</i>) syn.: Nimesil, Nimulid, Nice	Tab. 0,1 and 0,2; gel 1 % by 20,0
11.	Celecoxib (<i>Celecoxib</i>) syn.: Celebrex	Caps. by 0,1 and 0,2
12.	Ketorolak (<i>Ketorolak</i>) syn.: Ketanov	Tab. 0,01, amp. 3 % sol. 1 ml.
13.	Baralgin (<i>Baralgin</i>) syn.: Spazmalgon, Maksigan, Trigan	Tab. patented; amp. by 5 ml.; supp. rect.

Tasks for self-control. Choose the correct answers.

- What is the analgesic which doesn't have anti-inflammatory effects:
 - Aspirin
 - Paracetamol
 - Nimesulide
 - Analgin
 - Voltaren
- Specify the pharmacological effects of non – narcotic analgesics
 - Analgesic
 - Psychostimulant
 - Antipyretic
 - Anticonvulsive
 - Anti-inflammatory
- Choose combined preparations of non – narcotic analgesics
 - Indomethacin
 - Spazmalgon
 - Nimesulide
 - Meloxicam
 - Baralgin
- Ways of easing ulcerogenic action of NSAIDs
 - Take with coating demulcents
 - Use selective COX-2 inhibitors
 - Combine with β -blockers
 - Combine with glucocorticoids

E. Take on an empty stomach

5. Specify from what pain mostly relief non-narcotic analgesics?

- A. Traumatic
- B. Inflammatory
- C. Toothache
- D. Articular
- E. Inoperable tumors

II. Original practical work in class

1. To view the collection of drugs.
2. Work with the tests (Krok-1).
3. Prescribe and ground the choice of drug:

- 1) in the acute phase of rheumatism;
- 2) patented drug from the group of non – narcotic analgetic to relief of colic
- 3) NSAID with least ulcerogenic action;
- 4) NSAID with strongest antipyretic effect;
- 5) NSAID with strongest analgesic effect;
- 6) NSAID in case of gout;
- 7) NSAID with antiagregante action;
- 8) non – narcotic analgetic counter – indicated in case of leucopenia;
- 9) NSAID that produced increasing of BP, tachycardia;
- 10) NSAID with hepato – and nephrotoxic actions;
- 11) NSAID for local usage with fibrinolytic and antiseptic actions, good penetrated through tissue barriers;
- 12) in case of arthritis with gastric ulcer;
- 13) a highly active inhibitor of COG-2;
- 14) NSAIDs causing bronchospasm;
- 15) selective inhibitor of COG-1;
- 16) replacing meloxicam drug;
- 17) the drug indomethacin replacement;
- 18) the combination agent of the group of NSAID;
- 19) NSAID - aniline derivative. 13) a highly active inhibitor of COG-2;
- 14) NSAIDs causing bronchospasm;
- 15) selective inhibitor of COG-1;
- 16) replacing meloxicam drug;
- 17) the drug indomethacin replacement;
- 18) the combination agent of the group of NSAID;
- 19) NSAID - aniline derivative.

Unit 20. PSYCHOTROPIC DRUGS. PSYCHODISLEPTIC DRUGS. NARCOTIC ANALGESICS

Actuality of the unit. Narcotic analgesics are substances that capable with resorptive action to suppress intracental conduct and perception of pain, and with the reintroduction cause mental and physical dependence (morphinism). Each case of anaesthesia is individual, composed with various data. Pain is accompanied by many pathological conditions, complicating the flow of disease (myocardial infarction, renal and hepatic colic, burns, trauma, tumors). Narcotic analgesics are widely used to relieve shock, neuroleptanalgesia, sedation, in the postoperative period, etc. The use of these drugs is strictly controlled because of the danger of addiction. Pain is characteristic for many pathological states and complicates the disease. (colics, traumas, tumors, burns). The use of this highly effective group of drugs is under the strict control due to the danger of addiction.

I. Individual work

Control questions

1. Common conception of psychotropic drugs. Neurophysiologic mechanisms of action.
2. Classification of PSYCHOTROPIC drugs:
 - Psychodysleptic drugs (psychotomimetic drugs or hallucinogens): narcotic analgesics (Morphin, Fentanyl etc.), Mescaline, Lysergic acid diethylamide (LSD), Psilocybin, Tetrahydrocannabinol (“Hashish”, Marihuana).
 - Neuroleptic drugs: derivatives of Phenothiazine, Butyrophenone.
 - Tranquilizers (anxiolytic drugs): – derivatives of Benzodiazepine and other chemical groups.
 - Psychosedatives: Bromides, Valerian, Leonorum.
 - Antidepressants: MAO inhibitors, Tricyclic antidepressants.
 - Psychostimulants: Amphetamine, Sidnocarb, Caffeine, Cocaine.
3. NARCOTIC ANALGESICS. General characteristics.
4. Alkaloids. Physicochemical features. Common reactions rendering alkaloids detoxication.
5. OPIUM ALKALOIDS. Classification:
 - a) derivatives of *phenanthrene* (Morphine, Codeine);
 - b) derivatives of *isoquinolin* (papaverine).
6. Classification of narcotic analgesics **according to chemical structure**:
 - a) derivatives of *phenanthrene*:
 - natural alkaloids of Opium – Morphine, Codeine, Omnoponum;
 - synthetic analogues of Opium – Ethylmorphine, Buprenorphine, Nalbuphine, Nalorphine, Naloxone, Naltrexone;
 - b) Benzomorphans – Pentazocine;
 - c) Morphinans – Butorphanol;
 - d) derivatives of Phenylpiperidine – Promedolum, Fentanyl, Loperamide (Imodium);
 - e) derivatives of Heptanone – Methadone, Palfium;
 - f) derivatives of various chemical groups – Tramadol, Teledyne;
7. Opioid receptors. Endorphins and enkephalins.
8. Classification of narcotic analgesics **according to opiate receptors affinity**:
 - agonists of opiate receptors (strong – Morphine, Promedolum, Fentanyl, Methadone; weak – Codeine, Omnoponum);
 - agonists – antagonists (Buprenorphine, Nalbuphine, Butorphanol, Pentazocine, Tramadol, Teledyne, Nalorphine);
 - antagonists (Naloxone, Naltrexone);
9. Morphine’s pharmacodynamics and pharmacokinetics.
10. Comparative characteristics of narcotic analgesics.
11. Indications and contraindications. Adverse effects.
12. Acute and chronic poisoning with narcotic analgesics. Treatment. Medical and social aspects of narcomania.

List of practical works. Prescribe drugs with their application (*separately from the prescription!*):

Nº	Name of the drug	Drug form
1.	Morphine hydrochloride (<i>Morphini hydrochloridum</i>)	Amp. 1 % sol. 1 ml.; tab. 0,01
2.	Omnoponum (<i>Omnoponum</i>) syn.: Pantopon	Amp. 1 and 2 % sol. 1 ml.
3.	Codeine phosphate (<i>Codeini phosphas</i>)	Tab. 0,015
4.	Ethylmorphine hydrochloride (<i>Aethylmorphinum hydrochloridum</i>) syn.: Dionin	Tab. 0,015; (<i>Dioninum</i>), 1 – 2 % sol., eye drops

5.	Promedolum (<i>Promedolum</i>) syn.: Trimeperidine	Tab. 0,025; amp. 1%, 2% sol. 1 ml.
6.	Fentanyl (<i>Phentanylum</i>) syn.: Fentanest	Amp. 0,005% sol. 1, 2 and 10 ml.
7.	Pentazocine (<i>Pentazocinum</i>) syn.: Elixir, Fortre	Tab., supp. by 0,05; amp. 3 % sol. 1 – 2 ml.
8.	Tramadol (<i>Tramadolum</i>) syn.: Tramal	Tab., caps. 0,05, 0,1; amp. 5 % sol. 1 and 2 ml.; rectal suppositories by 0,1, drops 10% sol. 20 and 50ml.
9.	Buprenorphine (<i>Buprenorphinum</i>)	Tab. 0,0002; amp. 0,03 % sol. 1 and 2 ml.
10.	Naloxone (<i>Naloxonum</i>)	Amp. by 1 ml. (1 ml. — 0,0004)

Tasks for self-control. Choose the correct answers.

1. Specify analgesic for neuroleptanalgesia:
 - A. Morphine
 - B. Promedol
 - C. Fentanyl
 - D. Omnopon
 - E. Pentazocine
2. Specify the effects of morphine:
 - A. CNS stimulation
 - B. CNS depression
 - C. Euphoria
 - D. Abstinence
 - E. Increased pulmonary ventilation
3. Enter the leading cause of death in cases of poisoning by morphine:
 - A. Acute renal failure
 - B. Acute liver failure
 - C. Inhibition of the respiratory center
 - D. Inhibition of vasomotor center
 - E. Cardiac arrest
4. Specify pharmacological properties of promedol:
 - A. A strong painkiller
 - B. Weak analgesic
 - C. Spasmolytic
 - D. Anti – inflammatory
 - E. Antitussive
5. Mark the antagonist of narcotic analgesics:
 - A. Omnopon
 - B. Naloxone
 - C. Morphine
 - D. pentazocine
 - E. Phenobarbital

II. Original practical work in class

1. To view the collection of drugs.
2. Work with the tests (Krok-1).
3. Prescribe and ground the choice of drug:
 - 1) in case of traumatic shock;
 - 2) in case of inoperable form of cancer tumor;
 - 3) in case of neuroleptanalgesia;
 - 4) for cough relieve in case of pneumothorax;
 - 5) for analgesia in labors;
 - 6) in case of liver colica;

- 7) neo – Galen’s preparations of opium;
- 8) Morphine antidote;
- 9) Narcotic analgetic at inflammation of eye’s iris.
- 10) an antidote case of poisoning by morphine;
- 11) opiate agonist-receptor antagonist;
- 12) narcotic analgesic from the group phenylpiperidine;
- 13) drug replacement morphine;
- 14) derivative of benzomorfan.

Unit 21. NEUROLEPTIC DRUGS. TRANQUILIZERS. PSYCHOSEDATIVES

Actuality of the unit. Neuroleptics and tranquilizers – psychotropic drugs with depress (inhibitory) effect on the central nervous system. Under CNS depressants understand the substance of various origins that can reduce the excitability of the central nervous system of higher divisions on the CNS.

Neuroleptic drugs – special group of psychotropic drugs that primary blocks the activity of certain mediator systems of brain and capable to relieve psychical excitement of different genesis and to reduce dysfunction of perception, mental processes and social behavior. Tranquilizers are close to neuroleptics, but have the ability to selectively suppress the symptoms of emotional instability, tension, and fear (antifobic), weaken the symptoms of disadaptation to the unpleasant environment and have antianxiety (anxiolytic) action. Drugs in this group have in varying degrees anticonvulsant, myorelaxant, sedative, hypnotic, vegetostabilizing activities. Introduction of tranquilizers in clinical practice greatly enhanced the treatment of a range of nervous and psychic diseases – tions. The number of psychotropic drugs used in clinical practice, has a tendency to increase and, unfortunately, their use comes from under medical supervision. Psychosedative agents have a wide range of pharmacological psychosedative to wegetotropic and antispasmodic action.

I. Individual work

Control questions

NEUROLEPTICS (antipsychotic drugs, neuroplegics)

1. General characteristics of neuroleptics. History of creation. Classification
- 1) *Phenothiazine* derivatives (typical neuroleptics):
 - a) aliphatic derivatives – Chlorpromazine (Aminazinum), Levomepromazine;
 - b) piperazine derivatives – Perphenazine (Aethaperazinum), Triftazine, Ftorphenazine, Ftorphenazine – decanoate;
 - c) piperidine derivatives – Neuleptil.
- 2) Butyrophenone derivatives – Haloperidol, Trifluperidol, Droperidol;
- 3) Diphenylbutylpiperidine derivatives – Pimozide, Fluspirilenum;
- 4) Benzamide derivatives – Sulpiride (Eglonil), Tiapride, Metoclopramide*⁵ (Reglan), Sultopride;
- 5) derivatives of various chemical groups – Reserpine, Chlorprothixene, Azaleptinu (Clozapine).
2. Pharmacokinetics of neuroleptics.
3. Mechanism of neuroleptic (antipsychotic) action. Pharmacodynamic effects.
4. Comparative characteristics of different neuroleptic groups. Prolonged forms of the drugs (Flushpirilen, Pimozide, Ftorfenazin – decanoate).
- 5 Indications for clinical use.
6. Adverse effects. Contraindications. Treatment of the neuroleptic Parkinsonism.

TRANQUILIZERS (anxiolytics).

1. General characteristic.

⁵ It is used in gastroenterology

2. Classification by the chemical structure

- 1) *1.4 – benzodiazepine* derivatives – Chlordiazepoxide, Diazepam, Phenazepam, Nitrazepam, Flunitrazepam, Clonazepam, Alprazolam, Lorazepam, Temazepam, Gidazepam etc.
- 2) Derivatives of various chemical groups – Mebicar, Grandaxine, Amyzil, Litonit, Phenibut etc.

3. Pharmacodynamics of tranquilizers. Classification **according to mechanism of action:**

- direct agonists of the benzodiazepine receptors of the GABA – receptor – chlorionic channel – derivatives of benzodiazepine (diazepam, oxazepam, lorazepam, and others.);
- direct agonists of serotonin receptors – buspirone, etc .;
- different mechanism of action – amizyl, meprobamate, trioxazine and others.

4. Pharmacokinetics of tranquilizers. Classification **according to the duration of action:**

- short – acting ($T_{1/2}$ to 6 hours) – Triazolam, Midazolam.
- medium – acting (6 – 24 h) – Lorazepam, Nozepam, Flunitrazepam and others.
- long – acting ($T_{1/2}$ more than 24 hours) – Nitrazepam, Phenazepam, Diazepam, Phenazepam, Flurazepam (prodrug, $T_{1/2} \approx 100$ hours), and others.

5. Indications for clinical usage. Classification **according to spectrum of hypnotic action:**

- sedatives ("big", night) – nitrazepam, flurazepam, diazepam, phenazepamum, etc.
- day ("small"), having stress – protective activity with an activating component – mezepam, gidazepam, buspirone, mebicar.

6. Adverse effects. Contraindications. Acute poisoning, treatment (Flumazenil). Formation of drug addiction.

PSYCHOSEDATIVES.

1. General characteristic. Classification:

- plant origin – Valerian, Leonorum, Passiflora, and preparations on it's base (Novo – passit, Persen – forte, Cardiofit etc.);
- bromides – Sodium and Potassium bromide;
- complex preparations: Valokordin (Ethylic ether of bromisovalerian acid + Phenobarbital + peppermint and hop oil + Ethanol), Corvalol (like Valokordin but without hop oil), Valocormide (extract of valeriana, lily of the vally, belladonna, sodium bromide, mentol), Quarter's mixture (Infusion of Valerian + Infusion of Mentha + Sodium bromide + Magnesia sulfate + Amidopyrine + Caffeine), Ivanov – Smolensky mixture (Infusion of Valerian + Sodium bromide + Amidopyrine + Barbitol – sodium), etc.
- 2. Pharmacodynamics. Indications and contraindications for administration.

List of practical works. Prescribe drugs with their application (*separately from the prescription!*):

№	Name of the drug	Drug form
1.	Aminazine (<i>Aminasinum</i>) syn.: Chlorpromazine	Dragee 0,025, 0,05 и 0,1; amp. 2.5% sol. 1, 2, 5, 10 ml.; tab by 0,01;
2.	Aethaperazine (<i>Aethaperazinum</i>)	Tab. 0,004; 0,006 and 0,01
3.	Haloperidol (<i>Haloperidolum</i>)	Tab. 0,0005; 0,001; 0,002; 0,005 and 0,01; amp. 0,5 % sol. 1 ml.; vials 0,2 % sol. 10 ml.
4.	Droperidol (<i>Droperidolum</i>)	Amp. 0,25% sol. 2, 5 and 10 ml.
5.	Talamonal (<i>Thalamonal</i>)	Amp. by 2ml.
7.	Flushpirilen (<i>Fluspirilenum</i>)	Amp. by 2 ml. suspension (1 ml. – 0,002).
6.	Sulpiride (<i>Sulpiridum</i>) syn.: Eglonil	Caps. 0,05
8.	Azaleptine (<i>Azaleptinum</i>) syn.: Clozapine, Leponeks	Tab. 0,025 and 0,05; amp. 2,5% sol. 2 ml.
9.	Chlozepide (<i>Chlozapidum</i>) syn.: Chlordiazepoxide, Elenium	Tab., dragee, caps. 0,005, 0,01 and 0,025

10.	Diazepam (<i>Diazepam</i>) syn.: Seduksen, Sibazon, Relanium, Valium	Tab. 0,0001; 0,002 and 0,005; amp. 0,5% sol. 2 ml.
11.	Phenazepam (<i>Phenazepamum</i>)	Tab. 0,0005; 0,01 and 0,0025; amp. 0,3% sol. 1 ml.
12.	Gidazepam (<i>Gidazepamum</i>)	Tab. 0,02 and 0,05
14.	Mixture of Tinct. radix Valerian (<i>Valeriana</i>), SD – 0,5, and Sodium bromide (<i>Natrii bromidum</i>), SD – 0,3	
13.	Tinct. Leonuri (<i>T-ra Leonuri</i>)	Vial 50 ml.
15.	Valocordin (<i>Valocordin</i>)	Vial 20 ml.

Tasks for self-control. Choose the correct answers.

1. *What are the pharmacological properties of neuroleptics:*
 - A. Removal of psychomotor excitation
 - B. Antipsychotic (removal of delirium and hallucinosis)
 - C. Expressed hypertensive effect
 - D. Reduce body temperature only when hyperthermia
 - E. Antiemetic
2. *Specify the adverse effects of chlorpromazine:*
 - A. Changes of endocrine function
 - B. Local irritating action
 - C. Inhibition leukopoiesis (agranulocytosis)
 - D. Orthostatic collapse
 - E. Extrapyrarnidal disorders
3. *Additional sedative effect of chlorpromazine due to:*
 - A. Blockade of central D2 – dopaminoreceptors
 - B. Central α -adrenoblocking effect
 - C. Blockade of central 5HT2 – receptors
 - D. The blockade of central H1 histamine receptors
 - E. Central M – cholinoblocking effect
4. *The effects of tranquilizers are:*
 - A. Activation of the autonomic system
 - B. Anxiolytic effect
 - C. Anticonvulsant action
 - D. Stress – protective effect
 - E. Inhibition of action means depress the CNS
5. *Adverse effects of tranquilizers:*
 - A. Disturbance of motor coordination
 - B. Drowsiness
 - C. Hypertension
 - D. Drug dependence
 - E. Teratogenic, embryotoxicity

II. Original practical work in class

1. To view the collection of drugs.
2. Work with the tests (Krok-1).
3. Prescribe and ground the choice of drug:
 - 1) to manage maniac agitation;
 - 2) neuroleptic for neuroleptanalgesia;
 - 3) in case of neuroleptic Parkinsonism;
 - 4) in case of centrally – induced vomiting;
 - 5) sympatholytic with neuroleptic activity;
 - 6) in the case of neurotic hyposomnia;
 - 7) to relieve emotional tension;
 - 8) in complex therapy of the hypertonic disease;
 - 9) anxiolytic with expressed anticonvulsant action;

- 10) anxiolytic with expressed muscle relaxant action;
- 11) tranquilizer with less expressed hypnotic effect;
- 12) in case of neurotic pain in the heart region;
- 13) sedative in the form of tincture.
- 14) neuroleptic - phenothiazine;
- 15) drug haloperidol replacement;
- 16) Long-acting anxiolytic.

Unit 22. ANTIDEPRESSANTS. NORMOTHYMICS. PSYCHOSTIMULANTS

Actuality of the unit. Antidepressants – psychotropic drugs used to treat depression. In depressed patients, they improve mood, reduce or relieve depression, lethargy, apathy, anxiety and emotional stress, increase mental alertness, normalize the phase structure and the duration of sleep and appetite. However, it is unsafe drugs for causing very serious side effects, provoking suicide attempts

Normotimics – a group of psychotropic drugs, the main feature of which is the ability to stabilize mood in psychiatric patients, especially in patients with affective disorders, to prevent or soften their recurrence, to inhibit progression of disease. Normotimics also have the ability to soften "sharp corners of character", impatience, temper, impulsiveness, dysphoria in patients with various mental disorders. All normotimics have also antimanic effect and is used for the treatment of manic states.

Psychostimulators – psychotropic substances, stimulating mental and physical working – ability, improve the ability to perceive external stimuli (improve vision, hearing, etc., accelerate response reactions), decrease fatigue and need for sleep. The group also includes psychostimulators of public funds (tea, coffee, tobacco) and illegal drugs (amphetamines, cocaine).

I. Individual work

Control questions

ANTIDEPRESSANTS (thymoleptics, thymoanaleptics)

1. General characteristics. Classification **by the mechanism of action:**

- 1) *Monoamine oxidase (MAO) inhibitors* – irreversible (Nialamide), reversible – MAO – A – Pyrazidolum, Moclobemide; MAO – B – Selegiline, etc.);
- 2) Inhibitors of neurotransmitter reuptake:
 - *nonspecific inhibitors of neurotransmitter reuptake (Norepinephrine, Serotonin)* – tricyclic antidepressants (TAD, typical): Imipramine (Imisinum), Clomipramine, Amitriptyline;
 - *selective inhibitors of neurotransmitter reuptake:*
 - *serotonin reuptake* – Fluoxetine (prozac), Fluvoxamine, Trazodone;
 - *Norepinephrine* – Reboxetine, Atomoxetine; TDA: secondary amines – Desipramine, Nortriptyline; tetracyclic and others – Maprotiline;
 - *Serotonin and norepinephrine* – Venlafaxine, Duloxetine
 - *Serotonin and dopamine* – Bupropion.
- 3) Agonists of monoamine receptor (blockers of presynaptic α_2 -receptors, which suppress serotonin release, and the postsynaptic 5 – HT₂, 5 – HT₃ – receptor) – Mirtazapine, Mianserin, Trazodone, etc.;
- 4) Another mechanism – activators of reuptake serotonin and blockers of its time – violation: tianeptine (coaxil) melatonergic: agomelatine. – Sydnophenum, Tianeptine;

Note: Antidepressive activity also possess drugs of other pharmacological groups: anxiolytics (alprazolam, buspirone), antiparkinsonian drugs (midantan), antiepileptics (karbamazepin), low – dose of neuroleptics (Thioridazine, Levomepromazine, Clozapine), hepatoprotectors – Heptral etc. .

3. Pharmacokinetics of antidepressants.

4. Pharmacodynamics. The conception of the thymoretics, sedative and "balanced" action of antidepressants. Comparative characteristics of preparations from different groups. Classification depending on clinical effect.

5. Indications and special features of clinical usage.

6. Adverse effects. Contraindications for usage.

NORMOTHYMICS

1. *Lithium* preparations (Lithium carbonate / Lithionium – durelum, Quilinorm – retard, Micalitum), Lithium oxybutyrate. Pharmacokinetics. Pharmacodynamics. Indications and contraindications for usage. Adverse effects. Acute poisoning with lithium salts. First aid.
2. *Other preparations with a mood stabilizer activity* – antiepileptic (carbamazepine, sodium valproate, lamotrigine), neuroleptics (risperidone, clozapine), calcium channel blockers (verapamil, nifedipine, nimodipine), thyroid hormones (triiodothyronine, levothyroxine). General characteristics.

PSYCHOSTIMULANTS

1. General characteristics. Classification:

1) *phenylalkylamines* – Amphetamine⁶ (Phenaminum);

2) *sydnonimines* – Sydnocarbum;

3) *purine derivatives (xanthines)*⁷ – Caffeine, Caffeine – benzoate sodium.

4) *piperidine derivatives* – meridil

3. Pharmacokinetics, pharmacodynamics of phenylalkylamines. Adverse effects, clinical usage. Rules of application. Formation of dependence. Features of Sydnocarbum and Meridil destination.

4. Caffeine. Mechanism of action. Pharmacokinetics, pharmacodynamics. Indications and contraindications for usage.

5. Conception of actoprotectors.

List of practical works. Prescribe drugs with their application (*separately from the prescription!*):

№	Name of the drug	Drug form
1.	Pirazidol (<i>Pyrazidolum</i>)	Tab. 0,025 and 0,05
2.	Amitriptyline (<i>Amitriptylinum</i>)	Tab. 0,025; amp. 1 % sol. 2 ml.
3.	Imizine (<i>Imizinum</i>) syn.: Imipramine	Tab. 0,025; amp. 1,25 % sol. 2 ml.
4.	Maprotiline (<i>Maprotiline</i>)	Tab. 0,025
5.	Fluoxetine (<i>Fluoxetinum</i>) syn.: Prozac	Tab., caps. 0,01 and 0,02
6.	Bupropion (<i>Bupropion</i>)	Tab. 0,15
7.	Mirtazapine (<i>Mirtazapine</i>)	Tab. 0,03
8.	Coaxil (<i>Coaxil</i>) syn.: Tianeptine	Tab. 0,125
9.	Lithium carbonate (<i>Lithii carbonas</i>)	Tab. 0,3
10.	Sydnocarb (<i>Sydnocarbum</i>)	Tab. 0,005; 0,01 and 0,025
11.	Caffeine-sodium benzoate (<i>Coffeinum-natrii bensoas</i>)	Tab. 0,1 and 0,2; amp. 10% and 20% sol. 1 and 2 ml.

Tasks for self-control. Choose the correct answers.

1. *Thymoretics effect of antidepressants is due to:*

A Blockade of central α_2 -adrenoceptor

B. Blockade of central H₁ histaminoreceptors

⁶ In medical practice, are not used

⁷ Complete classification of xanthine, see the topic number 23.

- S. Central M – cholinomimetic effect
 - D. Blockade of central 5HT₂-receptors
 - E. Central adrenomimetic effect
2. *Adverse effects of SSRIs:*
- A. Movement disorders
 - B. Atropine effects
 - C. Increased appetite
 - D. «Serotonin" crises
 - E. Anterograde amnesia
3. *Adverse effect of lithium salts:*
- A. Tremor of extremities
 - B. Severe diarrhea
 - C. Hypertension
 - D. Respiratory depression
 - E. Polyuria, thirst
4. *Pharmacodynamic effects of psychostimulators are:*
- A. Bradyarrhythmia
 - B. Anorexia – genic
 - C. Improve the long – term memory
 - D. Improve attention, decrease creativity
 - E. Mobilization of energy resources of the body
5. *Specify the pharmacological effects of caffeine:*
- A. The exciting action on the cortex of cerebral hemispheres
 - B. The narrowing of blood vessels
 - C. Direct cardiostimulating effect
 - D. Deterioration of diuresis
 - E. Stimulation of gastric secretion

II. Original practical work in class

1. To view the collection of drugs.
2. Work with the tests (Krok-1).
3. Prescribe and ground the choice of drug:
 - 1) SSRI with thymoretic effect;
 - 2) antidepressant without cholinolytic action;
 - 3) antidepressant with sedative effect;
 - 4) antidepressant that affects on the dopamine reuptake;
 - 5) atypical tricyclic antidepressant that increases serotonin neuronal reserves in the depo and causing dependence in case of abuse;
 - 6) antidepressant with receptor mechanism of action;
 - 7) for chronic fatigue syndrome;
 - 8) for treatment of maniacal conditions;
 - 9) at an attack of migraine;
 - 10) in case of narcolepsy (rules for dosage).
 - 11) antidepressant - non-selective monoamine reuptake inhibitors;
 - 12) psychostimulant - derivative sydnominine;
 - 13) replacement drug caffeine.

Unit 23. NOOTROPIC DRUGS. ADAPTAGENS. ANALEPTICS. DRUGS OF ABUSE

Actuality of the unit. Nootropics – drugs, that have a specific positive impact on higher integrative functions of the brain. They improve mental activity and stimulate cognitive function, ability to study and memory, increases brain resistance to various damaging factors, including extreme pressure and hypoxia. There are a group of the "true" nootropic drugs for whom the ability to improve

mnemonic function is the main and sometimes the only effect, and a group of nootropics with mixed action ("neuroprotective"), in which the mnemonic effect is complemented, and often overlap with other important actions. A number of substances belonging to the group of nootropic drugs, has a rather broad spectrum of pharmacological activities, including antihypoxic, anxiolytic, sedative, anticonvulsant, myorelaxant and other effects. Adaptogens – a group of drugs that can increase the non-specific resistance to a broad spectrum of harmful effects of nature. For today analeptics mainly used in extreme conditions in the prehospital level. Their pharmacotherapeutic action differently and largely depends on the dose, type of higher nervous activity and a number of other factors.

I. Individual work

Control questions

NOOTROPIC DRUGS (psychometabolic stimulators, cerebroprotectores)

1. General characteristics. Classification:

– substances with predominantly *cholinomimetic action*:

- *racetam* (pyrrolidone derivatives) – piracetam (nootropil), aniracetam, etiracetam etc;
- derivatives *dimethylaminoethanol* (precursor of acetyl – choline) – deanol aceglumat, meclofenoxate (acefen);
- *thiamine* derivatives – sulbutiamine, fursultiamin;
- *choline* derivatives and substances that modulate its activity: – citicoline (ceriaxon) etc.

– substances with predominantly *GABA – mimetic effect*:

- *GABA – ergic* agents – gamma – aminobutyric acid (Aminalon), Neyrobutal, Sodium hydroxybutyrate, Pykamilonum, Pantohamum, Phenibutum, Sodium oxybutyrate;
- *precursors GABA and modulators its metabolism* – NMDA – receptor modulators: glutamic acid, memantine; pyridoxine derivatives: pyritinol membrane protectors (encephabol, piriditol), biotredin;
- drugs affecting the *peptidergic receptors* – neuropeptides and their analogues: semax, nooglutil;
- different substances with nootropic action component – cerebrovascular correctors: nicergoline, vinpocetine (cavinton), xantinola nicotinate, cinnarizine, cerebrolysin, actovegin; adaptogens: ginseng extract; antioxidants: mexidol and others.

2. Mechanism of action. Pharmacodynamics.

3. Indications and contraindications for usage. Features and application.

ADAPTOGENES (biostimulants)

1. General characteristics. Classification:

- plant origin – ginseng, Chinese magnolia vine, Leuzea, Rhodiola rosea, Aralia, Eleutherococcus, sterculia, Saparal etc General characteristics.
- animal origin – Pantocrinum and others.

2. Pharmacodynamics. Indications and contraindications for usage.

ANALEPTIC DRUGS (reviving or reanimated drugs)

1. General characteristics. Classification:

- drugs with primary action on the vital centers (breathing and cardiovascular) – Caffeine, Bemegride, Corazolium, Aethymisolum;
- drugs with the mixed mechanism of action – Camphora, Sulfocamphocainum, Cordiaminum.

2. Pharmacodynamics, indications for use, contraindications, side effects.

DRUGS OF ABUSE⁸: hallucinogens, opioids, amphetamines, Cocaine, Caffeine, antidepressants, Cannabis, barbiturates, barbiturates, tranquilizers, alcohol, nicotine etc.

⁸ There is another term "recreational" use (English recreation - rest, recovery.), so we use this psychoactive substances according not to medical indications to obtain satisfaction or for any other purpose. In any case, abuse of this substances lead to dependence.

Features of formation depending on each group, social value. The methods of struggle

List of practical works. Prescribe drugs with their application (*separately from the prescription!*):

№	Name of the drug	Drug form
1.	Piracetam (<i>Pyracetamum</i>) syn.: Nootropil	Tab. 0,4; 0,8 and 1,2; vials 20 and 33 % sol.
2.	Aminalon (<i>Aminalonum</i>)	Tab. 0,25
3.	Cavintone (<i>Cavinton</i>) syn.: Vinpocetine	Tab. 0,005; amp. 0,5 % sol. 2 ml.
4.	Tinct. Ginseng (<i>Tinctura Ginsengum</i>)	Vial 50 ml.
5.	Liquid extr. Echinacea (<i>Extractum Echinacea fluidum</i>)	Vial 50 ml.
6.	Pancrotin (<i>Pancrotinum</i>)	Tab. 0,15; amp. 1 ml.; vials 50 ml.
7.	Cordiamine (<i>Cordiaminum</i>)	Amp. 1 and 2 ml.; amp. 1 ml.; vial by 15 ml. for inner use
8.	Bemegrade (<i>Bemegridum</i>)	Amp. 0,5% sol. 10ml.
9.	Aethymizole (<i>Aethymizolum</i>)	Tab. 0,1; amp. 1% and 1,5% sol. 3 and 5 ml.
10.	Sulfocamfocain (<i>Sulfocamfocainum</i>)	Amp. 10 % sol. 2 ml.
11.	Camphor (<i>Camphora</i>)	Amp. 20 % oil sol. 1 and 2 ml. s/c; vial 10 % sol. 30 and 50 ml. for external use

Tasks for self-control. Choose the correct answers.

- Specify what will be after prolong administration of nootropics:
 - Cerebroprotective action
 - Pro – oxidant action
 - Causes euphoria, dependence
 - Improve cerebral blood flow
 - Improve brain function
- Which nootropic drug has the additional psychostimulant effect
 - Sulbutiamine
 - Lucidril
 - Aminalon
 - Pyritinol
 - Piracetam
- Which adaptogen is known as "golden root"?
 - Ginseng
 - Schisandra
 - Rhodiola rosea
 - Leuzea
 - Eleutherococcus
- Which analeptik do we use with an overdose of anesthetic and hypnotic drugs:
 - Caffeine
 - Bemegrade
 - Sulfokamfocain
 - Kordiamin
 - Etimizol
- What will be in overdose of analeptics?
 - Collaps
 - Acidosis
 - Cardiac arrest
 - Seizures
 - Hypoxia of the brain

II. Original practical work in class

1. To view the collection of drugs.
2. Work with the tests (Krok-1).
3. Prescribe and ground the choice of drug:
 - 1) nootropic drug (racetam group) to improve long-term memory;
 - 2) GABA drug to improve brain resistance to damaging factors;
 - 3) nootrop - a derivative of vitamin;
 - 4) analeptic, topically used as an antiseptic and irritant;
 - 5) adaptogen with nootropic activity;
 - 6) in case of faint, acute vasal insufficiency;
 - 7) analeptic – derivative of nicotinic acid;
 - 8) in case of respiratory center depression with symptoms of cardial failure;
 - 9) for increasing of vitality tonus and immune resistance;
 - 10) in rehabilitation period after cerebro – cranial trauma.
 - 11) analeptik with a mixed mechanism of action;
 - 12) nootropic agent with predominantly GABA-mimetic action;
 - 13) replacement drug Echinacea extract.

Unit 24. CHECKING OF PRACTICAL SKILLS ON “DRUGS ACTING ON CNS”

CONTENT MODULE 4. DRUGS THAT AFFECT THE FUNCTIONS OF THE CARDIOVASCULAR SYSTEM.

Actuality of the unit: Diseases of the heart and blood vessels are the main cause of global morbidity and mortality on the planet. They include many disorders that can affect the contractile properties of myocardial muscles, the function of arteries and veins, capillaries. The most common diseases of the cardiovascular system include hypertension (high blood pressure), angina (chest pain due to insufficient blood flow through the coronary arteries of the heart muscle), heart failure, myocardial infarction and arrhythmia (rhythm disturbance).

The treatment and scheme of taking cardiac drugs will depend on the specifics of the current disease, since not all of them are the same. For example, one of the diseases can be caused by excessive blood clotting or increased blood pressure. But this disease can also be caused by both factors. Therefore, several drugs for the heart with different mechanisms of action may be needed for successful therapy.

The training objectives. *Know:* the pharmacology of drugs affecting the cardiovascular system.

Be able to: solve test tasks, situational and pharmacotherapeutic tasks, write and analyze prescriptions for the drugs of this section.

Interdisciplinary integration. Anatomy, physiology, pathological physiology, biochemistry of the cardiovascular system

Unit 25. CARDIOTONIC DRUGS. CARDIAC GLYCOSIDES. NON – GLYCOSIDE CARDIOTONICS. CARDIOSTIMULANTS

Actuality of the unit. Cardiotonics used to treat acute and chronic heart failure. Congestive heart failure accompanies many acute and chronic heart diseases: ischemic heart disease, myocarditis, cardiac valve abnormalities, and dystrophic processes in myocardium. Currently, the management tactics of these patients has been changed. The first classical medicines for heart failure are the cardiac glycosides. Cardiac glycosides – nitrogenic – free compounds of plant origin, which have the steroid nucleus in their basis and cause cardiotonic effect. The exclusive position of cardiac glycosides among other cardiotonic drugs is defined by their pharmacodynamic characteristics, their ability to correct the metabolism and function of the patient's heart to restore the effective functioning of the heart and to improve the blood circulation in case of its insufficiency.

I. Individual work

Control questions

- I. Etiopathogenesis of heart failure. CARDIOTONIC DRUGS. General characteristics.

CARDIAC GLYCOSIDES

1. General characteristics. History of heart glycosides learning (W. Withering, E.V. Pelican, S.P. Botkin, N.A. Bubnov, I.P. Bogoyavlensky, I.P. Pavlov, N.Y. Chistovich). Plants, containing cardiac glycosides. Chemical structure of cardiac glycosides.
2. Classification:
 - a) *long – acting* glycosides with significant cumulation — preparations of *Digitalis purpurea* – (Digitoxin, Gitalen, Cordigid); preparations of *Digitalis ferruginea* (Digalen neo).
 - b) *intermediate – acting* glycosides with moderate cumulation — preparations of *Digitalis lanata* (Digoxin, Celanidum, Lantoside, Medilazid); preparations of *Adonis vernalis* (Adonisidum); preparations of oleander (Nereolin); preparations of *Erysimum diffusum* (Cardiovalenum);
 - c) glycosides with *rapid and short duration* of action and *insignificant cumulation* — drugs of *Strophanthus* (Strophanthin), drugs of *Convallaria majalis* (Corglyconum, tincture of Convallaria, drugs of *Drimia maritima* (Meprostsillarin) et al.

The notes: Glycosides of long and intermediate duration of action conditionally are called "as group of Digitalis" (on classification of group A and B); glycosides of Strophanthus, Convallaria – "as group of Strophanthus" (group C).

3. Pharmacodynamics of cardiac glycosides. Mechanism of cardiotoxic action. Changes in ECG.

therapeutic phase:

a) *positive inotropic* effect — increased strength of contraction of cardiac muscle;

b) *negative chronotropic* effect — reduction in heart rate;

c) *positive tonotropic* effect — increased tonus of myocardium;

toxic phase:

d) *negative dromotropic* action — reduction of conductivity of myocardium;

e) *positive bathmotropic* action — increase excitability of myocardium.

4. Changing of hemodynamics under influence of cardiac glycosides.

5. The most important additional effects of different cardiac glycosides (influencing the CNS, changes in water – salt exchange etc.).

6. Pharmacokinetics of cardiac glycosides.

7. Comparative characteristics of different cardiac glycosides.

8. Indications and contraindications for prescribing of cardiac glycosides.

9. The principles of digitalization (phase of saturation and phase of maintaining). Effectiveness criteria.

10. Overdosage by cardiac glycosides. Treatment (preparations of potassium, anti – arrhythmic, chelators and donators of sulfhydryl group).

NON-GLYCOSIDE CARDIOTONICS.

Classification:

- sympathomimetics — Dopamine, Dobutamine, etc.;
- phosphoesterase inhibitors — Amrinone, Milrinone;
- metabolic preparations — Glucagon, Riboxine, Neaton, Glutamine acid, etc.;
- from different groups — Sulmazol, Vesnarinone, Levosimendane.

Mechanisms of action. Indications and contraindications for prescription. Undesirable effects.

The concept of a cardiostimulators: adrenergic – and dofaminomimetiks, stimulants of glucagon receptors (Glucagon), analeptics (Cordiamin, Sulfocamfocain) and others. Indications and contra – indications. Undesirable effects.

List of practical works. Prescribe drugs with their application (*separately from the prescription!*):

№	Name of the drug	Drug form
1.	Digitoxin (<i>Digitoxinum</i>)	Tab. 0,0001; rectal suppositories 0,00015
2.	Digoxin (<i>Digoxinum</i>)	Tab. 0,00025; amp. 0,025 % sol. 1 ml.
3.	Celanidum , syn.: izolanid	Tab. 0,00025; vials 0,05 % sol. 10 ml.; amp. with 0,02 % sol. 1 ml.
4.	Infusion of Adonis vernalis grass (<i>Herba Adonis vernalis</i>), MD – 0,5	
5.	Adonisidum	Bot. 15 ml.
6.	Strophanthin (<i>Strophanthinum</i>)	Amp. 0,05 % sol. 1 ml.
7.	Corglyconum	Amp. 0,06 % sol. 1 ml.
8.	Cardiovalenum	Bot. 15 ml.
9.	Unithiol (<i>Unithiolum</i>)	Amp. 5 % sol., 10 ml.
10.	Panangin (<i>Panangin</i>) syn.: asparkam	Patented dragee and amp. 10 ml.
11.	Trilon B syn.: disodium edetate	Amp. 5 % sol. 5 and 10 ml.
12.	Dobutamine (<i>Dobutaminum</i>)	Amp. 5 % sol. 5 ml.
13.	Milrinone (<i>Milrinonum</i>)	Amp. 0,1 % sol. 1 ml.

Tasks for self-control. Choose the correct answers.

1. *What is the reason of cardiotoxic effect of cardiac glycosides?*
 - A. Reflex effect on the heart
 - B. Stimulation of Na⁺, K⁺ – ATP – ase
 - C. Blockade of Na⁺, K⁺ – ATP – ase
 - D. Blockade of beta – adrenergic receptors
 - E. Indirect activation of beta – adrenergic receptors
2. *To extracardiac effects of cardiac glycosides belong:*
 - A. Strengthening of stroke and minute volume of blood
 - B. Increasing of venous pressure
 - C. Reducing the pressure in the pulmonary vessels
 - D. Increasing of diastolic pressure in the ventricles
 - E. Diuretic effect
3. *On the background of administration of cardiac glycosides on the ECG T – wave decline, ST interval below the isoelectric line, reducing the QRS complex and increasing of R wave. As a result of what effect did this happen?*
 - A. «+» inotropic
 - B. «+» chronotropic
 - C. «–» dromotropic
 - D. «–» bathmotropic
 - E. «+» bathmotropic
4. *Patient with chronic heart failure who received Digoxin appeared headache, nausea, xanthopsia. Which drug may reduce the symptoms of intoxication?*
 - A. Naloxone
 - B. Dipyrroxim
 - C. Bemegride
 - D. Uritol
 - E. Atropine sulfate
5. *The patient with cardiogenic shock received cardiotoxic drug from the group of non – selective adrenomimetics with indirect action. Select a medicine:*
 - A. Dobutamine
 - B. Dopamine
 - C. Milrinone
 - D. Vesnarinone
 - E. Riboxinum

II. Original practical work in class

1. To view the collection of drugs.
2. Work with the tests (Krok-1).
3. Prescribe and ground the choice of drug:
 - 1) cardiac glycoside with high accumulation;
 - 2) cardiac glycoside with sedative activity;
 - 3) cardiac glycoside in case of acute heart failure;
 - 4) cardiac glycoside in case of chronic heart failure;
 - 5) cumulative glycoside for I.V. injection;
 - 6) potassium – containing drug in case of cardiac glycoside overdosing;
 - 7) donator of sulfhydryl groups used in case of intoxication with cardiac glycoside;
 - 8) cardiotoxic from group of stimulators of β_1 adrenoreceptors.
 - 9) cardiotoxic – a phosphodiesterase inhibitor.
 - 10) the drug replacement strofantin;
 - 11) the drug digoxin replacement;
 - 12) the drug replacement of amrinon;
 - 13) the drug digitalis purpurea;
 - 14) the drug digitalis woolly;
 - 15) preparation of lily of the valley;
 - 16) chelator in case of overdose of cardiac glycosides;

- 17) Korglikon Pananginum and in some recipes and explain the possibility of combined use;
- 18) digoxin and calcium gluconate in some recipes and explain the possibility of combined use;
- 19) the drug that causes xanthopsia;
- 20) the drug in case of overdose which there beats, ventricular fibrillation and cardiac arrest

Unit 26. ANTIARRHYTHMIC DRUGS

Actuality of the unit. Antiarrhythmic drugs (antiarrhythmics) used to normalize arrhythmic heart rate, eliminate or prevent the occurrence of arrhythmias. As a rule arrhythmias are not an independent disease and appear on the ground of disordering heart work in ischemic heart disease, myocarditis, pneumonia, endocrine disorders, hormonal disorders, and others.

I. Individual work

Control questions

1. Conception of arrhythmias, types of arrhythmias. Etiopathogenic factors of their occurrence.
2. Modern approaches to pharmacotherapy of arrhythmias:
 - *ethiotropic*: elimination of neurogenic and endocrinal disturbances (CNS suppressants, antithyroid agents); the inflammatory phenomena in a myocardium (NSAIDs, glucocorticoids); acute or chronic oxygen insufficiency of a myocardium (angioprotectors, coronarolytics, etc.), normalizing electrolytic exchange (preparations of potassium), etc.
 - *pathogenetic*: elimination of disturbances of electrolytic exchange and accompanying changes of automatism and excitability (membrane – stabilizing, blockers of Ca^{2+} and K^{2+} channels, preparations of potassium); nervous regulation of heart activity (conductivity) – in cases of tachyarrhythmia (beta – adrenoblockers), bradyarrhythmia (M – cholinoblockers, beta – adrenomimetics).
3. The requirements to antiarrhythmic drugs
4. Classification of antiarrhythmic drugs:
 - I. In cases of bradyarrhythmia:** M – cholinoblockers (Atropine, Platyphyllinum), beta – adrenomimetics (Isadrine, Dobutamine etc.), Glucagon.
 - II. In cases of tachyarrhythmia*:**

I class — *sodium channel blockers (membrane – stabilizing drugs):*

IA — prolonging the effective refractory period (ERP): Quinidine, Novocainamide, Disopyramide, Ethmozine, Ajmaline etc;

IB — shorting ERP: Lidocaine, Mexiletine, Tocainide, Diphenin;

IC — rendering various influence on ERP: Propafenone, Ethacizine.

II class — *beta – adrenoblockers:*

 - nonselective— Propranolol (Anaprilinum), Nadolol (Korgard), Oxprenolol** (Trazikor), Pindolol** etc.;
 - cardioselective — Atenolol, Metoprolol, Talinolol, Acebutolol** etc.

III class – *blockers of potassium channels (prolonging ERP):* Amiodarone, Sotalol, Bretylium.

IV class – *calcium channel blockers:* cardiotropic — Verapamil, Hallopamil and mixed — Diltiazem.
5. Pharmacology of I CLASS drugs. Mechanism of antiarrhythmic action. Comparative characteristics of drugs. Indications. Undesirable affects.
6. β – ADRENOBLOCKERS as the antiarrhythmics. Mechanism of action. Indications. Undesirable affects.
7. BLOCKERS OF POTASSIUM CHANNELS. Pharmacodynamics and pharmacokinetics. Indications. Undesirable effects.
8. CALCIUM CHANNEL BLOCKERS. General characteristics. Classification:
 - ⇒ I type — *cardiotropic* — phenylalkilamine derivatives: 1st generation — Verapamil (finoptinum), 2nd generation — Gallopamil etc.;
 - ⇒ II type — *vasotropic*:

- *general action* — dihydropyridine derivatives:
 - 1st generation — Nifedipine (Fenigidin, Corinfar);
 - 2nd generation — Nifedipine – GITS, Amlodipine, Isradipine, Nicardipine, etc.;
- *cerebrovasotropic* — difenilpiperazin derivatives:
 - 1st generation — Cinnarizine (Stugeron);
 - 2nd generation — Flunarizin (Nomigren), as well as some of the dihydropyridine derivatives of the 2nd generation (Nimodipine).

III type — *mixed* — benzodiazepine derivatives: 1st generation — Diltiazem, 2nd generation — Klentiazem.

Mechanism of action. Pharmacodynamic effects. Features of different types. Pharmacokinetics. Classification by duration of action. The differences between generations.

Indications. Undesirable effects.

Mechanism of antiarrhythmic action of calcium channel blockers.

9. Mechanism of antiarrhythmic action of potassium – containing preparations.

10. Features of clinical application antiarrhythmic drugs depending on kinds of infringements of the heart rhythm.

11. Antiarrhythmic preparations on the base of medicinal plants (cardiac glycosides, alkaloids Rauwolfia, aconites, cinchona tree, Hawthorn etc.). Indications to usage.

List of practical works. Prescribe drugs with their application (*separately from the prescription!*):

№	Name of the drug	Drug form
1	2	3
1.	Novocainamide (<i>Novocainamidum</i>) syn.: Procainamide	Tab. 0,25, amp. 10% sol. 5ml.
2.	Diphenin (<i>Dipheninum</i>) syn.: Phenytoin	Tab. patented.
3.	Lidocaine hydrochloride (<i>Lidocainum hydrochloridum</i>)	Amp. 2 % sol. 2 and 10 ml.; amp. 10 % sol. 2 ml.
4.	Propafenone (<i>Propafenone</i>) syn.: Ritmonorm	Tab. 0,15 and 0,3; amp. 0,35 % sol. 10 and 20 ml.
5.	Anaprilin (<i>Anaprilinum</i>) syn.: Propranolol	Tab. 0,01 and 0,04.
6.	Atenolol (<i>Atenololum</i>)	Tab. 0,05, 0,025 and 0,1
7.	Acebutolol (<i>Acebutololum</i>)	Tab. 0,2 and 0,4
8.	Amiodarone (<i>Amiodaronum</i>) syn.: Cordarone	Tab. 0,2, 0,05, amp. 5 % sol. 3 ml.
9.	Verapamil (<i>Verapamilum</i>) syn.: Izoptin, Finoptinum	Tab. 0,04, 0,08 and 0,12; amp. 0,25 % sol. 2 ml.
10.	Tincture of Hawthorn (<i>Grataegus</i>)	Bot. 25 ml.

Tasks for self-control. Choose the correct answers.

1. *Select the drug with local anesthetic activity for relief of post – infarction ventricular arrhythmias:*
 - A. Lidocaine
 - B. Anestezin
 - C. Verapamil
 - D. Panangin
 - E. Anaprilin
2. *To a patient with cardiac fibrillation with a history of bronchial asthma, is necessary to appoint an antiarrhythmic agent. Which drug from this group is contraindicated to the patient?*
 - A. Lidocaine
 - B. Anaprilin
 - C. Verapamil
 - D. Nifedipine
 - E. Novocainamid
3. *Which calcium channel blockers drug is indicated for tachyarrhythmia?*

- A. Verapamil
- B. Nifedipine
- C. Cinnarizine
- D. Nimodipine
- E. Amlodipine

4. *The patient suffers from sinus bradycardia. Which of the following drugs should be assigned?*

- A. Amiodarone
- B. Atropine sulfate
- C. Novocainamid
- D. Disopyramid
- E. Panangin

5. *Choose antiarrhythmic drug with M – anticholinergic, α -adrenoblocking, antipyretic, analgesic effects:*

- A. Novocainamid
- B. Quinidine
- C. Ajmaline
- D. Diphenin
- E. Etmozin

II. Original practical work in class

1. To view the collection of drugs.
2. Work with the tests (Krok-1).
3. Prescribe and ground the choice of drug:

- 1) drug with negative ino, chrono – , dromo – , bathmotropic effects;
- 2) antiarrhythmic, to which undesirable actions belong collapse reaction, systemic lupus erythematosus etc.;
- 3) antiarrhythmic with antiepileptic activity;
- 4) antiarrhythmic, by the application of which there can be pulmonary fibrosis, infringements of vision, etc.;
- 5) class IC antiarrhythmic;
- 6) selective β – blocker with intrinsic sympathomimetic activity during tachyarrhythmia;
- 7) calcium channel blocker that act mainly in the myocardium;
- 8) antiarrhythmic in case of overdose by cardiac glycosides;
- 9) antiarrhythmic of plant origin.
 - 10) the drug in case of bradycardia;
 - 11) the drug, prolongs the effective refractory period;
 - 12) drug class IV;
 - 13) the drug metoprolol replacement;
 - 14) gallopamil replacement drug;
 - 15) antiarrhythmic causing bronchospasm;
 - 16) antiarrhythmic, having a sedative effect;
 - 17) antiarrhythmic causing hypotension;
 - 18) antiarrhythmic causing tachycardia;
 - 19) antiarrhythmic that causes mydriasis.

Unit 27-28. ANTIANGINAL PREPARATIONS.

COMPLEX THERAPY OF MYOCARDIAL INFARCTION

Actuality of the unit: Antianginal preparations – group of medicinal preparations used for the prevention of coronary insufficiency, attacks of stenocardia, myocardial infarction and other forms of ischemic heart diseases. Into the list antianginal drugs enters peripheral vasodilators (organic nitrates – nitroglycerine and its analogues in the various medicinal forms), calcium channel blockers, spasmolytics, agents influencing on adrenergic system innervations of heart etc. Their action is explained by reaching of balance between oxygen need (requirement) of heart and it's supply (delivery

of oxygen to heart). This physiological task (decreasing intensity of job of heart and reduces its oxygen requirement) can be solved by different ways. Therefore antianginal drugs often are combined, due to which action of various elements is reached through action on cardiovascular systems (decreasing of arterial pressure, dilation of coronary vessels, reduction of force and frequency of cardiac systole etc.) and action on metabolism regulating energy needs of heart. Often included in complex therapy for ischemic heart disease are so – called additional preparations raising stability of organs and tissues to functioning in conditions of insufficient supply of oxygen. In certain kinds of angina it is perspective to use inhibitors of angiotensin converting enzyme, bradycardic action drugs – selective inhibitors of channels of the sinus node controlling spontaneous diastolic depolarization (Ivabradine), and others.

I. Individual work

Control questions

ANTIANGINAL DRUGS

1. Etiopathologic factors of ischemic heart disease. Requirements for antianginal drugs: promote the formation of collateral vessels without "steal" syndrome, have antiplatelet activity, without negative effect on the lipid, carbohydrate metabolism, and others.

2. Classification:

1) *Drugs decreasing requirements of myocardial oxygen and improving blood supply:*

a) Nitrovasodilators:

- Nitrates — Nitroglycerine and prolonged forms (Sustac – forte (mite), Trinitrolong, Nitrogranulong, Nitro – mak, Nitroderm etc.); Isosorbide dinitrate /Iso – mak, Isoket, Nitrosorbide, Dinitrosorbilong etc/; Isosorbide mononitrate, Isomonat, Moniside, Olicard etc./;

- sidnonimines — Molsidomine /Corvaton, Sidnofarm/.

b) Calcium channel blockers — Verapamil, Diltiazem, 2nd generation Dihydropyridine*;

c) Activators (Minoxidil and Pinocidil) and blockers (Amiodarone) of potassium channels;

2) *Drugs reducing requirement of myocardium in oxygen:*

a) beta – adrenoblockers — Propranolol, Atenolol, Metoprolol etc.**;

3) *Drugs improving delivery of oxygen to myocardium (coronarolytics):*

a) Myotropic action — Carbocromen, Dipyridamol, Papaverine, No – spa, Aminophylline etc.;

b) Reflectory action — Validol.

4) *Drugs raising resistance of myocardium to hypoxia:*

a) antihypoxants — Trimetazidine /Preductal/, Mildronate, ATP – long, Neoton, Ascorbic acid, Riboflavin, Nicotinic acid etc.;

b) anti – oxidants — Tocopherol, Dibunol, Thiotriazoline etc.;

c) anabolics — steroids (Retabolil, Nerobol), non – steroids (Inosine /Riboxin/, Potassium orotate);

d) normalizing of electrolytes exchange — Panangin /Asparkam/.

3. NITRATES. Mechanisms of action. pharmacodynamics, pharmacokinetics. Undesirable effects.

The comparative characteristic of nitrates. Others nitrovasodilators. Peculiarities of application.

4. CALCIUM CHANNEL BLOCKERS as antianginal drugs. Mechanisms of action. Undesirable effects.

5. Feature of application in treatment of the patients ischemic heart disease β – ADRENOBLOCKERS.

6. Agents that improve the delivery of oxygen to the myocardium. MYOTROPIC drugs. General characteristics. Classification of **nonselective myotropic drugs** by mechanism of action:

- phosphodiesterase inhibitors — isoquinoline derivatives: Papaverine, Drotaverine /Nospanum/; different chemical groups: Carbochromen /Intenkordin/ etc.;
- adenosinergic and phosphodiesterase inhibitors — Dipyridamole /Chimes/, Lidoflazin etc.;
- antagonists of adenosine (purine) receptors and phosphodiesterase inhibitors — methylxanthine (purine) derivatives:

* Classification of calcium channel blockers is given in topic № 22.

** Classification of β-adrenoblockers is given in topics № 10, 22.

- alkaloids: Caffeine (1,3,7 – trimethylxanthine), Theobromine (3,7 – dimethylxanthine), Theophylline (1,3 – dimethylxanthine);
- semisynthetic: Aminophylline /Eufillin/, Diprofillin, Pentoxifylline /Trental, Agapurin/ etc.***;
- mixed mechanism of action — Apressin, Dibazolium, Nicotinic acid and its derivatives (used as antihypertensive, see topic number 25); Bentsiklan /Halidorum/, Pinaveriya bromide, Arpenans (used mainly in spasm of smooth muscles of the abdominal cavity), and others.

Note: Depending on the origin of spasm other drugs has myotropic action: M – cholinoblockers, ganglioblockers, α -adrenoblockers selectively reduce the influence innervation that leads to spasm, β 2-adrenergic agonists increase the inhibitory effect through presynaptic β 2-adrenergic receptors, and others.

Main applications of myotropic medicine. Feature of application at the patients ischemic heart disease vasodilators, myotropic and reflectory – acting drugs. Concept about syndrome "stealing".

7. Drugs, which increase resistance to hypoxia of the myocardium. General characteristics of the main groups. Indications and contraindications.

8. Complex therapy of ischemic heart disease (IHD). Application of anti – aggregates (Acetylsalicylic acid, Dipyridamol, Clopidogrel), ACE inhibitors (Enalapril etc.), selective inhibitors If – channel of the sinus node (Ivabradine), selective antagonists of aldosterone receptors (Eplerenone) etc.

9. Principles of complex therapy of a myocardial infarction:

- 1) *prevention and treatment of thrombosis* — fibrinolytics (Streptokinase, Alteplase), direct anticoagulants (Heparin and low molecular weight heparin), antiplatelet agents (Acetyl salicylic acid, Clopidogrel);
- 2) *elimination of pain syndrome* — narcotic analgesics (Morphine, Promedol); if the therapy is not effective: I.V. β – adrenoblockers (Propranolol, Metoprolol), nitrates;
- 3) *elimination of fear, emotional excitation* — tranquilizers (Diazepam), antipsychotics (Haloperidol);
- 4) *prevention of vomiting* — antiemetic (Metoclopramide);
- 5) *elimination of hemodynamic disturbances:* in case of hypotension — adrenergic agonists (Dopamine, phenylephrine), glucocorticoids; in the case of hypovolemia — blood substitutes; in the case of hypertension — β – adrenoblockers, ACE inhibitors;
- 6) *elimination of heart failure, cardiogenic shock* — oxygen intranasally; depending on the severity of heart failure, hemodynamic state and others factors: nitrates, ACE inhibitors, loop diuretics (Furosemide), aldosterone antagonists (Spironolactone, Eplerenone), cardiotoxic (Levosimendan, Milrinone, Dobutamine, Dopamine);
- 7) *elimination of arrhythmia* — in case of tachycardia: Lidocaine, Amiodarone, β – adrenoblockers, Digoxin; in case of bradycardia: Atropine;
- 8) *restriction of necrosis* — nitrates, β – adrenoblockers orally;
- 9) *elimination of infringements electrolyte and acid – base balance* — Sodium bicarbonate, Panangin etc.;

General characteristic of groups.

List of practical works. Prescribe drugs with their application (*separately from the prescription!*):

No	Name of the drug	Drug form
1.	Nitroglycerine (<i>Nitroglycerinum</i>)	Tab. 0,0005; caps. 0,0005; Bot. 1% spirit sol. 10 ml.; aerosols in balloons 12,0 and 30,0
2.	Sustak (<i>Sustac</i>)	Tab. 0,0026 (– mite) and 0,0064 (– forte)
3.	Isosorbide mononitrate (<i>Isosorbidum mononitratum</i>)	Tab. 0,02 and 0,04; in ampoules with 1% sol. 1 ml.
4.	Isosorbide dinitrate (<i>Isosorbidum dinitratum</i>) syn.: Nitrosorbid	Tab. 0,005, 0,01 and 0,02; in ampoules with 1% sol. 10 ml.; caps 0,02 , 0,04 , 0,06

*** Xanthines are rarely used as antianginal agents.

5.	Molsidomine (<i>Molsidomin</i>) syn.: Corvaton	Tab. 0,002 and 0,004
6.	Trimetazidine (<i>Trimetazidinum</i>) syn.: Preduktal	Tab. 0,02
7.	Dipyridamole (<i>Dipyridamolum</i>) syn.: Curantylum	Tab. 0,025, in amp. 0,5 % sol. 2 ml.
8.	ATP – long (<i>Adenosinum phosphatum</i>)	Tab. 0,01 and 0,02, amp. 2 % sol. 1 and 2 ml.

Tasks for self-control. Choose the correct answers.

1. Choose antianginal drug – nitrous oxide donator.
 - A. Molsidomine
 - B. Papaverine
 - C. Trimetazidine
 - D. Verapamil
 - E. Nitroglycerin
2. Choose fact that is true to the nitrates:
 - A. Selectively dilate vascular smooth muscle
 - B. Reduce pre – and afterload on the heart
 - C. Cause syndrome "steal"
 - D. Improves coronary blood flow
 - E. Cause antiaggregation activity
3. Which adverse effects can nitrates cause?
 - A. Reflectory bradycardia
 - B. Orthostatic hypotension
 - C. Tolerance
 - D. Reduction of intracranial pressure
 - E. Withdrawal syndrome
4. What antianginal drug at the same time has antiarrhythmic properties specific to I, II, III, IV classes?
 - A. Atenolol
 - B. Verapamil
 - C. Panangin
 - D. Amiodarone
 - E. Nicorandil
5. The reason to use dihydropyridine calcium channel blockers as antianginal drugs:
 - A. Dilates blood vessels, decreasing of cardiac pre – and afterload
 - B. Selectively dilate the arteries, reducing the afterload of heart
 - C. Selectively dilate veins, reducing of cardiac preload
 - D. Reduce myocardial oxygen needs
 - E. Decreasing of coronarospasm

II. Original practical work in class

1. To view the collection of drugs.
2. Work with the tests (Krok-1).
3. Prescribe and ground the choice of drug:
 - 1) for stoppage of stenocardia attack;
 - 2) in the period of stenocardia from group of nitrates;
 - 3) nitrate, having the longest action;
 - 4) for stoppage of an attack stenocardia at idiosyncrasy to nitrate group;
 - 5) antianginal, causing reflective tachycardia;
 - 6) antianginal, with side effect like atherogenic, desensitization of receptors, rebound syndrom, etc .;
 - 7) antianginal, causing "stealing" syndrome;
 - 8) antianginal, improving energy supply of myocardium;
 - 9) for stoppage of pain syndrome during myocardial infarction;
 - 10) for elimination of bradycardia during myocardial infarction.
 - 11) a drug that enhances the arterioles and venules, reducing preload and afterload on the heart;

- 12) the drug, causing rapid tolerance;
- 13) the drug replacement isosorbide mononitrate;
- 14) koronarolitik;
- 15) the drug that causes bradycardia;
- 16) the drug that causes orthostatic collapse;
- 17) antihypoxant;
- 18) for limiting necrosis of myocardial infarction;
- 19) to eliminate the fear, excitement at an attack of angina pectoris.

Unit 29. DIURETIC DRUGS. COMPLEX THERAPY OF CONGESTIVE HEART FAILURE

Actuality of the unit. Diuretics — drugs of plant origin, non – organic and synthetic origin drugs with the ability to increase urine output by several ways: 1) increase filtration processes (formation of primary urine); 2) inhibition processes of electrolytes reabsorption (especially Na⁺ and Cl⁻) and water in the renal tubules (formation of secondary urine). Possibility of medical management of renal excretory ability is based on the knowledge of the mechanisms of neurohumoral regulation of water – salt metabolism and the role of the kidneys in the formation and elimination of urine. Neurohumoral regulation of water – salt metabolism is largely carried due to the functioning of major homeostatic processes – retaining sodium and water in the body. Knowledge of rational and safe use of diuretics contribute to successful treatment of various diseases, including heart failure.

I. Individual work

Control questions

DIURETICS

1. Etiopathogenesis of edema.

2. Classification of diuretic drugs **according to the chemical structure and mechanism of action:**

I. Na⁺ – reabsorption inhibitors:

- 1) Na⁺ – reabsorption inhibitors from the lumen of channels into the cell (affecting the luminal membrane):
 - aldosterone agonists — Spironolactone /Veroshpiron/;
 - Na – channel blockers — Triamterene, Amiloride;
- 2) Na⁺ – reabsorption inhibitors from the cell throughout the basal membrane:
 - carbonic anhydrase inhibitors — Diacarb (Acetazolamide), Dorzolamide;
 - “loop” diuretics* — Furosemide /Lasix/, Ethacrynic acid /Uregit/, Bumetanide /Bumetanide/, Torasemide, Xipamide;
 - sulphonamides*: thiazides — Hydrochlorothiazide /Dihlotiazid, Hydrochlorothiazide/, and thiazide like — Oxodolin /Ohlorthalidone/, Clopamide /Brinaldiks/, Indapamide and others.

II. Active on all channel longitude:

- osmotic diuretics: Mannitol /Mannit/, Urea;
- acidifying — Ammonium chloride.

III. Affecting renal blood flow — xanthines (Theophylline, Aminophylline), Furosemide.

IV. Plants with diuretic activity — horsetail, Adonis, bearberry leaf, birch buds, juniper berries, leaf orthosiphon, cranberries, strawberries, flowers, cornflower, special charges (kidney tea, Nephrophyt) and others.

V. Combined diuretics — Moduretik (Hydrochlorothiazide + Amiloride), Triampur (Hydrochlorothiazide + Triamterene), Furezis (Furosemide + Triamterene) and others.

3. Classification of diuretic drugs **according to the potency of action:**

- quick and short effect — “loop” diuretics, osmotic diuretics;

* Termin saluretics mean primarily inhibitors of Na⁺ and Cl⁻ reabsorption.

- medium strength and duration — thiazide, potassium – saving (Triamterene), carbonic anhydrase inhibitors, xanthine;
- delayed and long – acting — thiazide like, potassium – saving (Spironolactone).
 4. Sites of action of the main groups.
 5. Xanthine diuretics. Mechanisms of action. Indications for use. Undesirable effects.
 6. Carbonic anhydrase inhibitors. Mechanisms of action. Indications for use. Undesirable effects.
 7. Osmotic diuretics. Mechanisms of action. Indications for use. Undesirable effects.
 8. Loop diuretics. Mechanisms of action. Indications for use. Undesirable effects. The concept of forced diuresis.
 9. Thiazide and thiazide like diuretics. Mechanisms of action. Indications for use. Undesirable effects.
 10. Potassium – saving diuretics. Mechanisms of action. Undesirable effects.
 11. Plants with diuretic activity.
 12. General principles of diuretics appointment.

COMPLEX THERAPY OF CONGESTIVE HEART FAILURE

- **main:**
 - ACE inhibitors;
 - diuretics, and selective antagonists of aldosterone receptor: Eplerenone (Inspra);
 - cardiac glycosides;
 - β – adrenoblockers (in combination with ACE inhibitors): Bisoprolol, Carvedilol, Metoprolol retard.
- **supporting:** antagonists of angiotensin II receptors, potassium channel blockers (Amlodipine);
- **additional** (in certain clinical situations): vasodilators (nitrates, calcium channel blockers), antiarrhythmic, non – glycoside cardiotoxic, anti – aggregant agents, indirect anticoagulants, glucocorticoids, synergists of cardiac glycosides — vitamin preparations (Thiamine, Cocarboxylase, Pyridoxine, Nicotinic acid, Tocopherol), neurotrophic (Glucose, steroidal and nonsteroidal anabolic agent).

URICOSURIC AGENTS. General characteristics. Classification:

- A. *Drugs, inhibiting the synthesis of uric acid:*
- suppressing xanthinoxidase — Allopurinol;
 - with various mechanisms of action — Benzobromarone (Desurik).
- B. *Drugs, increasing excretion of uric acid:*
- suppressing reabsorption of uric acid in kidney's channels — Benzobromarone, Probenecid®, Sulphinpyrazone (Anturane®), Urodane, Kebuzone;
 - drugs, decreasing acidification of urine — Uralit (Soluran), Magurlit, Blemaren;
 - combination drugs — Allomarone (Allopurinol + Benzobromarone).
- C. *Drugs in case of stone formation in urinary tract (expelling of blood ammonia products) —* Urolesane, Phytolisinum, Cisternal.
- D. *In the case of acute attack of of gout —* NSAIDs (Butadion, Indomethacin), Colchicine, corticosteroids.

Mechanism of action. Indications and contraindications. Pharmacological safeness and interchangeability of medicines.

List of practical works. Prescribe drugs with their application (*separately from the prescription!*):

№	Name of the drug	Drug form
1	2	3
1.	Mannit (<i>Mannitum</i>) syn.: mannitol	Bot. 500 ml., containing 30 g of substance; amp. 15% sol. 200, 400, 500 ml. each
2.	Aminophylline (<i>Aminophyllinum</i>)	Tab. 0,15; ampoules 2,4% – 10 ml. and 24% –

	syn.: Euphyllin	1 ml.
3.	Diakarb (<i>Diacarbium</i>) syn.: <i>Dorzolamidum</i>	Tab. 0,25; vial 2 % sol. 5 ml.
4.	Hydrochlorothiazide (<i>Hydrochlorthiazidum</i>) syn.: Dihlotiazid, Hydrochlorothiazide	Tab. 0,025 and 0,1
5.	Cloпамide (<i>Cloпамidum</i>) syn.: Brinaldix	Tab. 0,02
6.	Furosemide (<i>Furosemidum</i>) syn.: Lasix	Tab. 0,04; amp. 1% 2 ml. (<i>Lasix</i>)
7.	Torasemide (<i>Torasemidum</i>) syn.: Trifas	Tab. 0,005, 0,02, 0,2
8.	Ethacrynic acid (<i>Acidum etacrynicum</i>) syn.: Uregei	Tab. 0,05
9.	Triamterene (<i>Triamterenum</i>)	Caps. 0,05
10.	Spironolactone (<i>Spironolactonum</i>) syn.: veroshpiron	Tab. 0,025
11.	Triampur (<i>Triampur</i>)	Patented tab.
12.	Amiloride (<i>Amiloridum</i>)	Tab. 0,005
13.	Allopurinol (<i>Allopurinolum</i>)	Tab. 0,10
14.	Dorsolamide (<i>Dorzolamidum</i>)	Bot. 2 % sol. 5 ml
15.	Fitolisin (<i>Phytolysin</i>)	Cream in tubes 100,0

Tasks for self-control. Choose the correct answers.

- Xanthine diuretics have the following effects:*
 - Cardiostimulation
 - Bronchospasm
 - Vasodilator
 - Spasmolytic
 - Immunomodulating
- Atherogenic effect present in:*
 - Furosemide
 - Diakarb
 - Hydrochlorothiazide
 - Triamterene
 - Aminophylline
- Severe metabolic acidosis causes:*
 - Bufenox
 - Oxodolin
 - Furosemide
 - Diakarb
 - Hydrochlorothiazide
- In patients with hypertension during treatment with hydrochlorothiazide appeared drowsiness, loss of appetite, extrasystoles, muscle aches. What could be the reason?*
 - Hyponatremia
 - Hyperuricemia
 - Hypokalemia
 - Hyperkalemia
 - Hypercalcemia
- Patient with urarthritis. What preparation is necessary to appoint to inhibit synthesis and increased excretion of uric acid?*
 - Allopurinol
 - Urolesan
 - Benzbromarone
 - Ural
 - Phytolysinum

II. Original practical work in class

- To view the collection of drugs.
- Work with the tests (Krok-1).

3. Prescribe and ground the choice of drug:

- 1) diuretic increasing renal blood flow;
- 2) diuretic for “reinforced diuresis”;
- 3) diuretic of choice in case of chronic heart failure (indicate assignment rules);
- 4) diuretic, which onset of action is 7 – 10 days;
- 5) diuretic used for treatment of glaucoma;
- 6) diuretic, which infringe tolerance to glucose;
- 7) diuretic, causing hypercalcemia;
- 8) preparation reducing the basic undesirable action of Saluretics;
- 9) preparation used for the treatment of Gout.
- 10) for the relief fit of gout;
- 11) a drug that reduces uric acid excretion;
- 12) a drug that increases the excretion of uric acid;
- 13) the drug, inhibiting sodium transport from the tubule lumen into the cell;
- 14) amiloride replacement drug;
- 15) the drug ethacrynic acid substitutions;
- 16) combined a diuretic;
- 17) the average diuretic potency and duration of action;
- 18) a drug that increases the excretion of nitrogenous wastes;
- 19) diuretics acting throughout the tubule;
- 20) a diuretic, causing hyperkalemia.

**Unit 30. DRUG AFFECTING ON BLOOD PLESURE.
ANTIHYPERTENSIVE, HYPERTENSIVE DRUGS**

Actuality of the unit. Medicines regulating arterial blood pressure (BP) are related with various mechanisms of action (from central up to peripheral) concerns to medicinal means. They rather conditionally can be divided into 2 groups: hypertensive (raising BP) and hypotensive (lowering BP). Hypertensive agents are subdivided into two groups: a) used for treatment of sharp reduction of BP (direct and indirect adrenomimetics); b) at, so – called, neurocirculating dystonia on hypotonic types (adaptogens, GABA – ergic, psychostimulators). Hypotensive, in turn, are subdivided into means working systematically and consequently used for treatment of arterial hypertension, and Hypertonic illness; the second group – adjusts circulation locally (brain, coronary and peripheral). The greatest practical importance for the doctor hypotensive drugs represent. The arterial pressure depends on cardiac output (minute, shock volume), peripheral resistance of vessels to current of blood, viscosity of blood, its electrolyte balance and elasticity of artery. The volume of circulating blood has great importance attached to it. These factors are regulated by nervous and endocrine systems, condition of an exchange of substances, quantity (amount) of a liquid and salts in vessels. The action of hypotensive drugs can be directed on different parts physiological and biochemical regulating blood pressure (neurotropic, myotropic, influencing on activity of renin – angiotensin system etc.).

I. Individual work**Control questions****ANTIHYPERTENSIVE DRUGS**

1. Etiology of hypertension. Mechanisms for blood pressure control.
2. Classification

I. *Neurotropic* — tranquilizers (Diazepam, Gidazepam et al.), antipsychotics (Chlorpromazine, Droperidol, Eglonil) psychosedative (Valerian, Leonurus), magnesium salts (Magnesium sulfate);

II. *Drugs, affecting synaptic transmission:*

- 1) mainly centrally acting:
 - central α_2 -adrenomimetics — Clonidine /Clonidine, Gemiton/, Methyldopa, Guanfacine;
 - selective agonists of imidazoline receptors — Moxonidine, Rilmenidine;

2) mainly peripheral action:

- β – Adrenergic blockers: nonselective — Propranolol, Oxprenolol, Pindolol; cardioselective — Atenolol, Metoprolol, Bisoprolol, Acebutolol;
- α -Adrenergic blockers: nonselective — Pirroxan; α_1 -Adrenergic blockers — Prazosin, Doxazosin;
- α and β – blockers — Labetalol, Carvedilol, Proxodolol;
- sympatholytic drugs — Reserpine, Raunatin, Octadin;
- ganglioblockers — Benzohehexony, Pentamin;
- blockers of serotonin receptors — Ketanserin, Ritanserin.

III. *Myotropic (vasodilators)*:

1) nonselective* (spasmolytics):

- phosphodiesterase inhibitors — isoquinoline derivatives (Papaverine, Drotaverine /No – spa/);
- antagonists of adenosine (purine) receptors and inhibitors of phosphodiesterase — Xanthines (Theophylline, Aminophylline);
- mixed mechanism of action — Apressin /Hydralazine/, Dibazolium, nicotinic acid and its derivatives (Ksantinola Nicotinate /Komplamin/, Nikoshpan) and others.

2) selective:

- Calcium channel blockers — Verapamil, Nifedipine, Amlodipine, Diltiazem**;
- Potassium channel activators — Minoxidil, Diazoxide;
- nitric oxide donors — Sodium nitroprusside and others.***

IV. *Drugs affecting renal function and electrolyte metabolism*:

a) diuretics;

b) ACE – inhibitors:

- short – acting (6 – 12 hours) containing sulfhydryl group — Captopril;
- long – acting (24 h) containing a carboxyl group — Lisinopril, Enalapril, Perindopril, Ramipril, Trandolapril, and others;
- extremely long action (36 hours), containing a phosphoryl group — Fosinopril.

c) antagonists of angiotensin II receptors — Losartan, Valsartan, Irbesartan.

V. *Herbal – origin* drugs — hawthorn, linden flowers, raspberries, black elderberry flowers, grass cudweed toplanoy.

VI. *Combined* drugs — Adelphanum (Reserpine+Dihydralazine+Hydrochlorothiazide), Sinepres (Reserpine+Dihydroergotoxin+Hydrochlorothiazide), Kristepin (Reserpine+Dihydroergocristine+Clonidine), Kapozid (Captopril+Hydrochlorothiazide), Co – Renitek (Enalapril+Hydrochlorothiazide), Papazol (Papaverine+ Dibazolium) and et al.

3. Comparative characteristic of separate groups.

4. Principles pharmacotherapy hypertonic disease.

5. First aid at hypertonic crisis.

HYPERTENSIVE DRUGS. General characteristics.

Classification:

- Adrenergic agonists — Adrenaline, Ephedrine, Noradrenaline, Mesatonum;
- Dopaminergic agonists — Dopamine;
- Glucocorticoids — Hydrocortisone, Prednisolone;
- Mineralocorticoids — Deoxycorticosterone;
- Analeptics — Corazolium, Cordiaminum, Caffeine, Camphora;
- Drugs acting on angiotensin system — Angiotensinamide;

* Full classification of miotropic agents is given in unit № 23.

** Classification of calcium channel blockers is given in unit № 22.

*** From clinical view, peripheral vasodilators are classified into: arteriolar (calcium channel blockers, potassium channel blockers, hydralazine /apressin/ etc.); arteriolar and venous (α -adrenoblockers, ganglionic blockers, nitrovasodilators (nitroglycerin, sodium nitroprusside), no-spa, papaverin etc.).

- Adaptogens — Ginseng, Eleutherococcus, Schizandra etc.
Mechanisms of action, therapeutic effects, adverse effects, indications and contraindications.

List of practical works. Prescribe drugs with their application (*separately from the prescription!*):

№	Name of the drug	Drug form
1.	Clonidine (<i>Clonidine</i>)	Tab. 0,000075, 0,00015, amp. 0,01 % sol. 1 ml.
2.	Bisoprolol (<i>Bisoprolol</i>) syn.: Concor	Tab. 0,005, 0,01
3.	Nifedipine (<i>Nifedipinum</i>) syn.: Fenigidin	Tab. 0,01 and 0,02
4.	Amlodipine (<i>Amlodipin</i>) syn.: Norvasc	Tab. 0,005, 0,01
5.	Dibazol (<i>Dibazolium</i>) syn.: Bendazol	Tab. 0,004 and 0,02, amp. 0,5 and 1 % sol. 1, 2, 5 ml.
6.	Nospanum (<i>Nospanum</i>) syn.: drotaverine	Tab. 0,04, amp. 2 % sol. 2 ml.
7.	Papaverini hydrochloridum (<i>Papaverini hydrochloridum</i>)	Tab. on 0,04; amp. 2 % sol. 2 ml.; rectal suppositories 0,02
8.	Magnesii sulfas (<i>Magnesii sulfas</i>)	Amp. 20 % sol. 5 ml., 25 % sol. 10 and 20 ml.
9.	Xantinoli nicotinas (<i>Xantinoli nicotinas</i>)	Tab. 0,15, amp. 15 % sol. 2 and 10 ml.
10.	Captopril (<i>Captoprilum</i>)	Tab. 0,025, 0,05, 0,1
11.	Enalapril (<i>Enalaprilum</i>)	Tab. 0,005, 0,01, 0,02
12.	Fosinopril (<i>Fosinopril</i>) syn.: Monopril	Tab. 0,01, 0,02
13.	Losartan (<i>Losartanum</i>)	Tab. 0,05

Tasks for self-control. Choose the correct answers.

- Which hypotensive drug is characterized by analgesic, hypothermic, sedative, nootropic, M – anticholinergic effects?
 - Captopril
 - Nifedipine
 - Dibazol
 - Metoprolol
 - Clonidine
- Note the effects typical to calcium channel blockers?
 - Spasmolytic effect
 - Uterotonic effects (increased uterine contractions)
 - Atherogenic effect
 - Nephroprotective, diuretic effect
 - Antiaggregant effect
- Choose a calcium channel blocker, causing reflex tachycardia
 - Verapamil
 - Nifedipine
 - Amlodipine
 - Cinnarizine
 - Nimodipine
- What adverse effects can occur during the use of ACE inhibitors?
 - Dry cough
 - Hypokalemia
 - Violations of renal function
 - Violations of vision
 - Violation of sexual function
- The aldosterone receptor antagonists unlike ACE inhibitors:
 - Reduce the hypertrophy of the left ventricle of the heart
 - Do not change the level of potassium in the blood
 - Affects the level of bradykinin, prostaglandins, prostacyclin in the blood
 - Diuretic effect, nephroprotective effect

E. Angioprotective action

II. Original practical work in class

1. To view the collection of drugs.
2. Work with the tests (Krok-1).
3. Prescribe and ground the choice of drug:
 - 1) for treatment of hypertensive crisis;
 - 2) for treatment of hypertonic disease with accompanying ischemic heart disease (IHD);
 - 3) calcium channel blocker prolonged action;
 - 4) for treatment of hypertension with accompanying pyelonephritis;
 - 5) hypotensive, causing orthostatic collapse;
 - 6) hypotensive, after which there is a burning sensation, redness of the face, extending on their own in 20 – 30 minutes;
 - 7) vasodilator that improves neuromuscular transmission;
 - 8) myotropic having immunostimulatory activity;
 - 9) hypotensive – antagonist of angiotensin – II receptors;
 - 10) in case of acute hypotension.
 - 11) short-acting ACE inhibitor;
 - 12) antihypertensive drug - a central α_2 -adrenomimetic;
 - 13) antihypertensive drug - trunkviizator;
 - 14) vasodilator mixed mechanism of action;
 - 15) antihypertensive drug, affecting synaptic transmission;
 - 16) the drug lisinopril replacement;
 - 17) the drug papaverine replacement;
 - 18) antihypertensive drug - a selective BPC;
 - 19) antihypertensive drug that causes orthostatic collapse;
 - 20) hypotensive drug that causes bradycardia.

**Unit 31. AGENTS THAT AFFECT BLOOD CIRCULATION AND
MICROCIRCULATION.**

Actuality of the unit. Nowadays cardiovascular pathology becomes «young» that leads to disability in persons of working age. Medications making better microcirculation, normalizing permeability of vessels, diminishing the edema of tissues and making better metabolic processes in the vessels walls found wide application at treatment of different angiopathy: diabetic (including retinopathy, nephropathy, defeats of cerebral and coronal vessels); violations of vessel's permeability at the rheumatic fever; atherosclerotic pathology of vessels etc. During the last decades in the treatment of coronary artery disease, hypertension and other cardiovascular diseases a group of hypolipidemic agents has been widely used. Primary prophylaxis with these drugs is accompanied by a decrease in the mortality rate, but it increases the deaths from non – cardiac diseases, including many serious adverse effects, affecting almost all systems and organs. Therefore, the appointment of hypolipidemic agents should be strictly determined by the type of hyperlipoproteinemia, clinical disease, efficacy and tolerability of the drug. The effectiveness of these drugs, their impact on the duration and the "quality" of life in patients suffering from atherosclerosis and other cardiovascular diseases, remains the subject of numerous clinical studies and scientific discussions. Thus, despite the rather large arsenal of angioprotectors (hypolipidemic, anti – aggregants, and others.), the problem of treatment of disorders bloodflow and peripheral microcirculation remains unresolved.

I. Individual work**Control questions****ANGIOPROTECTORS**

1. General characteristics. Reasons of infringements of peripheral blood circulation (atherosclerosis, diabetes mellitus etc.).

2. Classification:

1) *Hypolipidemic drugs*:

- *bile acid absorption inhibitors* — cholesterol absorption inhibitors (Cholestyramine, Colestipol);
- *bile acid and cholesterol absorption inhibitors* — Neomycin, Orlistat;
- *inhibitors of lipids synthesis* (cholesterol, triglycerides):
 - statins or inhibitors of hydroxymethyl – glutaric coenzyme A (HMG – CoA) reductase – (Lovastatin, Simvastatin, Fluvastatin);
 - fibrates — Fenofibrate, Bezafibrate, Gemfibrozil and others;
 - nicotinic acid /Niacin, Enduratsin/ and its derivatives (Ksantinola nicotinate);
 - different — biguanides, Probucol;
- *drugs that promote catabolism and excretion of sterols* — unsaturated fatty acids drugs (Linetol, Lipostabil, Omacor, Omega – 3 and others.), Essentiale, lipoic acid, plant origin (Polisponin, garlic preparations), and others.

2) **Hyperalphalipoproteinemic** drugs — Diphenin, bioflavonoids.

3) Drugs **stabilizing atherogenic lipoproteins** — Heparin, Chonsuridum, Chondroitin sulfate.

4) **Platelet aggregation inhibitors**:

- *inhibit the synthesis of thromboxane A₂*: COX inhibitors (Acetylsalicylic acid, Aspirin – cardio); thromboxane inhibitors (Dazoxiben);
- *blockers of receptors on platelets*: Ticlopidine, Clopidogrel; platelet – activating factor – PAF (Ketotifen, Ginkgo biloba); Serotonin (Ketanserin); glycoprotein of IIb / IIIa type (Reopro, Lamifiban, Tirofiban, Ksemilofiban et al.);
- *adenosinergic and phosphodiesterase inhibitors*: Dipyridamole, Pentoxifylline;
- *drugs that increase activity of prostacyclin system*: Epoprostenol.

5) **Antioxidants**:

- *direct acting*: fat – soluble — Tocopherol acetate, Aevitum, Ubiquinone, Dibunol; water – soluble – Ascorbic acid, bioflavonoids (Rutin, Quercetin); thiol – glutathione, Cystamine, Lipamid, lipoic acid, etc.;
- *indirect acting*: glutathione precursors (Glutamic acid, Complamin) inducers of peroxidases (sodium selenite), etc.;

6) **Endothelia-tropic** drugs:

- *drugs that decrease activity of bradykinin* — Parmidin /Anginin, Prodektina, Veranterol/;
- *antigialuronidase agents* — Etamzilat /Dicynonum/, calcium dobesilate, Troxerutin /Troksevazin, Venoruton/;
- *plant origin* — extracts of fruits horse chestnut (Escin, Aescusan), ginkgo biloba leaves (Ginkgo biloba /Tanakan/), etc.

7) **Calcium channel blockers** — Nifedipine, Aml.odipine, etc.

3. General characteristics of drugs. Mechanisms of action, side effects. Indications and contraindications for usage.

COMPLEX THERAPY OF INFRINGEMENTS OF CEREBRAL BLOOD FLOW.

Etiopathogenesis. Classification of preparations:

- *myotropic* (spasmolytics) — preparations of dyes (Vinpocetine /Cavinton/, Vincamine), xanthine derivatives (Theophylline, Aminophylline, Instenone, Pentoxifylline (Trental), isoquinoline derivatives (Papaverine, Drotaverine /No – spa/, Dibasole, Nicotinic acid and it's derivatives (Xanthinol nicotinate, Nicospan etc.);
- *alpha – adrenoblockers* — Nycergolyn /Sernyon/, Dihydroergotamine, Dihydroergotoxine etc.;
- *calcium channel blockers* — Nimodipine, Cinnarizine, Flunarizine;
- *antagonists of serotonin* — Methysergide, Peritol, Pyzotiphen /Sandomygran/ etc.;

- *drugs that improve metabolic processes* — nootropes (Aminalon, Piracetam, Pycamilon), albumin hydrolysates (Cerebrolysin, Aktovegyn, Solcoseryl) etc.;
- *anti – thrombotic* drugs – anti – aggregates (acetylsalicylic acid), anticoagulants (Heparin, Fraxyparin), fibrinolytics (Streptolyase, Actelyse); and *fibrinolysis inhibitors* (Aminocaproic acid).
General description of separate groups. Mechanisms of action. Undesirable effects. Indications and contraindications to application.

PREPARATIONS APPLIED FOR THE PHARMACOTHERAPY OF MIGRAINE:

Etiopathogenic factors. Classification of drugs:

– *for a treatment of migraine attacks:*

- specific (anti – migraine) action: alpha – adrenoblockers (ergotamine, dihydroergotamine) and 5 – HT₁ receptor agonists (Sumatriptan, Zolmitriptan etc.);
- unspecific (analgesic) action: NSAID (Paracetamol, Acetylsalicylic acid, Naproxen, Indomethacin), anti – emetics (dopaminolytics – Metoclopramide etc.);

– *for prophylaxis of migraine:* beta – adrenoblockers (Propranolol), anticonvulsants (Carbamazepine, Valproic acid derivatives), calcium channel blockers (Cinnarizine, Nimodipine), antidepressants, 5 – HT₂ receptor antagonists (Methysergide, Pizotiphen, Peritol etc.), NSAID, Caffeine, Clonidine, Magnesium sulfate etc.

Mechanisms of action. Undesirable effects.

DRUGS APPLIED AT DISTURBANCE OF PERIPHERAL BLOOD FLOW. General

characteristics. Classification of drugs:

1. *α-adrenoblockers* — Tropafene, Pyroxene etc.
2. *miotropic* — (phosphodiesterase inhibitors and adenosine receptors blockers): xanthine derivatives (Aminophylline, Instenone, Pentoxifylline /Trental/, Xanthinol nicotinate), isoquinoline derivatives (Papaverine, Drotaverine /No – spa/, benzofuran derivatives (Phencyclerban), imidazole derivatives (Dibasole), drugs of vegetable and animal origin (Andekalyn etc.).
3. *angioprotectors* — hypocholesterinemic, endotheliotropic etc.

Concept about VEINOTONIC DRUGS: endotheliotropic, drugs and other ergot alkaloids.

Indications and contra – indications.

The concept venotonics: endothelium-tropic, ergot alkaloids and other drugs.

- preparations containing horse chestnut: escin (aestsin, Veni-tang, Reparil) Aescusan;
- preparations containing biflavonoid diosmin: dposmin (diovenor);
- preparations containing Rutoside (semi-synthetic derivative of rutin): troxerutin (venoruton, rutinoven, rue, troksevazin);
- preparations containing glyukofuranozid: tribenzid (glivenol), proctitis-glivenol;
- combined means: Anavenol (esculin, digidroar-gokristin, Rutoside); detraleks (diosmin, hesperidin), indovazin (troxerutin, indomethacin), etc.

Indications and contraindications. Pharmacological safeness and interchangeability of medicines.

List of practical works. Prescribe drugs with their application (*separately from the prescription!*):

№	Name of the drug	Drug form
1.	Fenofibrate (<i>Phenofibrate</i>)	Caps. 0,1
2.	Lovastatin (<i>Lovastatinum</i>)	Tab. 0,1; 0,2; 0,4
3.	Cinnarizine (<i>Cinnarizine</i>) syn.: Stugeron	Tab. 0,025; caps. 0,075
4.	Nimodipine (<i>Nimodipine</i>)	Tab. 0,03; Bot. 0,02 % sol.
5.	Cavinton (<i>Cavinton</i>) syn.: Vinpocetine	Tab. 0,005; amp. 0,5 % 2 ml.

6.	Sumatriptan (<i>Sumatriptan</i>) syn.: Imigran	Tab. 0,05; 0,1
7.	Dihydroergotamine (<i>Dihydroergotaminum</i>)	Tab. 0,0025; amp. 0,1 % sol. 1 ml.
8.	Troxevasin (<i>Troxevasin</i>) syn.: Troxerutin, Venoruton	Caps. 0,3, amp. 10 % sol. 3 ml.
9.	Pentoxifylline (<i>Pentoxifylline</i>) syn.: Trental	Tab. 0,1; amp. 2 % 5 ml.

Tasks for self-control. Choose the correct answers.

1. Choose hypolipidemic drug after application of which may occur undesirable effects such as myopathy, rhabdomyolysis, hepatitis, vasculitis, hemolytic anemia, alopecia, and others.

- A. Fenofibrate
- B. Lovastatin
- C. Niacin
- D. Cholestiramin
- E. Linoleamid

2. Select hypolipidemic drugs without resorptive action.

- A. Lovastatin
- B. Niacin
- C. Cholestiramin
- D. Fenofibrate
- E. Probukol

3. In rehabilitation after craniocerebral trauma was prescribed drug, improves cognitive function. What is a drug?

- A. Cinnarizine
- B. Nootropil
- C. Xsantinola nicotinate
- D. Cavinton
- E. Cerebrolysin

4. Choose anti – aggregant that has anti – anginal activity:

- A. Tanakan
- B. Aspirin
- C. Dipyridamole
- D. Clopidogrel
- E. Reopro

5. Choose endotheliotropic plant – origin drug that has anti – aggregatory action:

- A. Parmidin
- B. Pentoxifylline
- C. Aescusan
- D. Tanakan
- E. Etamsylate

II. Original practical work in class

1. To view the collection of drugs.

2. Work with the tests (Krok-1).

3. Prescribe and ground the choice of drug:

- 1) calcium channels blocker in a post – stroke period;
- 2) *Vinca rosecea* drug in atherosclerotic changes in cerebral vessels;
- 3) after a cranial – cerebral trauma;
- 4) anti – atherosclerotic, undesirable effects of which are allergic reactions, muscles pain, muscles weakness, cholestatic hepatitis etc.;
- 5) competitive inhibitor of HMG – CoA – reductase;
- 6) lipid-lowering drugs - an inhibitor of lipid synthesis;
- 7) giperalfalipoproteinemicheskie drug;

- 8) endotheliotropic means;
- 9) drug substitution of simvastatin;
- 10) replacement drug bezafibrate;
- 11) the drug from the group fibrates;
- 12) to relief of migraine.
- 13) tserebrovazotropny bpc;
- 14) preparation of specific antimigraine action;
- 15) α -adrenoblocker at peripheral vascular spasm;
- 16) venotonic;
- 17) for preventing migraine;
- 18) myotropic drud - xanthine derivative;
- 19) nootropic drug in the treatment of disorders of cerebral circulation;
- 20) antispasmodic - isoquinoline derivative;
- 21) antimigraine drug;
- 22) an anticonvulsant for the prevention of migraine attacks.
- 23) a drug for the complex treatment of varicose veins that stabilize hyaluronic acid with a p – vitamin activity.

***Unit 32. CHECKING OF PRACTICAL SKILLS ON “DRUGS ACTING ON
CARDIOVASCULAR SYSTEM”***

CONTENT MODULE V. DRUGS THAT AFFECT METABOLISM, BLOOD SYSTEM AND IMMUNE PROCESSES

Actuality of the unit. This section discusses preparations of hormones, vitamins, amino acids and other biologically active substances that have both positive and adverse metabolic effects on the human body, which the doctor of any specialty should know.

The training objectives. *To know:* main types of hormone and of a vitamin therapy; pharmacology of hormones, vitamin and enzyme preparations and their synthetic substitutes and antagonists. *To be able:* to write and justify the choice of drugs this chapter in different pharmaceutical forms to solve the test tasks, situational and pharmacological challenges.

Intersubject integration. Normal and pathological physiology, histology, biochemistry.

Unit 33. HORMONAL PREPARATIONS OF POLYPEPTIDE, THEIR SYNTHETIC ANALOGS AND ANTAGONISTS.

Actuality of the unit. Hormones are incretory substances of endocrine glands. They control the growth and development processes of organism, reproductive processes, model the defense reactions by influencing the metabolism. They are highly biologically active and specifically active. Hormonal preparations are widely used not only in clinical endocrinology but also in other fields of medicine (replacement, stimulating and non – specific therapy). Hormonal preparations together with antihormonal drugs can be used for suppression of endocrine glands function.

I. Individual work

Control questions

1. Principles of neuro-humoral regulation. The concept of liberins (releasing factor) and statins (inhibitory factor).

2. General mechanisms of biological effects of hormonal substances. Creation of synthetic analogues of hormones, their advantages and disadvantages. Concept about hormonal and anti-hormonal preparations.

3. Types of hormonotherapy – *substitution, stimulating, inhibitory, pharmacodynamics* (not specific).

4. Classification of HORMONAL PREPARATIONS according chemical structure:

- 1) substances of *protein* and *peptide* structure — preparations of hormones of hypothalamus, hypophysis (pituitary), epiphysis, parathyroid and pancreas, calcitonin;
- 2) derivatives of *aminoacids* — preparations of thyroid gland, adrenal medulla;
- 3) *steroids* — preparations of adrenal cortex and sexual glands, prostaglandins.

5. Preparations and analogues of hormones of HYPOTHALAMUS:

- 1) *Secretion stimulators*:
 - somatotropin releasing – hormone — Sermorelin, Somatoliberin;
 - corticotropin releasing hormone — CRH;
 - thyrotropin releasing hormone — Protirelin /Rifatiroin/;
 - gonadotropin releasing hormone — Gonadotropin, Leuprolide, Nafarelin, Buserelin and others.
- 2) *Inhibitors of hormone secretion*: somatotropin inhibiting hormone — Somatostatin, Octreotide, Lanreotide; different — Danazol, Bromocriptine.

Pharmacological properties. Application.

6. Preparations and analogues of ANTERIOR PITUITARY:

- somatotropin (growth hormone),
- adrenocorticotropic (Corticotropin, Tetrakozactid, Sinakten – depo),

- thyrotrophic (thyrotropin),
- gonadotropin: follicle – stimulating hormone (FSH, urofollitropin, follitropin alpha and beta) and luteinizing hormone (LH, human menopausal gonadotropin / menotropin /), similar to the luteinizing from the placenta (human chorionic gonadotropin), prolactin (prolactin).

Pharmacodynamics. Application. Undesirable effects.

7. Preparation of hormones of INTERMEDIATE PITUITARY (melanotropic) — Intermedin. Pharmacological properties. Application.

8. Preparations of POSTERIOR PITUITARY HORMONES — Oxytocin, Vasopressin (Desmopressin, Terlipressin) and containing both hormones – Pituitrinum. Pharmacological properties. Application.

9. Preparations of EPIPHYSIS hormones — Melatonin. Pharmacological properties. Application.

10. Preparations of THYROID hormones:

1) Levothyroxine, triiodothyronine hydrochloride (Triiodothyronine), thyroidin and combination drugs (Thyreocombum, tireotom). Pharmacodynamics. Application. Undesirable effects.

2) Calcitonin (Calcitonin, Calcitriol, Miakaltsik). Participation in calcium and phosphorus metabolism. Indications for use. Adverse effects.

Anti – thyroid preparations – Thioamide (Mercazolil, Propylthiouracil), preparations of iodine, radioactive iodine. Mechanisms of action. Undesirable effects. Applications.

11. Preparations of PARATHYROID HORMONES — parathyroid hormone (Parathyroidin, Teriparatide). Pharmacodynamics. Indications.

12. Preparations of PANCREATIC hormones:

1) Glucagon, Somatostatin. Pharmacological effects. Application.

2) INSULIN. A structure. Classification **by origin**:

a) animal origin — porc, bovine: badly/intermediately/highly purified;

b) human (HM), obtained by: a semi – synthetic; genetic engineering (recombinant insulin analogues).

Substances added to insulin drugs that improve their properties (prolongation of action, crystallization etc.).

Classification of insulin preparations by **duration of action**:

I. *Short – acting*:

1) ultra – short (analog corresponds to the human, the action in 5 – 10 min, peak – 2 hours, duration – 3 – 4 hours; introduced before eating for 5 – 10 minutes or after a meal): semi – synthetic analog of human insulin (insulin lispro) – Humalog; insulin glulisine – Epaidra; insulin aspart – NovoRapid Penfill, NovoRapid flekspen;

2) short (regular/soluble, the action in 15 – 30 minutes, peak – 2 hours, duration – 5 – 8 hours; administered 30 – 40 minutes before a meal):

- human genetic engineering — Actrapid HM, Humulin regular, Biosulin P, ginsulin P, P insuman;
- human semisynthetic — Biosulin P, Humodar P;
- pork monocomponent — Aktrapid MC, Monodar, Monosuinsulin MK.

II. *Long – acting* (basal) insulin:

1) the average duration (action 2 – 4 h, peak – 6 – 8 hours, duration – 12 – 14 hours, the usual dose – 24 U / day in 2 admission): *insulin zinc suspension amorphous* — Monotard MC; *protamine – insulin (isophane insulin)*:

- human genetic engineering — Insuman base, Protafan HM, Monotard HM, Humulin H, Biosulin H, H gansulin;
- human semisynthetic — Biogulin H, Humodar B.
- pork monocomponent — Protafan MC.

2) long (action 4 – 5 h, peak – over 8 – 12 hours, duration – 24 – 36 h): *zinc – insulin crystal suspensions*: Ultralente MC Ultratard HM, Humulin ultralente, Semilente MC; *insulin analogues*: insulin glargine – Lantus, insulin detemir – Levemir Penfill etc.

III. *Combined* (biphasic; a mixture of short and prolonged insulin; introducing the morning, in the evening in 30 minutes before a meal):

- human genetic engineering — Insulin 30P, Mixtard 30 HM, Humulin M30;
- human semisynthetic — Biogulin 70/30, Humalog Mix 25, Humodar K25;
- biphasic insulin aspart — Novomix 30 Penfill, Novomix 30, Flekspen.

Modern drug forms and delivery systems.

Pharmacological effects. The indications, principles of prescription and dosage calculation. Complications of insulin therapy. Preventive measures, treatment of hypo and hyperglycemia.

13. SYNTHETIC ANTIDIABETIC drugs. Classification:

- *derivatives of sulphonylureas*: 1 – st generation – Butamide, Bucarban; 2nd generation – Chlorpropamide, Glibenclamide /Maninil/, Glicvidon, Gliclazide); 3 – rd generations – Glimepiride /Amaryl/;
- *biguanides*: Buformin /Glibutide/, Metformin;
- *antidiabetic drugs of various chemical groups*: thiazolidones – Rosiglitazone, Pioglitazone; Acarbose /Glucobay/, Gliphazine, combined "Arphazetin").

Distinctions in mechanisms of action. The indications and contra – indications to prescription.

List of practical works. Prescribe drugs with their application (*separately from the prescription!*):

№	Name of the drug	Drug form
1.	Corticotropin (<i>Corticotropinum</i>)	Vials 10 – 20 – 30 – 40 U
2.	Octreotide (<i>Corticotropinum</i>), syn.: Sandostatin	Amp. 1 ml. (1 ml. – 0,0001 and 0,0005)
3.	Pituitrin (<i>Pituitrinum</i>)	Amp. 1 ml. (1 ml. – 5 U).
4.	Desmopressin (<i>Desmopressinum</i>) syn.: Diprivan	Vials 1 ml. (1 ml. – 0,0001) for nasal application
5.	Oxytocin (<i>Oxytocinum</i>)	Amp. 1 and 2 ml. (5 and 10 U)
6.	Levothyroxine (<i>Levothyroxinum sodium</i>)	Tab. 0,000025; 0,00005 and 0,0001
7.	Potassium iodide (<i>Kalii iodidum</i>)	Tab. 0,04; 0,125; 0,25 and 0,5; vials 3 % sol 200 ml.
8.	Merkazolil (<i>Mercazolilum</i>)	Tab. 0,005
9.	Calcitrin (<i>Calcitrium</i>)	Vials 10 and 15 IU
10.	Actrapid HM (<i>Aktrapid HM</i>)	Vials 10 ml. (1 ml. – 40 and 100 IU)
11.	Protaphan HM (<i>Protaphan Insulinum NM</i>)	Vials 3 ml. (1 ml. — 100 U)
12.	Glibenclamide (<i>Glibenclamide</i>) syn.: Maninil	Tab. 0,005
13.	Glimepiride (<i>Glimepiridum</i>) syn.: Amaryl	Tab. 0,001; 0,002; 0,003; 0,004; 0,006
14.	Metformin (<i>Metforminum</i>)	Tab. 0,25

Tasks for self-control. Choose the correct answers.

1. Physician appointed replacement therapy to patients with hypothyroidism. Select preparation which is suitable in this case:

- A. Levothyroxine
- B. Parathyroidin
- C. Propylthiouracil
- D. Merkazolil
- E. Calcitriol

2. The patient with diabetes mellitus was appointed insulin. What is the main mechanism of insulin action?

- A. Inhibition of amino acid transport
- B. Inhibition of gluconeogenesis
- C. Activation of glucose transport into the cell
- D. Activation of triglyceride synthesis
- E. Inhibition of glycogen synthesis

3. Women in childbirth with weakness of labor activity was introduced drug Pituitrin. Choose hormones which are inside of Pituitrin:

- A. Vasopressin and Progesterone

- B. Oxytocin and Estradiol
- C. Oxytocin and Progesterone
- D. Vasopressin and Estradiol
- E. Oxytocin and Vasopressin

4. Choose indications for use of calcitonin:

- A. Osteoporosis
- B. Myxedema (hypothyroidism)
- C. Vascular calcification
- D. Tetany
- E. Hypercalcemia

5. Endocrinologist appointed glibenclamide to patients with diabetes mellitus. Choose mechanism of action of this agent:

- A. Inhibits gluconeogenesis
- B. Stimulates insulin secretion from the beta cells of Langerhans islets
- C. Enhances glucose metabolism
- D. Enhances glucose uptake by peripheral tissues
- E. Enables the transport of glucose into the cell

II. Original practical work in class

1. To view the collection of drugs.
2. Work with the tests (Krok-1).
3. Prescribe and ground the choice of drug:
 - 1) for preoperational preparation of the patients thyrotoxicosis;
 - 2) thioamide for the treatment of hyperthyroidism;
 - 3) for treatment of thyrotoxicosis;
 - 4) for stimulation of parturitional activity;
 - 5) for treatment of diabetes insipidus;
 - 6) inhibitor of somatotropin secretion for treatment of acute pancreatitis;
 - 7) for treatment of insulin dependant diabetes with 150 g of sugar in daily urine;
 - 8) for diabetic coma (hyperglycemic);
 - 9) at overdosage of insulin;
 - 10) from group of synthetic hypoglycemic drugs, to which undesirable effects are the allergic reactions, disturbances of bone marrow, hepatotoxicity, development of secondary resistance etc;
 - 11) for treatment of non – insulin dependant diabetes mellitus during ineffective production of sulfonylureas;
 - 12) for treatment of osteoporosis.
 - 13) a drug that stimulates the secretion of insulin β -cells of the islets of Langerhans;
 - 14) short-acting insulin.

Unit 34. HORMONAL PREPARATIONS OF STEROID STRUCTURE AND THEIR SYNTHETIC SUBSTITUTES. MINERALOCORTICOIDS AND GLUCOCORTICOIDS. PECULIARITIES OF USAGE.

Actuality of the unit. Steroid hormone preparations and anti – hormonal drugs are widely used in medicine for the specific therapy (treatment of diseases arising from a deficiency or excess of certain hormones), and as an agents of non – specific medication to treat non – endocrine pathology. Moreover, the development of modern contraceptives is one of the important directions of pharmacology and medicine. However, oral contraceptives are not safe drugs. Their appointment must be strictly reasonable and based on clinical and laboratory studies of hormonal background of women. Anabolic agents also play an important role in metabolic pharmacology and therapeutic practice. However, anabolic of steroid structure agents have many unwanted effects in the case of irrational use.

I. Individual work

Control questions

1. Hormones of adrenal cortex. Biological role.
2. Preparations of MINERALOCORTICOIDS (Aldosterone, Desoxycorticosterone) — Desoxycorticosterone acetate (DOCSA) and Trimethyl acetate, Fludrocortisone acetate. Pharmacological effects. Indications and contraindications for use.
3. Preparations of GLUCOCORTICOIDS — Cortisone acetate, Hydrocortisone acetate, Hemisuccinate and its synthetic analogs (Prednisolone, Prednisone, Dexamethasone, Triamcinolone). Characteristics. Indications and contraindications for use. Principles of pharmacotherapy with glucocorticoids, prophylaxis of complications.
4. Inhibitors of synthesis and agonists of adrenocorticoids — mineralocorticoids (Spironolactone), glucocorticoids (Mitotane, Amphenone B, Metyrapone, Ketoconazole). Usage.

List of practical works. Prescribe drugs with their application (*separately from the prescription!*):

№	Name of the drug	Drug form
1.	Desoxycorticosterone acetate (<i>Desoxycorticosteroni acetas</i>) syn.: DOCSA	Amp. 0,5 % oil sol. 1 ml.; tab. 0,005 sublingual
2.	Prednisolone (<i>Prednisolonum</i>)	Tab. on 0,001, 0,005
3.	Prednisolone hemisuccinate (<i>Prednisoloni hemisuccinas</i>)	Amp. 0,025 powder, ampoules 3 % sol. on 1 ml.
4.	Hydrocortisone Acetate (<i>Hydrocortizoni acetas</i>)	Amp. 2,5 % suspension 2 ml.
5.	Triamcinolone (<i>Triamcinolonum</i>) syn.: Kenakort	Tab. 0,004
6.	Dexamethasone (<i>Dexamethazonum</i>)	Tab. 0,0005
7.	Beclometasone dipropionate (<i>Beclometasonum dipropionas</i>) syn.: Bekotid, Beklomet	Aerosols for inhalation, 50, 100, 200 micrograms / dose, the balloon for 200 doses
8.	Sinaflan (<i>Synaflanum</i>)	0,025 % ointment in tubes on 10 and 15 gms

Tasks for self-control. Choose the correct answers.

1. *Glucocorticoids have anti-inflammatory activity. This is due to the increase in their participation in the synthesis of specific proteins that inhibit the activity of phospholipase A2. What compound is released as a result of the action of this phospholipase and is a precursor of anti-inflammatory substances?*
 - A Arachidonic acid
 - B Diacylglycerol
 - C Phosphoinositol
 - D Phosphatidic acid
 - E Phosphocholine
2. *The patient took glucocorticoids for a long time. Discontinuation of the drug caused an exacerbation of the disease, a decrease in blood pressure, weakness. How can you explain it?*
 - A Hyperproduction of ACTH
 - B Increasing tolerance to the drug
 - C Sensitization
 - D Adrenal insufficiency
 - E Cumulation
3. *A patient with neurodermatitis has been taking prednisone for a long time. The examination revealed a high level of sugar in the blood. The side effect of this drug is related to the effect on which link of carbohydrate metabolism?*
 - A Activation of gluconeogenesis
 - B Activation of glycogenogenesis
 - C Activation of glucose absorption in the intestines

D Inhibition of glycogen synthesis

E Activation of insulin utilization

4. A patient suffering from allergic dermatitis went to the hospital. What drug should be prescribed for the purpose of anti-inflammatory and anti-allergic action?

A Retabolil

B Ethamid

C Oxytocin

D Insulin

E Prednisolone

5. After taking a hormonal agent for the treatment of arthritis, the patient developed hypokalemia and hypocalcemia. What medicine did the patient take?

A Retabolil

B Ethamid

C Oxytocin

D Insulin

E Prednisolone

II. Original practical work in class

1. To view the collection of drugs.

2. Work with the tests (Krok-1).

3. Prescribe and ground the choice of drug:

- 1) for treatment of collagenosis;
- 2) at allergic bronchospasm;
- 3) in case of Addison's disease;
- 4) for local treatment of allergic dermatitis;
- 5) for the topical treatment of allergic dermatitis;
- 6) hydrocortisone replacement drug;
- 7) Preparation of mineralocorticoids;
- 8) a hormonal preparation with ulcerogenic action;
- 9) hormone preparation for bronchial asthma in aerosol.

Unit 35. HORMONAL DRUGS OF STEROID STRUCTURE. PREPARATIONS OF MALE AND FEMALE SEX HORMONES.CONTRACEPTIVES.

Actuality of theme. Sex hormones are produced by the gonads — the ovaries, testicles and, in small amounts, the reticular zone of the adrenal cortex. The biological action of sex hormones consists in their participation in the formation of primary and secondary sexual characteristics, ensuring reproductive function, in the regulation of protein metabolism, etc. The function of the gonads is controlled by pituitary gonadotropins. Hormonal therapy is carried out in order to replace the insufficient production of hormones in endocrine glands and treat hypofunction, as well as in non-endocrine diseases to increase the body's resistance, in case of metabolic disorders, during infectious and allergic diseases, etc.

In addition, the development of modern means of contraception remains one of the topical areas of pharmacology and medicine. However, oral contraceptives are dangerous means. Their appointment should be strictly justified and based on clinical and laboratory studies of the woman's hormonal background. Anabolic agents are also important in metabolic pharmacology and therapeutic practice. However, anabolic agents of steroid structure have many undesirable effects, especially when they are used irrationally.

1. Preparations of FEMALE SEXUAL HORMONES and their synthetic analogs. Classification:

A) *Estrogens* (follicles hormones):

- steroid estrogens — Estrone (Folliculin), Estradiol, Estradiol benzoate and Dipropionate, Ethinyl estradiol, conjugated estrogens;
- non – steroid estrogens — Synestrol, Diethylstilbestrol propionate, Dimestrol, Sigitin etc.

B) *Gestagens, progestins or progestogens* (hormones of the corpus luteum) — Progesterone, Oxiprogesteron, Levonorgestrel, Norethisterone /Norkolut/, Pregnin, Atsetomepregenol, Allilestrenol.

C) *Combined* (estrogen – progestin, estrogen – progesterone – antiandrogen) — oral contraceptives, anti – climacterical (Climonorm, Pregestrol) etc.

Mechanism of action, side effects. Indications and contraindications for use.

6. Conception of hormonal contraception. Classification of *contraceptives* (see unit № 64).

General characteristic. Undesirable effects.

7. *Inhibitors and antagonists of estrogen* (Clomiphene, Tamoxifen) and *progesterone* (Mifepristone). Application.

8. Preparations of ANDROGEN HORMONES (androgens) and their synthetic analogs (Testosterone propionate, Methyltestosterone, Testoenatum). Mechanisms of action, side effects. Applications.

9. ANABOLIC STEROIDS. Classification:

- *steroid* — Retabolil, Fenobolin, Methandrostenolone, Metylandrostendiol and others.;
- *non – steroidal* — purine derivatives (Riboxinum /Iosine/), Pyrimidine derivatives (Potassium orotate, Pentoxyl, Methyluracil), the hydrolysis products of the nucleic acids (Sodium nukleinat).

Pharmacodynamics. Indications for. Adverse effects of anabolic steroid abuse in sport.

Contraindications.

10. *Androgen secretion inhibitors* — analogues of gonadoreleasing – hormone (Buserelin, Leuprolide), antiandrogenic preparations (Finasteride, Cyproterone, Flutamide). Applications.

List of practical works. Prescribe drugs with their application (*separately from the prescription!*):

1.	Estrone (<i>Oestronum</i>) syn.: Folliculin	Amp. 0,05 % and 0,1 % oil sol. 1 ml.
2.	Sinestrol (<i>Synoestrolum</i>) syn.: Estronal	Tab. 0,001; in ampoules 0,1 % and 2 % oil sol. 1 ml.
3.	Progesterone (<i>Progesteronum</i>) syn.: Lutein	Amp. 1 and 2,5 % oil sol. 1 ml.
4.	Rigevidon (<i>Rigevidon</i>)	Tab. patented.
5.	Testosterone propionate (<i>Testosteroni propionas</i>) syn.: androfort	Amp. 1 – 5 % oil sol. 1 ml.
6.	Retabolil (<i>Retabolilum</i>) syn.: Nandrolol	Amp. 5 % oil sol. 1 ml.

Tasks for self-control. Choose the correct answers.

1. A patient with rheumatoid arthritis has been taken a glucocorticosteroid agent for several weeks, then suddenly stop taking it. What complications can occur?

- A. Hyperglycemia
- B. Increased blood pressure
- C. Withdrawal syndrome
- D. Exacerbation of chronic infectious processes
- E. Ulceration gastric mucosa and duodenum

2. Patients had been taking corticosteroids for 2 weeks. A remission of the main disease developed, but he had the exacerbation of chronic tonsillitis. Why complication happened?

- A. Antiallergic
- B. Anti – inflammatory
- C. Antishock
- D. Immunosuppressive

E. Desintoxication

3. *The 37 years old patient was suffering from a tumor of the ovary. What agent administered in this case?*

- A. Estriol
- B. Progesterone
- C. Non – ovlon
- D. Methandrostenolone
- E. Synestrol

4. *The 45 years old patient with acute adrenal insufficiency was appointed a replacement therapy. Choose medication:*

- A. Mercazolil
- B. Adrenaline
- C. Retabolil
- D. Corticotropin
- E. Prednisolone

5. *Pregnant women, in anamnesis has a few cases of spontanousmiscarriage. What is the hormonal medication can be assigned to maintain pregnancy?*

- A. Progesterone
- B. Testosterone propionate
- C. Methandrostenolone
- D. Estrone
- E. Hydrocortisone

II. Original practical work in class

1. To view the collection of drugs.
2. Work with the tests (Krok-1).
3. Prescribe and ground the choice of drug:
 - 1) for treatment of a malignant tumour of prostate gland;
 - 2) for treatment of a malignant tumour of milk glands in 35 – year – old woman;
 - 3) oral contraceptive;
 - 4) an estrogen of steroid structure;
 - 5) preparation of male sex hormones;
 - 6) the anabolic steroid drug.
 - 7) in the period of reconvalence (recovery)
 - 8) for climacteric syndrome.

Unit 36. WATER-SOLUBLE VITAMINS. LIPID – SOLUBLE VITAMINS. ENZYME AND ANTI-ENZYME PREPARATIONS. AMINOACIDS DERIVATIVES

Actuality of the unit. Biosynthesis of vitamins occurs mainly outside the human body. Endogenous biosynthesis of some of them, carried out by intestinal microflora, is not always able to cover the needs of the body. Therefore, a person mainly receives vitamins from the outside with food. Although vitamins are not a plastic material and do not serve as a source of energy, they are absolutely necessary for all life processes and are biologically active even in small doses. Insufficient intake of certain vitamins in the body or violation of their assimilation leads to the development of pathological processes in the form of hypo- and avitaminosis. For the treatment of these processes, the specific action of the corresponding vitamins is used. In increased doses, vitamins are used for therapeutic purposes as powerful non-specific pharmacodynamic agents. In connection with the wide application in various pathologies, a doctor of any profile needs to know the pharmacology of vitamins for their rational and safe appointment.

Along with hormonal and vitamin preparations, many substances can influence and regulate the processes of metabolism. Some have antioxidant and antihypoxic effects, others normalize or activate

metabolic processes in cells, stimulate regeneration processes. Thus, enzyme preparations and their inhibitors are widely used in medical practice (for purulent-necrotic processes, thrombosis, thromboembolism, digestive disorders, oncological diseases, etc.). It is promising to develop a group of immobilized enzymes chemically and physically connected to the matrix of the carrier, which stabilizes the active substance and prolongs its effect. Enzyme preparations placed in liposomes are created, which are used for targeted entry into the cell. Amino acids also play an important role in modern pharmacology, some of which have found independent use as medicines (methionine, glycine, cerebrolysin, etc.). Mixtures of amino acids, as well as their combinations with micro- and macroelements, used as means for parenteral nutrition are of special importance

I. Individual work

Control questions

1. The role of vitamins in the tissue metabolism. Concept about vitamins.
2. Classification of the VITAMIN PREPARATIONS: water – and fatsoluble.
3. Types of vitamin supply disturbances and their causes: a) hypovitaminosis (endo – and exogene); b) hypervitaminosis.
4. Types of vitamin therapy: a) *replacement*; b) *adaptatory*; c) *pharmacodynamic*.
5. WATER – SOLUBLE VITAMINS *:
 - 1) *Thiamine (vitamin B₁)*** – thiamine chloride, thiamine bromide, cocarboxilase; vitamins — benfotiamine, and others. Pharmacodynamics. Undesirable effects. Application.
 - 2) *Riboflavin (vitamin B₂)*** – riboflavin, riboflavin mononucleotide. Pharmacodynamics. Indications and contra – indications.
 - 3) *Nicotinic acid (vitamin PP, B₃)*** – nicotinic acid, nicotinamide; combined preparations (Nikoverin, nikoshpan, pikamilon). Pharmacodynamics. Undesirable effects. Indications and contraindications. Nicotinic acid derivatives, synthesized at the department of general and clinical pharmacology ONMedU (Nicotines potassium and magnesium, Xantinole nicotinate, Lithonit).
 - 4) *Pyridoxine (vitamin B₆)*** – pyridoxine hydrochloride and combined preparations – Milgamma, Magne B₆ and others. Pharmacodynamics. Indications and contraindications.
 - 5) *Ascorbic acid (vitamin C)*. Pharmacodynamics and pharmacokinetics. Indications and contraindications. Combined drugs based on ascorbic acid ("Aspirin UPSA", "Aspro C forte", "Coldrex").
 - 6) *Bioflavonoids (Vitamin P)* – quercetin, rutin. The biological role. Indications for use.
 - 7) *Pantothenic acid (vitamin B₅)*** – calcium pantothenate, panthenol. The biological role. Indications for use.
 - 8) *Pangamic acid (vitamin B₁₅)* – pangamate calcium. The biological role. Indications for use.
 - 9) *Vitamin U (methylmethionine)* – metiosulfoniya chloride. The biological role. Indications for use.
 - 10) *Lipoic acid* – alpha – lipoic acid (thioctic acid, Valium). The biological role. Indications for use.

Pharmacology safety and the combined use of vitamins.
6. FAT – SOLUBLE VITAMINS *:
 - 1) Retinol (*vitamin A*) — Retinol acetate, Retinol palmitate, and others. Pharmacodynamics. Application. Hypo – and hypervitaminosis.
 - 2) Tocopherols (*vitamin E*) — Tocopherol acetate. The biological significance. Application.
 - 3) Calciferols (*vitamin D*). Drugs D₂ — Ergocalciferol, α – kaltsidol; D₃ — cholecalciferol; 25(OH)D₃ — Calcifediol; 1,25(OH)₂D₃ — Calcitriol (Osteotriol, Rokaltrol); Dihydrotestosterone. Pharmacodynamics. Application. Hypo – and hypervitaminosis.
7. The interaction of vitamins among themselves and with other drugs.
8. Polyvitamins (Neurorubin, Milgamma, Neurovitam, vitamins in complexes with enzymes (Vitrum, Aevitum, Undevit, Unicap, Oligovit etc.). Indications and contraindications.
9. Plants with high contents of vitamins (sea buckthorn, wild rose, cranberries, currants, etc.).

* Cyanocobalamin (vitamin B₁₂), folic acid (vitamin B_c, B₉) are discussed in unit № 31.

** Coenzyme-composing.

* Vitamin K (naphthoquinones) discussed in unit № 32.

10. Conception about avitaminosis.

DRUGS AFFECTING ON THE DIFFERENT METABOLIC PROCESSES:

- *improve energy supply* — Glucose, Trimetazidine, ATP, Riboxinum and others.;
- *amino acids drugs* — Glutamic acid, Methionine, Cerebrolysin, Cysteine and others.;
- *containing bee poison, snakes, their metabolic products* — Apilak, Propolis, Apizartron, Viprosal and others.;
- *biogenic stimulators* — Carnitine, Aloe, etc.;
- *cytoprotectors and improvers of tissue regeneration* — Actovegin, Solkoseril and others.;
- *antioxidants and antihypoxants* — Emoxipin, Tocopherol, etc.

General characteristics. Therapeutic indications.

3. ENZYME PREPARATIONS. Classification:

- 1) Drugs that primary use in *purulent – necrotic processes* — Trypsin, Chymotrypsin, Chymopsin, Terrilytin, Desoxyribonuclease, Collagenase, Prophezym etc.;
- 2) Drugs for improvement of *digestive processes* — Pepsin, natural gastric juice, Abominum, Oraza, Pancreatin, Panzynom, Festal Mezym – forte etc.;
- 3) *Fibrinolytic agents* — Fibrinolysin, Streptokinase, Streptodecase, Urokinase, Alteplase etc.;
- 4) *different preparations* — Lydase, Cytochrome C, Penicillinase, Asparaginase etc.

General characteristics of the products. Indications and contraindications. Undesirable effects.

4. ENZYME INHIBITORS. Classification

- 1) Proteinases and fibrinolysis inhibitors — Aprotinin (Contrycal, Gordoks), Aminocaproic acid;
- 2) Anticholinesterases — Proserinum, Physostigmine, Galanthamine;
- 3) MAO inhibitors — Nialamide;
- 4) Carbonic anhydrase inhibitors — Diacarb (Acetazolamide);
- 5) Xanthinoxidase inhibitors — Allopurinol;
- 6) Acetaldehyde dehydrogenase inhibitors — Disulfiram (Teturamum).

General characteristics. Application.

Pharmacology safety and the combined use of drugs.

List of practical works. Prescribe drugs with their application (*separately from the prescription!*):

№	Name of the drug	Drug form
1.	Thiamine chloride (<i>Thiamini chloridum</i>) syn.: aneurine	Tab. 0,002, 0,005 and 0,01; amp. 2,5 and 5 % sol. 1 ml.
2.	Coccarboxylase hydrochloride (<i>Coccarboxylasi hydrochloridum</i>)	Amp. 0,05 of lyophilized powder
3.	Riboflavin mononucleotide (<i>Riboflavinum – mononucleotidum</i>)	Amp. 1 % sol. 1 ml.
4.	Pyridoxine hydrochloride (<i>Pyridoxini hydrochloridum</i>)	Tab. 0,005 and 0,01; amp. 1% and 5 % sol. 1 ml.
5.	Nicotinic acid (<i>Acidum nicotinicum</i>)	Tab. 0,05; in amp. 1 % sol. 1 ml.
6.	Ascorbic acid (<i>Acidum ascorbinicum</i>)	Tab., powder 0,05 and 0,1; amp. 5% and 10% sol. 1 ml.
7.	Ascorutin (<i>Ascorutinum</i>)	Patented tab.
8.	Panthenol (<i>Panthenol</i>) syn.: Dexpanthenol	Aerosol 140 g
9.	Tocopherol acetate (<i>Tocopheroli acetas</i>)	Amp. 5 %, 10 %, 30 % oil sol.s 1 ml.; vials. 5, 10 and 30% sol.s 10, 20, 25 and 50 ml.
10.	Retinol acetate (<i>Retinoli acetas</i>)	Bot. 3.44% (100000 units in 1 ml.) oil sol., 10 ml.
11.	Ergocalciferol (<i>Ergocalciferolum</i>)	Bot. 0,125 % oil sol. or 0,5 % spirit sol. 10 ml.; dragee 500 IE; caps. 500 and 1000 IE
12.	Vitrum (<i>Vitrum</i>)	Tab.patent

13.	Oleum Hippophae (<i>Oleum Hippophae</i>)	Bot. 100 ml.
14.	Trypsin crystalline (<i>Trypsinum crystallisatum</i>)	Amp. and vials containing 0,005 and 0,01
15.	Teraflex (<i>Theraflex</i>)	Caps. patented.
16.	Lidaza (<i>Lydasum</i>)	Vials 64 units a lyophilized powder
17.	Pancreatin (<i>Pancreatin</i>)	Tab.patent
18.	Methionine (<i>Methioninum</i>)	Tab. 0.25

Tasks for self-control. Choose the correct answers.

1. Which vitamin preparation should be assigned to patients with chronic alcoholism, with symptoms of polyneuritis and heart failure?

- A. Filoquinon
- B. Ergocalciferol
- C. Retinol
- D. Routine
- E. Thiamine

2. What is **WRONG** about ascorbic acid:

- A. Increases vascular permeability
- B. Increases adaptability of the organism
- C. Enhances the synthesis of glucocorticoids
- D. Has detoxification action
- E. Increases the immune system

3. Choose which of these vitamins does not belong to the group B:

- A. Pyridoxine
- B. Ruthin
- C. Nicotinic acid
- D. Riboflavin
- E. Pangamic acid

4. In case of insufficiency of this vitamin pyruvic and lactic acids accumulate in the tissues, the content of acetylcholine is reduced, beriberi disease may develop. Determine this vitamin:

- A. Pyridoxine hydrochloride
- B. Ascorbic acid
- C. Thiamine chloride
- D. Nicotinic acid
- E. Riboflavin

5. A vitamin B₆ deficiency is found in the appointment of anti-TB drugs from the group of isonicotinic acid hydrazide. Choose mechanism of hypovitaminosis.

- A. It inhibits the absorption of vitamin in the GI tract
- B. Hydrazides destroy vitamin in the gut
- C. Hydrazides inhibit the synthesis of pyridoxal phosphate
- D. Hydrazides stimulate the synthesis of pyridoxal phosphate
- E. Hydrazides inhibit the decarboxylation of the vitamin in the liver

II. Original practical work in class

1. To view the collection of drugs.
2. Work with the tests (Krok-1).
3. Prescribe and ground the choice of drug:

- 1) at alcoholic polyneuritis;
- 2) at viral hepatitis;
- 3) at obliterated endoarteritis;
- 4) at hemeralopia;

- 5) for prophylaxis and in prodromal period of flu;
- 6) in gerontological practice;
- 7) for prophylaxis and treatment of atherosclerosis;
- 8) for treatment of metabolic acidosis;
- 9) for acceleration of wound healing of a burn.
- 10) insulin synergist;
- 11) vitamin preparation, possessing cardiogenic action;
- 12) when a spasm of cerebral vessels;
- 13) replacement drug of thiamine bromide.
- 14) in case of menorrhoea dysfunctions;
- 15) at myocardial dystrophy;
- 16) at hyperkeratosis;
- 17) for the treatment of rickets;
- 18) at ulcer disease of stomach;
- 19) at postoperative scars;
- 20) at chronic pancreatitis;
- 21) for increasing of appetite;
- 22) at pneumonia for expectoration of sputum;
- 23) at post – stroke period;
- 24) at chronic hepatitis.
- 25) amino acid preparation;
- 26) vitamin preparation combined with macro and micro elements;
- 27) an antioxidant;
- 28) the drug is contraindicated in acute pancreatitis;
- 29) the drug that causes "cheese syndrome".

Unit 37. DRUGS ACTING ON CALCIUM-PHOSPHORUS BALANCE.

Actuality of the unit. Actuality of theme. In recent years, there have been significant changes in the ideas about the physiology and pathology of calcium and phosphorus metabolism, and the arsenal of relevant medicines has significantly expanded. The formation of the concept of the hormonal nature of vitamin D and its metabolites should be considered among the most serious achievements, which allows us to consider them not only as "calcium-storing" endogenous regulators, but also in a much broader biological context. Successes in the study of such a common pathology as osteoporosis contributed to the creation of a new class of drugs (for example, bisphosphonates), the development of special dosage forms of estrogen and combined hormonal drugs for the prevention and treatment of osteoporosis in the postmenopausal period. The list of new targeted drugs includes fluoride drugs, new hormonal drugs, herbal drugs, improved bi-pharmaceutical forms of calcium drugs and their combinations with vitamin D.

I. Individual work

Control questions

Physiology and pathophysiology of calcium and phosphorus.

1. Drugs affecting CALCIUM AND PHOSPHORUS METABOLISM. Classification regulators of bone metabolism

⇒ *suppress the bone resorption:*

- sexual hormones;
- calcitonins — Calcitonin, Miakaltsik;
- active metabolites of vitamin D** — Calcitriol, α – caltsidol;

** Activate remodeling of physiologic structure of osseal tissues.

- bisphosphonates ** — Etidronate, Clodronate, Alendronate, Ibandronate;
- salts of calcium — Calcium chloride, Calcium carbonate and others.;
- ossein – hydroxyapatite (Osteogenon);

⇒ *increase bone mass:*

- fluorides — sodium fluoride (Ossein) and others.;
- active metabolites of vitamin D ** — Calcitriol, α – caltsidol;
- anabolic steroids — Methandienone, Nandrolone;
- fragments of human of parathyroid hormone ** — Teriparatide;
- growth hormone — Somatotropin.

⇒ *affect the metabolism of cartilage tissue (chondroprotectors):* Rumalon, Chondroitin, Glucosamine, Teraflex (Glucosamine + Chondroitin), Alflutop, Piaskledin and others.

There are 3 generations in the group of chondroprotectors:

- ⇒ Extracts from products of animal origin (including cartilage of fish and crustaceans): alflutop, rumalon, mucarthrin.
- ⇒ Monocomponent preparations:
- ⇒ - based on chondroitin sulfate: structum, mucosate, chondroksid;
- ⇒ - based on glucosamine: dona, elbona, stopartrosis.
- ⇒ Combined products, which include glucosamine, chondroitin sulfate and additional components, such as vitamins, non-steroidal anti-inflammatory drugs: teraflex, arthrogard, geladrink.

Classification according to the method of introduction:

1. for oral administration in the form of powders, capsules or tablets;
2. for injections of intramuscular or intra-articular solutions;
3. for external use - ointments.

Drugs of CALCIUM, FLUORINE, PHOSPHORUS and bisphosphonates. General characteristics. Therapeutic indications.

List of practical works. Prescribe drugs with their application (*separately from the prescription!*):

№	Name of the drug	Drug form
	Osteotriol (<i>Osteotriol</i>) syn.: Calcitriol	Caps. 0,00025 and 0,0005
1.	Alendronate sodium (<i>Alendronate sodium</i>)	Tab. 0,1
2.	Calcium chloride (<i>Calcii chloridum</i>)	Bot. 5 and 10 % sol.; amp. 2,5 % sol. 5 ml. and 10% solution 10 ml.
3.	Ergocalciferol (<i>Ergocalciferolum</i>)	500 IU dragees; capsicum 500 and 1000 MO each; fl. 0.0625, 0.125, 0.5% oil solution and 0.5% alcohol solution, 10 ml each
4.	Teraflex (<i>Theraflex</i>)	Капс. комбін.
5.	Dona (<i>Dona</i>)	Powder for preparing a solution for oral use in sachet No. 20, No. 30
6.	Struktum (<i>Structum</i>)	hard capsules 500 mg blister, No. 60

Tasks for self-control. Choose the correct answers.

1. What preparation is necessary to choose for the treatment of osteoarthritis?

- A. Actovegin
- B. Glucosamine
- C. Cerebrolysin
- D. Methionine
- E. Riboxin

2. For the night blindness doctor prescribed a water – soluble vitamin preparation. Choose this drug.

- A. Lipoic acid
- B. Retinol acetate
- C. Riboflavin
- D. Niacin

- E. Ergocalciferol
3. Which of the following drugs are suitable these 4 definitions: growth vitamin, anti – infective, epithelial, and vitamin against xerophthalmia?
- Ergocalciferol
 - Riboflavin
 - Retinol acetate
 - Tocopherol acetate
 - Vikasol
4. Patient with ischemic heart disease was appointed Tocopherol. What effect a doctor expected to get?
- Spasmolytic
 - Antiatherosclerosis
 - Increase the delivery of oxygen to the myocardium
 - Antioxidant
 - Negative inotropic
5. In a patient with myocardial infarction and coronary artery thrombosis. Which of the drugs used for thrombolysis?
- Streptokinase
 - Trypsin
 - Lidase
 - Pentoxifyllin
 - Acetylsalicylic acid

II. Original practical work in class

- To view the collection of drugs.
- Work with the tests (Krok-1).
- Prescribe and ground the choice of drug:
 - drug metabolite of vitamin D3 for osteoporosis in a postmenopause;
 - bisphosphonates for the treatment of deforming ostitis (Paget's disease);
 - in osteoarthritis to stimulate the regeneration of cartilage tissue;
 - the combined agent containing glucosamine and chondroitin.

DRUGS AFFECTING THE BLOOD SYSTEM

Classification of drugs that affect the blood system:

- affecting hematopoiesis:**
 - erythropoiesis — stimulants and suppressors;
 - leucopoiesis — stimulants and suppressors;
- influencing blood coagulation:**
 - antithrombotic — 1) antiagregants, 2) reducing coagulation (anticoagulants), 3) increase fibrinolysis (fibrinolytic);
 - hemostatic — 1) proagregants, 2) increase coagulation (procoagulants); 3) inhibitors of fibrinolysis;
- affecting the volume and composition of the blood** (blood – substituting and plasm – substitutes).

The training objectives. *To know:* pharmacology of drugs stimulating and depressing bone marrow, and blood clotting. *To be able to:* solve the test tasks, situational and pharmacological tasks, to prescribe and analyze recipes for preparations of this section.

Intersubject integration. Physiology, pathological physiology, biochemistry of the hematopoietic system and hemostasis.

Unit 38. DRUGS AFFECTING THE ERYTHROPOIESIS. BLOOD SUBSTITUTES.

Actuality of the unit. Modern pharmacotherapy of erythropoiesis disorders allows influence on diseases such as hypochromic anemia (normoblastic), hyperchromic anemia (megaloblastic), hemolytic and aplastic anemias. The problem of studying the drugs used for controlling dehydration and disorders of acid – base balance, is one of actual for modern intensive therapy. The requirement of these drugs is generally increasing, in connection with this new preparations are created.

I. Individual work

Control questions

1. Basic forms of pathology of blood composition and volume.
2. Classification of drugs affecting the **ERYTHROPOIESIS**:

A) Stimulators of erythropoiesis:

- in case of **hypochromic** (iron deficient) anemia — iron preparations;
- in case of **hyperchromic** (megaloblastic) anemia — Cyanocobalamin, Folic acid;
- in case of anemia of **different genesis** — preparations of hematopoietic growth factors: Erythropoietin (Epocomb, Recormon, Epomaks); granulocyte colony – stimulating factor (Filgrastim); granulocyte – macrophage colony stimulating factor (Sargramostim).

B) Suppressors of erythropoiesis — radioactive P.

3. Agents used in HYPOCHROMIC ANEMIA. Iron preparations. General characteristics.

Classification:

1) for peroral using:

- monocomponent: Ferronal (*Ferrous gluconate*), Actiferrin, Fero – gradumet (*Ferrous sulfate*), Ferrous lactate, Ferrous sulfate, Heferol (*Ferrous fumarate*), Hemofer (*Ferrous chloride*), Maltofer (*Ferrous hydroxide polymaltose complex*);
- combined: Tardiferon, Ferroplex, (+*ascorbic acid*), Ferrocal (+*cerebrolecithin + calcium fructosodiphosphate*), Haemostimulinum (+ *copper*), Maltoferfol (+ *folic acid*) etc.

2) for parenteral using: Ferbitol, Gectofer (*ferrosorbitol complex*), Fercoven, Ferrum Lek, (*Ferrous saccharate*), Coamide (+*cobalt*).

Pharmacokinetics, pharmacodynamics. Comparative characteristics. Indications for use. The dosage regimen. Undesirable effects. Poisoning by iron preparations and assistance measures (*Deferoxamine*).

4. Drugs, used in case of HYPERCHROMIC ANEMIA. General characteristics. Cyanocobalamin (Vitamin B₁₂) and its preparations — Cyanocobalamin, Hydroxycobalamin, Cobamamid (desoxyadenosilcobalamin) vitohepat. Folic acid (vitamin B_C, B₉, M). Pharmacokinetics, pharmacodynamics. Indications for use. Undesirable effects. Interaction with other drugs.

5. ERYTHROPOIETINS. General characteristics. Classification:

- *epoetin alfa* — Epocomb, Epocrin, Eprex;
- *epoetin beta* — Recormon, Eritrea;
- *epoetin omega* — Epomaks.

Pharmacodynamics. Application. Undesirable effects.

6. Phytotherapeutic agents and drugs of animal origin used in anemia.

7. Drugs that INHIBIT ERYTHROPOIESIS. Therapeutic indications.

8. **BLOOD – , PLASMA SUBSTITUTERS.** General characteristics. Classifications:

I. By composition:

- *protein structure*: from blood cells — red cell, platelet concentrate; from plasma — serum, antihemophilic plasma;
- *protein hydrolysates* — casein hydrolyzate, infuzamin, aminotrof, alvezin and others.; *amino acid sol.s* — polyamine, moriamin, freamin;
- *lipid emulsions* — intralipid, lipofundin;

- *colloid: animal origin* — gelatinol, plasmogel; *plant origin* — pectin; *synthetic* — dextrans (polyglukin, reopolyglucin) based on polyvinylpyrrolidone (neohemodes, polidez);
- *crystalloids: saline* — 0.9% sol. of sodium chloride, Ringer – Locke, potassium chloride, kvintasol, laktosol etc.; *buffers* — sodium bicarbonate, trisamin; *sugar sol.s and polyhydric alcohols* — glucose, fructose, sorbitol.

II. By functional properties and purpose:

- *hemodynamic* (antishock) — polyglucin, rondeks, reopolyglucin, gelatinol;
- *detoxification* — neogemodase, polides, reopolyglucin, gelatinol;
- *correctors of acid – base and water – salt balance* — saline, buffers;
- *for parenteral nutrition* — protein hydrolysates, amino acid sol.s, sugar, lipid emulsions;
- *drugs, performing the function of the oxygen transfer* — perftoran;
- *multifunctional* — Polifer (hemodynamic, hematopoietic) reoglyuman (hemodynamic, hematopoietic, detoxification, diuretic) poliglyusol, reosorbilakt (hemodynamics and acid – alkaline balance).

Requirements for blood substitutes. Indications and contra – indications. Undesirable effects.

9. **ACIDS AND ALKALIS:** local and resorptive effect. Acute poisoning, assistance measures.

10. The role of ions **SODIUM, POTASSIUM, MAGNESIUM*** in the regulation of body functions. Application of drugs in medical practice. Undesirable effects.

Pharmacology safety and the combined use of drugs.

List of practical works. Prescribe drugs with their application (*separately from the prescription!*):

№	Name of the drug	Drug form
1.	Ferropleks (<i>Ferroplex</i>)	Dragee patented
2.	Ferro – gradumet (<i>Ferro – Gradumet</i>)	Tab. 0,525
3.	Ferrum Lek (<i>Ferrum Lek</i>)	Amp. 2 and 5 ml.
4.	Ferbitol (<i>Ferbitolum</i>)	Amp. 2 ml.
5.	Coamid (<i>Coamidum</i>)	Amp. 1 % sol. 1 ml.
6.	Cyanocobalamin (<i>Cyanocobalaminum</i>)	Amp. 0,003, 0,01, 0,02, 0,05 % sol. 1 ml.
7.	Folic acid (<i>Acidum folicum</i>)	Tab. 0,001
8.	Poliglyukin (<i>Polyglucinum</i>)	Vial 400 ml.
9.	Lipofundin (<i>Lipofundinum</i>)	Amp. 100 and 500 ml.
10.	Neogemodez (<i>Neohaemodesum</i>)	Vial 100, 200, 400 ml.
11.	Glucose (<i>Glucosum</i>)	Vial 5, 10, 20, 40 % 200 and 400 ml.
12.	Sodium chloride (<i>Natrii chloridum</i>)	Isotonic (0,9%) and hypertonic sol.
13.	Sodium hydrocarbonate (<i>Natrii hydrocarbonas</i>)	Tab. 0,3 and 0,5; amp. 4 % sol. 20 ml.; supp. 0,3, 0,5 and 0,7.
14.	Potassium chloride (<i>Kalii chloridum</i>)	Tab. 0,5 and 1,0; 10 % sol.; amp. 4 % sol. 50 ml.

Tasks for self-control. Choose the correct answers.

1. A patient with hypochromic anemia receives ferronal. What substance improves the absorption of iron?

- Sodium bicarbonate
- Trypsin
- Festal
- Gastrocepin
- Ascorbic acid

2. A woman after childbirth started significant bleeding due to which developed anemia. What preparation should be assigned to the patient?

- Epomax

* Role of calcium, phosphorus and flour are discussed in unit № 30.

- B. Pentoxil
- C. Ferrum lek
- D. Cyanocobalamin
- E. Sargramostim

3. *Iron drugs in powder form for oral use are assigned in the capsule. Why is this done?*

- A. For prevention of vomiting
- B. In order to prevent constipation
- C. To eliminate the bitter taste of the drug
- D. To prevent interaction with hydrogen sulfide
- E. To eliminate the unpleasant odors of the drug

4. *Desintoxication blood fluid should:*

- A. Be metabolized and absorbed by the body
- B. Have a high molecular weight (30000 – 70000)
- C. Have a low molecular weight (6000 – 15000)
- D. Circulate for a long time in the blood
- E. Be free from organotoxicity

5. *Sodium chloride is the antidote to:*

- A. Magnesium sulphates
- B. Bromide
- C. Calcium chloride
- D. Cyanides
- E. Anticholinesterase agents

II. Original practical work in class

1. To view the collection of drugs.
2. Work with the tests (Krok-1).
3. Prescribe and ground the choice of drug:

- 1) for treatment of posthemorrhagic anemia;
- 2) preparations of Fe with ascorbic acid;
- 3) preparations of Fe in case of esophageal stricture;
- 4) for treatment of hypoplastic anemia, resistant for Fe preparations;
- 5) for treatment of malignant megaloblastic anemia (Addison – Biermer anemia);
- 6) in case of intoxication;
- 7) for parenteral nutrition in postoperative period;
- 8) isotonic sol. of glucose for I.V. injection;
- 9) blood substitute with long circulation in the body;
- 10) for correction of acid – base balance at a poisoning of salicylates;
- 11) at poisoning of magnesium sulphate.
- 12) monocomponent preparation of iron;
- 13) the drug replacement ferronal;
- 14) antishock liquid;
- 15) drug, what having detoxication and hemodynamic properties.

Unit 39. DRUGS AFFECTING THE LEUCOPOIESIS AND BLOOD COAGULATION. ANTI-CANCER AGENTS AND RADIOPROTECTORS.

Actuality of the unit. Drugs influencing leucopoiesis and blood coagulation take significant place in contemporary pharmacology. Deepening of knowledges about the reasons of leukopoietic disorder is determinating the new ways of these states complex therapy, particularly stimulators of leucopoiesis. During the last years the definite success in healing of bone marrow cancer is reached and as the result, the sufficient prolonging of the expected patient life duration has been reached. The knowledge of the preparations influencing on blood coagulation and fibrinolysis is necessary for every medician, as a

result of their use in case of sharp cardiovascular pathology (thrombosis, infarction of myocardium), in the postoperative period, injuries and others.

I. Individual work

Control questions

1. Agranulocytosis. Ethioopathogenesis. **LEUCOPOESIS STIMULATORS**. Classification:

- vitamin preparations — Pyridoxine, Folic acid;
- non – steroidal anabolic agent — Pentoxil, Methyluracilum, Sodium nucleinate;
- myeloid growth factors (colony stimulating factors) — Filgrastim (G – CSP, Neupogen), Sargramostim (GM – CSP), Molgramostim (Leucomax) et al.;
- others — Leucogen, Lithium carbonate.

Mechanism of action. Comparative characteristics and efficacy. Indications and contraindications for use.

2. **LEUCOPOESIS SUPPRESSORS** (anti – cancer). General characteristics. Classification:

1) *cytotoxic*:

- a) *alkylating agents* — Dopanum, Sarcylisine, Cyclophosphane, Myelosan, Cyclophosphamide;
- b) *antimetabolites* — analogs: folic acid (Methotrexate); purine (Mercaptopurine, Purine); pyrimidine (Fluorouracil, Ftorafur);
- c) *different synthetic substances* — Prospidin, Procarbazine, platinum drug (Cisplatin);
- d) *anticancer antibiotics* — actinomycetes (Dactinomycin); anthracyclines (Doxorubicin, Rubomycin); others (Bleomycin, Mitomycin);
- e) *alkaloids* — Vinblastine, Vincristine;

2) *hormones and their antagonists* — corticosteroids (Prednisolone); androgens (Testosterone); estrogens (Sinestrol, Fosfestrol); progestogens (Megestrol); antiestrogens (Tamoxifen, Toremifene); antiandrogen (Flutamide);

3) *enzymes* — Asparaginase;

4) *cytokines* — recombinant human interferon – α , interleukin – 2 (Proleukin), colony stimulating factors;

5) *radioactive isotopes* — radioactive iodine, gold.

Mechanisms of action. Indications and contraindications for use. Complications of chemotherapy, prophylaxis and treatment. Radioisotope preparations, indications, adverse effects.

3. Concept about **RADIOPROTECTORS** and drugs promoting of radionuclides removing — sulfur – containing preparations (Methionine, Cystamine, Taurine, Acetylcysteine, Unithiol, Cystophos), vitamin preparations, aminoacids, antioxidants, complexons, sorbents (Enterosgelum), biopolymers (Zymosan) etc. General characteristics. Mechanisms of action. The basic principles of application.

4. Drugs influencing on the **BLOOD COAGULATION**. Modern representations about coagulation and anticoagulation blood system.

5. Drugs **INCREASING BLOOD COAGULATION and INHIBITING OF FIBRINOLYSIS**: (hemostatic):

1) *Procoagulant agents*:

- a) direct acting: *topically* — Thrombin, Hemostatic sponge, Collagen sponge, Fibrin glue; *systemically* — preparations of coagulation factors (Fibrinogen, Factor VIII concentrate, IX, Cryoprecipitate);
- b) indirect acting — Vikasol (Menadione), Phytonadione, Etamzilat (Dicynonum), Desmopressin;

2) *inhibitors of fibrinolysis*:

- a) synthetic — Aminocaproic acid, Tranexamic acid, Ambene;
- b) animal origin — Aprotinin (Contrycal, Gordoks, Trasilol);

3) *Proagregants* — Calcium chloride, Calcium gluconate, Serotonin adipate, Adroxon;

4) *Thrombo – formers* — Decilat;

5) Coagulants of *animal and plant origin* — Gelatinolum, Water pepper;

6) *Heparin antagonists* — Protamine sulfate.

General characteristics of drugs. Mechanisms of action, side effects. Indications and contraindications for use.

6. ANTICOAGULANT, FIBRINOLYTIC, AND ANTIPLATELET DRUGS:

1) *anticoagulants*:

- a) direct action — Heparin and low – molecular – weight heparins (Fraxiparine, /Nadroparin/, Enoxaparin, Dalteparin, Ardeparin), Sulodexide, Hirudin and its preparations, Sodium citrate;
- b) indirect action — cumarin derivatives (Neodicumarin, Syncumar, Warfarin), indandione derivatives (Phenylin);

2) *fibrinolytic drugs* (thrombolytics):

- a) direct action — Fibrinolysin, Heparin, Trypsin;
- b) indirect action (profibrinolysin activators) — Streptokinase, Streptodectase, Urokinase, Alteplase;

3) *antiplatelet drugs* * — Aspirin, Ticlopidine, Dipyridamole, Pentoxifylline, Ticlodipine, Clopidogrel (Plavix), Reopro, IIb and IIIa platelet receptor blockers (Tirofiban)

General characteristics of drugs. Mechanisms of action, side effects. Indications and contraindications for use.

Pharmacology safety and the combined use of drugs.

List of practical works. Prescribe drugs with their application (*separately from the prescription!*):

№	Name of the drug	Drug form
1.	Pentoxyl (<i>Pentoxylum</i>)	Tab. on 0,025 and 0,2
2.	Filgrastim (<i>Filgrastim</i>)	Vials 0,0003 and 0,00048
3.	Cystamine dihydrochloride (<i>Cystamini dihydrochloridum</i>)	Tab. 0,2
4.	Methotrexate (<i>Methotrexatum</i>)	Tab. 0,0025; vials 25 mg/ml.
5.	Vinblastine (<i>Vinblastinum</i>)	Amp. 0,005
6.	Fibrinogen (<i>Fibranogenum</i>)	Vials 1,0 and 2,0
7.	Vikasol (<i>Vikasolum</i>)	Tab. 0,015, amp. 1 % 1 ml.
8.	Aminocaproic acid (<i>Acidum aminocapronicum</i>)	Vials 5 % 100 ml., tab. 0,5, rectal supp. 0,5
9.	Contrycal (<i>Contrykalum</i>)	Amp. 10000 and 50000 IU
10.	Heparin – Sodium (<i>Heparinum – natrium</i>)	Vials 5 ml. (5000, 10000 and 20000 IU in 1 ml.); ointment in tubes 10,0 and 25,0
11.	Fraxiparin (<i>Fraxiparine</i>) syn.: Nadroparin – calcium	Syringe – tube 0,3 and 0,5 ml.
12.	Protamine sulfate (<i>Protamini sulfas</i>)	Amp 1 % 2 and 5ml.
13.	Alteplase (<i>Alteplase</i>) syn.: Actilyse	Vials 0,05
14.	Neodicumarin (<i>Neodicumarinum</i>)	Tab. 0,05 and 0,1
15.	Warfarin (<i>Varfarinum</i>)	Tab. 0,002; 0,003; 0,005
16.	Clopidogrel (<i>Clopidogrel</i>) syn.: Plavix, Zilt	Tab. 0,075

Tasks for self-control. Choose the correct answers.

1. Due to the uncontrolled receiving Levomycetin patient revealed leukopenia. What preparation is assigned for leukopoiesis correction?

- A. Mercaptopurine
- B. Methotrexate
- C. Pentoxil
- D. Cyanocobalamin
- E. Prednisolone

2. For the prevention of thromboembolism in the postoperative period heparin is appointed. Specify, which is typical for heparin:

* Classification of anti-aggregants is given in unit № 26.

- A. It is effective orally
- B. Inhibits blood coagulation *in vitro* and *in vivo*
- C. The action develops within 18 – 24 hours and lasts for several days
- D. Able to significant accumulation
- E. This is coagulant

3. After heart by – pass surgery to improve the rheological properties of blood the patient is assigned blocker of ADP receptors on platelets. Specify the medication:

- A. Aspirin
- B. Clopidogrel
- C. Pentoxifylline
- D. Dipyridamole
- E. Lamifiban

4. For the treatment of acute pancreatitis, preparation of animal origin is assigned for the patient. Specify the medication:

- A. Aminocaproic acid
- B. Pancreatin
- C. Contrycal
- D. Ambene
- E. Mezym forte

5. Specify fibrinolytic of indirect action, which does not cause allergies, tolerance after repeated administration?

- A. Fibrinolizin
- B. Streptodeksase
- C. Streptokinase
- D. Alteplase
- E. Anistreplase

II. Original practical work in class

1. To view the collection of drugs.
2. Work with the tests (Krok-1).
3. Prescribe and ground the choice of drug:
 - 1) for treatment of agranulocytosis;
 - 2) vitamin preparation for leucopenia treatment;
 - 3) anticancer – antimetabolite;
 - 4) plant – derived anticancer drug;
 - 5) at radiation illness;
 - 6) at gastric bleeding;
 - 7) for thrombolysis during myocardial infarction;
 - 8) for thrombophlebitis treatment;
 - 9) prevention of myocardial infarction from the group of NSAIDs;
 - 10) for the prevention of thrombosis after coronary by – pass;
 - 11) at overdose of direct – acting anticoagulants;
 - 12) at overdose of indirect – acting anticoagulants.
 - 13) an inhibitor of fibrinolysis;
 - 14) indirect anticoagulants;
 - 15) fibrinolytic of indirect action;
 - 16) antiaggregant;
 - 17) Indirect procoagulants;
 - 18) hepato- and gematotoxyc drug;
 - 19) radioprotective drug.

Unit 40. IMMUNOTROPIC AGENTS AND ANTIALLERGIC DRUGS

Actuality of the unit. Wide range of application of immunocorrective agents in the treatment of congenital and acquired immune deficiencies, autoimmune aggression, led to the development of immunotherapy – a complex ethiotropic and pathogenetic measures, providing an active influence on the immune reactivity of the organism. At the current moment, in connection with the growth of HIV/AIDS morbidity, the problem of searching and creating of effective immune stimulators is especially important.

Prevention and treatment of allergic diseases is an actual problem of modern medicine. Attention of medicians of all specialties to this problem is explained mostly by the high percentage of allergic diseases out of all diseases. Morbidity with bronchial asthma in the number of countries is higher than cancer, rheumatism, tuberculosis, etc. Under the allergologists prognoses in connection with the increase of allergization factors quantity in future we can wait for stable growth of allergic diseases spreading.

I. Individual work

Control questions

IMMUNOTROPIC AGENTS

1. Concept about immunopharmacology. Definition of immunomodulating, immunostimulant and immunosuppressive drugs. Phenomenon of “pendulum”. Types of immunocorrection (substitutive, stimulant, suppressive).

2. **IMMUNOSUPPRESSANTS.** Classification:

- *antimetabolites* — Mercaptopurine*, Azathioprine*, Methotrexate*, Brequinar, Allopurinol* etc.;
- *alkalating agents** — Cyclophosphamide, Chlorbutin etc;
- *antibiotics* — Tacrolimus (FK 506), Rapamycin, Chloramphenicol, Cyclosporine A*, anticancer agents* (Dactinomycin, Daunorubicin, Mitomycin, Bleomycin) etc.;
- *alkaloids** — Vincristine, Vinblastine;
- *glucocorticoids* — Hydrocortisone, Prednisolone, Dexamethasone etc.;
- *antibodies* — antilymphocyte globulin, antithymocyte globulin, monoclonal antibodies (OKT – 3, Simulect®, Zena – pax®) etc.;
- *from different chemical groups* — NSAIDs (Acetylsalicylic acid, Paracetamol, Voltaren, Naproxen, etc.), enzyme preparations (Asparaginase*), 4 – aminoquinoline derivatives (Chloroquine), Salazopiridazina*, Heparin, Aminocaproic acid, gold preparations, Penicillamine, etc.

Characteristics of groups. Indications and contraindications for application. Immunosuppressants – as immunostimulators. Undesirable effects of immunosuppressive therapy. Control of immunosuppressive therapy.

3. **IMMUNOSTIMULANTS.** Classification by origin:

⇒ *endogenous and their synthetic analogues:*

- thymus preparations (Timalin, T – activin, Timactid, Vilozen, Imunofan, Timogen), red bone marrow (Mielopid), placental (placenta extract);
- immunoglobulins — human normal immunoglobulin (Intraglobin, Sandoglobulin, Octagam, Immunovenin, etc.); human immunoglobulin anti – staphylococcal, human immunoglobulin anti – cytomegalovirus (Cytotect);
- interferons* — recombinant interferon – gamma (Gammaferon, Imukin, Immunoferon);
- interleukins — recombinant interleukin – 1 beta (Betaleukin), recombinant interleukin – 2 (Proleukin, Roncoleukin);
- growth factors — recombinant human granulocyte – macrophage colony stimulating factor (Molgramostim);
- regulatory peptides — Tuftsin, Dalargin;

* Also used as anticancer (unit № 32).

* Classification of interferons is given in unit № 39.

- ⇒ *bacterial origin* and their analogues — vaccines (BCG etc.), extracts (Biostim), lysates (Bronhomunal, Immudon, Rinovak, Respivax), lipopolysaccharide cell wall (Pyrogenal, Prodigiozan, Likopid), a combination of ribosomes and cell wall fractions (Ribomunil), fungal (Bestatin, et al.) and yeast polysaccharides (Zymosan, Sodium nukleinat), probiotics (Linex, Blasts);
- ⇒ *synthetic* — purine and pyrimidine (Methyluracil, Pentoxil, Isoprinozin, Diutsifon, et al.), imidazole derivatives (Dibazolium), interferon inducers (Cycloferone, Amiksin, Neovir), polyoxidonium etc.;
- ⇒ *plant* and their analogues — adaptogens (Echinacea preparations (Immunal), Eleutherococcus, ginseng, Rhodiola rosea), other (aloe, garlic, beans, onions, red peppers, and others.);
- ⇒ *other classes* — preparations of vitamins C, A and E; metals (zinc, copper, etc.).

Classification according to the **mechanism of action**: mostly —

- *stimulate nonspecific factors of protection* — anabolic nonsteroidal and steroid structure, preparations of vitamins A, E, C; plant;
 - *stimulating monocytes* (macrophages) — Sodium nukleinat, Zymosan, vaccines, Pyrogenal, Prodigiozan, Biostim;
 - *stimulating T lymphocytes* — Dibazolium, Timalin, Taktivin, Timogen, zinc drugs, interleukins (IL – 2);
 - *stimulating B lymphocytes* — Myelopid, Tuftsin, Dalargin, Bestatin, Amastatin;
 - *stimulating NK cells and K cells* — interferons, antivirals (izoprinozin), placenta extract.
- Characteristics of the individual groups. Indications and contraindications.
4. Non – specific an immunocorrection.
 5. Basic principles on the use of immune preparations.

ANTIALLERGIC DRUGS.

1. Conception of allergy, types of allergic reactions. Modern conceptions of ethio – pathogenesis of allergic diseases. Stages of allergic processes. Common principles of treatment of allergic diseases (ethiotropic, pathogenetic, symptomatic therapy).

2. Classification:

A. Drugs used to treat IMMEDIATE HYPERSENSITIVITY reactions:

- *glucocorticoids* – Prednisolone, Triamcinolone, Betamethasone etc;
- *H₁ – histamine blockers* — Diphenhydramine (Dimedrolum), Diprazin, Suprastinum et al.;
- *stabilizers basophilic granulocytes* (inhibiting release, activation of histamine and other mediators of allergy) — Ketotifen (Zaditen), Cromolyn sodium (Intal), Oxatomidum (Tinset), Phenspirid;
- *antileukotriene drugs* — leukotriene – receptor blockers (Zafirlukast, Montelukast); 5 – lipoxygenase inhibitors (Zileuton);
- *reducing tissue damage* — anti – inflammatory (NSAID), steroidal and non – steroidal;
- *reduce allergy symptoms* (allergy functional antagonists) — adrenergic agonists, spasmolytics, M – cholinoblockers.

B. Drugs used to treat DELAYED HYPERSENSITIVITY reactions:

- *immunosuppressants* — glucocorticoids, etc.;
- *reducing tissue injury* — anti – inflammatory steroid and non – steroidal structure, anti – inflammatory with slow action (quingamine, penicillamine, gold – containing drugs (Solganal), Dalson etc.).

3. GLUCOCORTICOIDS. The mechanism of anti – allergic effect. Indications.

4. H₁-HISTAMINE BLOCKERS *. General characteristics. Classification:

I generation — derivatives:

- *ethanolamine* — diphenhydramine (Diphenhydramine hydrochloride, Benadryl), Tavegil (Clemastine);

* Termin of «anti-histamins» regarding H₁-histamine blockers is oldfashion, cause it does not reflect all pharmacodynamics peculiarities of new drugs from that group.

- *ethylenediamine* — suprastin (Chloropyramine);
- *phenothiazine* — promethazine (Promethazine hydrochloride, Pipolfen);
- *alkylamine* — Fenistil (Dimethindene), Pheniramine;
- *quinuclidine* — Phencarolum (Hifenadina);
- *etrahydro – carboline* — Diazolin (Mebhydrolin, Omeril);
- *piperidine* — Cyproheptadine (Peritol);

II generation — derivatives:

- *azetidinyll* — Loratadine (Claritin, Sanoral);
- *piperazine* — Cetirizine (Zyrtec, Tsetrin);
- *triprolidine* — Acrivastine (Sempreks);
- *oxyipyridin* — Ebastine (Kestin), Levocabastine (Gistimet);
- *benzimidazole* — Mizolastine;
- *piperidine* — Terfenadine (Seldan)*;
- *imidazole* — Astemizole (Gismanal)*;

III generation (active metabolites of the II generation): Fexofenadine (Telfast, Altiva, Allegra), Desloratadine (Aerius), Norastemizol (Seprakor), Karebastin, Levocetirizine (Ksizal).

Pharmacodynamics, pharmacokinetics, advantages and disadvantages of different generations. Undesirable effects.

5. STABILIZERS OF BASOPHIL GRANULOCYTES. Mechanism of action. Indications. Concept of anti – leukotrien drugs.

6. Anaphylactic shock. Types. Principles of treatment.

7. Drug – caused disease. Terms and conditions of its development. Clinical forms. Pathological manifestations. Principles of treatment.

Pharmacology safety and the combined use of drugs.

List of practical works. Prescribe drugs with their application (*separately from the prescription!*):

No	Name of the drug	Drug form
1.	Thymalin (<i>Tymalinum</i>)	Vials 0,01
2.	Azathioprine (<i>Azathioprinum</i>)	Tab. 0,05
3.	Filgrastim (<i>Filgrastimum</i>) syn.: Filstim	Vials 1 ml.(0,3 mg) a sol. for injections
4.	Immunal (<i>Immunal</i>)	Drops for intake in vials. 50 ml.; Tab. 0.08
5.	Dimedrol (<i>Dimedrolum</i>) syn.: Diphenhydramine	Powder and tab. on 0,02, 0,03, 0,05; supp. 0,005 and 0,01; amp. and syringe – tube 1 % 1 ml.
6.	Diazolin (<i>Diazolinum</i>)	Dragee and tab. 0,05 and 0,1
7.	Diprazin (<i>Diprazinum</i>) syn.: Pipolfen	Tab. 0,025, dragee 0,025 and 0,05, amp. 2,5 % 2 ml.
8.	Suprastin (<i>Suprastinum</i>)	Tab. 0,025, amp. 2 % 1 ml.
9.	Loratadine (<i>Loratidinum</i>)	Tab. 0.01; vials. 0.1 % syrup 100 ml. and 120; 0.1 % suspension to 30 ml. and 100 ml. for oral use
10.	Cetirizine (<i>Cetirizine</i>) syn.: Cetrin	Tab. 0.01; vials. 1% sol. of 10 and 20 ml. for oral use
11.	Fexofenadine (<i>Fexofenadinum</i>) syn.: Telfast	Tab. 0.12, 0.18
12.	Cromolyn sodium (<i>Cromolyn Sodium</i>) syn.: Intalum	Caps 0,02 for inhalation

Tasks for self-control. Choose the correct answers.

* Banned in many countries because of fatal arrhythmia development.

1. Find out an inducer of endogenous interferon production:
 - A. Imudon
 - B. Immunal
 - C. Methyluracilum
 - D. Amixin
 - E. Thymalin
2. Specify an immunomodulator, which is characterized by the effect of "pendulum"?
 - A. Naproxen
 - B. Heparin
 - C. Azathioprine
 - D. Hydrocortisone
 - E. Dibazol
3. The doctor in the complex therapy appointed an immunostimulant. Specify the indications for use of immunostimulants.
 - A. The allergy of immediate type
 - B. Sluggish infection
 - C. Delayed type allergy
 - D. Reaction of transplant rejection
 - E. All of above mentioned
4. Sedative – hypnotic effect of 1st generation of H₁ – histamine blockers is associated with?
 - A. The blockade of central – HT receptors
 - B. The blockade of central dopamine D – receptor
 - C. The blockade of central alpha – adrenergic receptors
 - D. The blockade of peripheral M – cholinergic receptors
 - E. The blockade of the central M – choline and H – histamine receptors
5. Which H₁ – histamine blockers allowed as a hypnotic for use on the territory of Ukraine?
 - A. Dimedrolum
 - B. Promethazine.
 - C. Suprastin
 - D. Loratadine
 - E. Doxylamine

II. Original practical work in class

1. To view the collection of drugs.
2. Work with the tests (Krok-1).
3. Prescribe and ground the choice of drug:
 - 1) in case of kidney transplantation;
 - 2) an immunostimulant from adaptogens;
 - 3) an immunosuppressant with anti – tumor activity;
 - 4) H₁ – histamine blockers with a strong hypnotic effect;
 - 5) Anti – histamine agent with minimal hypnotic effect;
 - 6) H₁ – histamine blockers, used to treat influenza;
 - 7) H₁ – histamine blockers, use of which is independent from food intake;
 - 8) myotropic with spasmolytic action for relief of asthma attack;
 - 9) for the prevention of asthma attacks;
 - 10) adrenergic agonist for relieve of anaphylactic shock.
 - 11) H₁-histamine blockers II generation;
 - 12) a drug that stimulates T-lymphocytes;
 - 13) the drug, inhibiting the release and activation of histamine;
 - 14) H₁-histamine blockers from the group of ethylene diamine;
 - 15) immunosuppressant from the group of glucocorticoids;
 - 16) immunosuppressant - antimetabolite;
 - 17) for the treatment of immediate type allergic reactions;
 - 18) for treating delayed type of allergic reactions.

Unit 41. CHECKING OF PRACTICAL SKILLS ON “DRUGS ACTING ON METABOLISM, BLOOD AND IMMUNITY”

CONTENT MODULE 6. ANTIMICROBIAL AND ANTIPARASITIC DRUGS

Actuality of the unit. Antimicrobial, antiparasitic agents – are drugs with disastrous effects on the pathogens that are used to prevent and treat infectious diseases. Due to introduction of antiseptics, disinfectants, chemotherapeutics at the end of XIX – the first half of the twentieth century it became possible significantly reduce mortality from infectious diseases such as cholera, typhoid fever, etc. Due to antimicrobial agents mankind overcame the first "wave of death" – infectious diseases, especially in childhood. However, due to irrational appointments of chemotherapeutic agents it is noticed an increasing of drug resistance of microbes, the development of non – specific sensitization, increasing the frequency of superinfection. Therefore, knowledge about the features of different groups of chemotherapeutic agents, rational rules of chemotherapy are a necessary condition for the successful treatment of infectious diseases. Also it becomes important to treat viral diseases such as HIV/AIDS, influenza and others. Till now malaria, tuberculosis remain widespread. In order to successfully deal with these various illnesses are a prerequisite knowledge of the respective groups of antimicrobial agents.

The training objectives. *To know:* Pharmacology of antimicrobial, antiparasitic medicines. *Be able to:* prove the choice of drugs and write this section in a variety of dosage forms to solve the test tasks, situational and pharmacological challenges.

Intersubject integration. Microbiology, general surgery, biochemistry, pathology and physiology.

Unit 42. DISINFECTANTS AND ANTISEPTICS

Actuality of the unit. Drugs with antimicrobial properties are divided into two groups. The first group, drugs which kill microorganisms, but highly toxic of host cell. They include antiseptic and disinfectant drugs. The second group (chemo – therapeutic) is selective in its action. These drugs have the ability to kill an invading microorganisms without harming the cells of the host. Disinfectants are used to kill microorganisms in the environment (tools treatment care items, tableware and so on.). Antiseptics are used to kill microorganisms on the surface of body (skin, mucous membranes, cavity wounds). The first means for preventing infectious processes were heavy metal salts and ethyl alcohol. Later, instead of too toxic carbolic acid ("Antiseptic Lister") began to be used salicylic acid and boric acid, thymol and others. At the present time it is impossible to imagine almost any one direction in medicine without the use of antiseptics and disinfectants. It is hard to line a border between antiseptic and disinfectant preparations, because a lot of antiseptics with the increase of concentration can be used as disinfection agents.

I. Individual work

Control questions

1. General characteristics of antimicrobial agents. The conception of disinfective, antiseptic, and chemotherapeutic substances. The requirements for disinfectant, antiseptic and chemotherapeutic agents.

2. Concept about antibacterial and chemotherapeutic spectrum.

3. Classification of DISINFECTANTS and ANTISEPTICS:

- *Halogen* – containing compounds: preparations of chlorine (Chloramine B, Chlorhexidine, Pantocide) and iodine (Iodine spirit sol., Iodinol, Lugol sol. etc.);
- *Oxidants*: Hydrogen peroxide, Potassium permanganate, Sodium hypochlorite;
- *Acids and alkalines*: Salicylic acid, Boric acid, Ammonia sol., Peroxide etc.;
- *Phenols*: Resorcin, Vagotil, etc.;
- *Tars, pitches, mineral oils*, products of oil refining: Tar birch, Ichtiolum, Naphthalan, Ozokerite, Citral, Sulsen etc.;

- *Aldehydes and alcohols*: Formaldehyde, Glutaraldehyde, Ethanol;
- *Metal compounds*: Silver nitrate, Zinc sulfate, Zinc oxide, Copper sulfate, Copper oxide etc.;
- *Dyes or tints*: Brilliant green, Methylene blue, Ethacridine lactate;
- *Detergents*: Cerigelum, Roccal, Aethonium, Decamethoxin, Potassium soap, Miramistin etc.;
- *Derivatives of different chemical groups*: nitrofurans (Furatsilin); thiosemicarbazone (Faringosept); containing hexetidines (Stomatidin, Geksoral, Givalex) etc.
- *Agents from plant source*: Clary, Calendula, Camomile etc.

4. Classification CHEMOTHERAPEUTIC AGENTS*:

Antibiotics;

Sulfonamides;

Miscellaneous synthetic antimicrobials:

- Fluoroquinolones (Ciprofloxacin, Ofloxacin, Moxifloxacin) and quinolones (Nalidixic acid, Oxolinic acid etc.);
- 8 – Oxyquinolone derivatives (Chlorquinaldol, Nitroxoline, Oxolinic acid etc.);
- Nitrofurans derivatives (Furazolidone, Furadoninum, Furoplast, Furaginum etc.);
- Imidazole derivatives (Metronidazole, Tinidazole etc.);
- oxazolidinones (Linezolid);
- Quinoxaline derivatives (Dioxydinum, Chinoxydin, Dioxicol).

Anti – infectives used under special indications:

Antituberculosis;

Antisiphilitic;

Antiprotozoal;

Antiviral;

Antifungal;

Anthelmintic;

Anticancer.

5. Conditions, which define antimicrobial activity: a) chemical structure, physical and chemical properties; b) concentration and grade of dissociation; c) time of exposition; d) temperature; e) species of microbe, ability to the spore – production; f) quantity of microbe cells; g) presence of organic substances (proteins, pus, etc), which may inactivate the agents.

6. Basic types and mechanisms of antimicrobial action (antiseptics and disinfectants).

7. Characteristics of the basic representatives of every group. Antimicrobial spectrum, mechanism of action, usage.

8. Poisoning by acids and alkalines, heavy metal compounds and phenols. First aid, usage of antidotes.

9. Concept about *dermato – protectors, wound cleaning and wound healing* preparations (Panthenol, Iruksol, Solcoseryl, etc.).

Pharmacology safety and the combined use of drugs.

List of practical works. Prescribe drugs with their application (*separately from the prescription!*):

№	Name of the drug	Drug form
1.	Chlorhexidine digluconate (<i>Chlorhexidinum bigluconas</i>)	Vials 0,5 % – 100 ml.
2.	Iodine, spirit sol. (<i>Solutio Iodi spirituosa</i>)	Sol. 2 – 10 %, 5 ml.
3.	Potassium permanganate (<i>Kalii permanganas</i>)	0,02 %, 0,5 %, 10 % sol.s
4.	Hydrogen peroxide diluted (<i>Solutio Hydrogenii peroxydi diluta</i>), concentrated (<i>concentrata</i>)	Vials 3% 25, 30, 50 ml.; Solutio Hydrogenii peroxydi concentrata 30 – 33 %.

* Some chemotherapeutic agents, depending on pharmacokinetic parameters and toxicity, could be used as antiseptics

5.	Methylene blue (<i>Methylenum coeruleum</i>)	1 – 3 % spirit sol.s and water sol.s; <i>Chromosmon</i> — 1 % sol in 25 % sol of glucose in amp. 20 and 50 ml.
6.	Brilliant green (<i>Viride nitens</i>)	2 % spirit sol.s
7.	Salicylic acid (<i>Acidum salicylicum</i>)	Spirit sol. 1% and 2 %
8.	Zinc sulphate (<i>Zinci sulfas</i>)	0,25 %, 0,5 % sol.s
9.	Protargol (<i>Protargolum</i>)	1 – 5 % sol.s
10.	Hexamethylenetetramine (<i>Hexamethylenetetraminum</i>) syn.: Urotropine	Tab. 0,25; 0,5 and amp. 40 % 5 ml. and 10 ml.
11.	Ethyl alcohol (<i>Spiritus aethylicus</i>)	40 %, 70 %, 95 % sol.s
12.	Resorcin (<i>Resorcinum</i>)	Water and spirit sol.s 2 – 5 %; ointments 5 – 10 – 20 %
13.	Decametoxine (<i>Decamethoxinum</i>)	Tab. 0,1 for sol. preparation (0,025%; 0,5%); vials 0,05% alcohol sol. 10 ml. (ear drops)
14.	Furatsilin (<i>Furacilinum</i>) syn.: Nitrofurazone	Tab. 0,02 for sol. preparation (1:5000); 0,2 % ointment

Tasks for self-control. Choose the correct answers.

- Which drug belongs to organic antiseptics?
 - Salicylic acid
 - Potassium permanganate
 - Resorcin
 - Chlorhexidine
 - Protargol
- Antiseptic, which bactericidal mechanism of action is based on the formation of atomic oxygen:
 - Potassium permanganate
 - Boric acid
 - Furacillin
 - Ethonium
 - Silver nitrate
- Which antiseptic has additional anti – itching and regenerative properties:
 - Pantocid
 - Zinc sulphate
 - Hydrogen peroxide
 - Ethyl alcohol
 - Ethonium
- Name the antiseptic that is used parenterally in the case of cyanide poisoning:
 - Silver nitrate
 - Ethacridine lactate
 - Ethyl alcohol
 - Methylene blue
 - Potassium permanganate
- Specify the antiseptic that can be used for local intravaginal contraception:
 - Potassium permanganate
 - Resorcin
 - Benzalkonium chloride
 - Vagotil
 - Furacillin

II. Original practical work in class

- To view the collection of drugs.
- Work with the tests (Krok-1).
- Prescribe and ground the choice of drug:
 - Antiseptic from halogens group for hands processing;
 - Antiseptic from halogens group for operation area and wound's edges processing;

- 3) Eye drops containing an antiseptic from the group of metals;
- 4) Agent from the dye group for treatment of pyoderma;
- 5) Oxidizing agent for wound irrigation;
- 6) From the group of oxidizing agents for gastric lavage;
- 7) Derivative of nitrofurans for rinsing the mouth and throat during tonsillitis, pharyngitis, stomatitis;
- 8) Agent for treatment urogenital tract inflammation;
- 9) Agent with keratolytic and keratoplastic activity.
- 10) of the metal group;
- 11) from the group of detergents;
- 12) cuprous sulphate replacement drug;
- 13) the replacing drug of methylene blue.

Unit 43. CHEMOTHERAPEUTIC AGENTS. ANTIBIOTICS. PRINCIPLES OF ANTIBIOTIC THERAPY. CLASSIFICATION. MECHANISM OF ACTION.

Actuality of the unit. Antibiotics are the most important chemotherapeutic agents. Thanks to them it became possible to cure the pulmonary form of plague, to decrease abruptly mortality in case of such infectious diseases as typhus, meningitis, tuberculosis, etc. Excessive use of this highly – effective group of chemotherapeutic drugs and underestimation of its potential danger, irrational and noneffective use causes a row of undesirable results of antibiotic therapy: increasing of drug – resistance of microbes, damaging of separate organs and systems, development of non – specific sensitization, increasing of frequency of endogenous, mixed as well as superinfections. The facts, mentioned above, led us to the decision of more careful use of antibiotics and strict observing rational antibiotic therapy principles.

I. Individual work

Control questions

1. History of antibiotics discovery and usage (Erlach P., Domagha G., Fleming A., Ermolyeva Z.).
 2. Main principles of the chemotherapy (rational choice of preparation, the initialization of therapy, the pathway of introduction, dose, the interval of introduction, the duration of the therapy, the combined therapy, increasing of the immunological reactivity).
 3. Criteria of an estimation of the chemotherapeutic drugs.
 4. ANTIBIOTICS. History of discovery and application. Producing sources.
 5. Main principles of antibiotic therapy. Information about main and reserve antibiotics.
 6. Classification of antibiotics according to **the mechanism of action** *:
- 1) Antibiotics, *inhibiting the cell wall synthesis*: β – lactams (Penicillins, Cephalosporins), Ristomycin, Vancomycin, etc.
 - 2) Antibiotics, affecting the *permeability of microbial cell membrane*: polyenes (Nystatin, Amphotericin B etc.), polymyxins etc.
 - 3) Antibiotics, *inhibiting the protein synthesis*: macrolides, aminoglycosides, tetracyclines, levomycetin, lincomycin etc.
 - 4) Antibiotics, *inhibiting the synthesis of nucleic acids*: Rifampicin, Griseofulvin. That mechanism is also actual for the anticancer and immunodepressant drugs.
7. Classification according to the **spectrum of antimicrobial activity and chemical structure**:
- I. *With primary activity against Grampositive bacteria*:
 - 1) β – lactam antibiotics (penicillins, cephalosporins);
 - 2) macrolides and azalides;
 - 3) antibiotics for special indications — rifamycins (Rifampicin), lincosamins (Lincomycin, Clindamycin), glycopeptides (Ristomycin, Vancomycin), sodium fuzidin, etc.
 - II. *With primary activity against Gram – negative bacteria*:

* In general, mentioned 4 mechanisms of action actual not only for antibiotics, but other chemotherapeutic agents as well.

1) aminoglycosides — Streptomycin, Gentamicin, Amikacin, etc.;

2) polymyxins — Polymyxin B and E.

III. *Influencing on the Gram – positive and Gram – negative bacteria:*

1) tetracyclines;

2) levomycetin group.

IV. *Influencing on the Gram – positive and Gram – negative bacteria for local usage — aminoglycosides (Neomycin, Monomitsin), Polymyxins, Syntomycin, Bacitracin, Lincomycin, Gramicidin.*

V. *Antifungal antibiotics — polyenes (Nystatin, Levorin, Amphotericin B, Amphoglucaminum, Mycoheptinum), Griseofulvin.*

VI. *Anticancer antibiotics — actinomycetes (Dactinomycin), anthracyclines (Doxorubicin, Rubomycin); others (Bleomycin, Mitomycin).*

8. COMPLICATION OF ANTIBIOTIC THERAPY:

1) development of antimicrobial resistance (biological, species, secondary, persistent, cross);

2) development of allergic reactions (anaphylactic shock, angioedema, urticaria, rhinitis, conjunctivitis, dermatitis etc.);

3) development of super – infection during treatment of the primary disease (candidosis, staphylococcosis, vitamin deficiencies);

4) direct organotoxic effects (nephrotoxicity, hepato, nephrotoxicity, myelotoxicity, gastrointestinal disorders, etc.);

5) the development of acute reactions (endotoxic);

6) mutagenic, teratogenic, embryotoxic effects.

9. General requirements and criteria of antibiotics differences (acid resistance, beta – lactamase stability, antibacterial spectrum etc.).

10. PENICILLINS. Classification:

a) biosynthetic:

- short – acting — Benzylpenicillin sodium, potassium salts, Phenoxymethylpenicillin;

- depot preparations — Benzylpenicillin – benzathine (Bicillin – 1, Extencillin), Bicillin – 3, Bicillin – 5.

b) semisynthetic penicillins:

- *wide spectrum* (aminopenicillins) — Ampicillin, Amoxicillin;

- *antistaphylococcal or penicillinaz resistant* (isoxazolilpenicillins) — Oxacillin, Dicloxacillin, Flucloxacillin;

- *antipseudomonal* — carboxypenicillins (Carbenicillin, Ticarcillin) and ureidopenicillins (Azlocillin, Piperacillin);

- *Combined* — Ampiox, Helicoid (moxicillin + metronidazole), Amoxiclav, Augmentin (amoxicillin + clavulanate), Ampicillin + Sulbactam, Ticarcillin + Clavulanic acid, Piperacillin + Tazobactam, and others.

Antimicrobial spectrum. Features of each subgroup. Beta – lactamase inhibitors (clavulanic acid, sulbactam). Pharmacokinetics. Chemotherapeutic spectrum. Side effects.

11. CEPHALOSPORINS. Classification:

- *1st generation* — Cefazolin (Kefzol), Cefalotin, Cefalexin, Cephalexin, etc.;

- *2nd generation* — Cefoxitin, Cefamandole, Cefprozil, Cefuroxim, Cefaclor, etc.;

- *3rd generation* — Cefotaxime (Klaforan), Ceftriaxone, Cefotaxime, Ceftazidime, Cefixim, Cefibuten and others.;

- *4th generation* — Cefepime, Cefpirome and others.

Comparative characteristics of drugs from different generations (antimicrobial spectrum, pharmacokinetic parameters). Chemotherapeutic spectrum. Side effects.

12. Pharmacological characterization of β -LAKTAM LIKE drugs – carbapenems (Imipenem, Meropenem) and monobactams (Aztreonam). The mechanism of action and spectrum of action. Side effects. Pharmacology safety and the combined use of drugs.

List of practical works. Prescribe drugs with their application (*separately from the prescription!*):

№	Name of the drug	Drug form
1.	Benzylopicillin sodium salt (<i>Benzylopicillinum – natrium</i>)	Powder in vials 500,000 and 1,000,000 units
2.	Bicillin – 5 (<i>Bicillinum – 5</i>)	Vials 1,500,000 units
3.	Oxacillin sodium salt (<i>Oxacillinum natrium</i>)	Tab. 0,25 and 0,5; Caps 0,25; vials 0,25 and 0,5
5.	Amoxiclav (<i>Amoxiclav</i>)	Caps. 0,325, 0,625; suspension for oral usage in vial 100 ml.; vial 0,6 and 1,2
6.	Cefazolin (<i>Cefazolinum</i>) syn.: Kefzol	Vials 0,25; 0,5; 1,0; 2,0; 4,0
7.	Cefuroxime (<i>Cefuroximum</i>)	Tab. 0,25; 0,5 g., vials. suspension for oral use 100 ml.
8.	Ceftriaxone (<i>Ceftriaxonum</i>)	Vials 0,25; 0,5; 1,0
9.	Cefpirome (<i>Cefpirom</i>)	Vials 0,5; 2,0; 4,0
10.	Meropenem (<i>Meropenem</i>)	Vials 0,5 and 1,0

Tasks for self-control. Choose the correct answers.

- Specify the antibiotic that is administered once every four weeks:
 - Bicillin-5
 - Extencillin
 - Penicillin
 - Phenoxymethylpenicillin
 - Benzylopicillin potassium salt
- What mechanism of bactericidal action of penicillin:
 - Increasing of permeability of the cytoplasmic membrane
 - Inhibition of intracellular protein synthesis
 - Inhibition of microbial cell wall synthesis
 - Inhibition of SH – groups of enzymes of microorganisms
 - Antagonism with para – aminobenzoic acid
- Point out a cephalosporin agent for meningitis treatment:
 - Cefazolin
 - Cefalothin
 - Cefaclor
 - Ceftriaxone
 - Cefalexir
- Which of these substances belongs to a group of β -lactamase inhibitors?
 - Acid carbolic
 - Acid mefenamic
 - Salicylic acid
 - Clavulanic acid
 - Benzoic acid
- Name the antibiotic that is used for eradication of *H.pylori* in gastric ulcer:
 - Benzylopicillin sodium salt
 - Bicillin – 5
 - Amoxicillin
 - Cefazolin
 - Aztreonam

II. Original practical work in class

- To view the collection of drugs.
- Work with the tests (Krok-1).
- Prescribe and ground the choice of drug:
 - biosynthetic antibiotic during streptococcal infection;
 - in case of infection caused by penicillinase – producing pneumococcus;

- 3) for the prevention of acute rheumatic fever;
- 4) from the group of penicillin for treatment of bacillary dysentery;
- 5) acid – resistant penicillin;
- 6) cephalosporin, for enteral usage;
- 7) cephalosporin, which resistant to cephalosporinase;
- 8) β – lactam antibiotic effective against *Pseudomonas aeruginosa*;
- 9) a group of carbapenem antibiotic.
- 10) cephalosporin of 1st generation;
- 11) antistafillococcus penicillin;
- 12) combinade penicillin;
- 13) inhibitor protected penicillin;
- 14) depot preparation penicillin;
- 15) cephalosporin of 3rd generation;
- 16) the drug replacement tsefoksitina;
- 17) Antibiotics that inhibit the synthesis of biopolymer membrane microbial cells;
- 18) the beta-lactam antibiotic.

Unit 44. ANTIBIOTICS. ANTIMICROBIAL AND CHEMOTHERAPEUTIC SPECTRA OF DIFFERENT GROUPS. USE

Actuality of theme. Nowadays, antibacterial drugs are widely used in medical practice for the purpose of eradicating the causative agents of infectious diseases and are one of the most frequently used groups of drugs. Monitoring data indicate that over the past ten years, the global consumption of antibiotics in medicine has increased by 36%, although the dynamics of consumption varies by country. In Ukraine, the consumption of antibiotics is at a lower level compared to other European countries. At the same time, the most frequently prescribed antibiotics are penicillins, and the level of their use is almost 2 times higher than that of drugs of other groups. Fluoroquinolones are in second place.

Antibiotic groups have different antimicrobial spectrum and pharmacological activity. Rational pharmacotherapy with antibiotics involves taking into account the characteristics of each group.

I. Individual work

Control questions

1. MACROLIDES AND AZALIDES. Classification of macrolides:

- *1st generation* – Erythromycin, Oleandomycin;
- *2nd and 3rd generation* – Roxithromycin, Spiramycin, Clarithromycin.

Azalides – Azithromycin (Sumamed).

Mechanism of action. Comparative characteristics of drugs (antimicrobial spectrum, pharmacokinetics). Application. Adverse reactions.

2. AMINOGLYCOSIDES. Classification:

- *1st generation* – Streptomycin, Kanamycin, Neomycin, etc.;
- *2nd generation* – Gentamicin;
- *3rd generation* – Amikacin, Sizomitsin, Tobramycin, and others.

Mechanism of action. Comparative characteristics of drugs (antimicrobial spectrum, pharmacokinetics). Application. Adverse reactions. The interaction between other drugs (Furosemide, muscle relaxants, cephalosporins and Vancomycin).

3. POLYMYXINS B and E. Mechanism of action. The antibacterial and chemotherapy spectrum. Undesirable effects.

4. TETRACYCLINES. Classification:

- *biosynthetic* – Tetracycline, Oxytetracycline;
- *semisynthetic* – Metacyclin, Doxycycline;

▪ *combined* – Oletetrin.

Mechanism of action. The antimicrobial and chemotherapeutic spectrum. Pharmacokinetics. Undesirable effects.

5. Pharmacology of LEVOMYCETIN (chloramphenicol, synthomycin).

6. Antibiotics, used according to *special indications*: rifamycins (Rifampicin), linkosamine (Lincomycin, Clindamycin), glycopeptides (Ristomycin, Vancomycin), fuzidin – sodium and others. Undesirable effects.

6. Characteristics of the effect of antibiotics *for topical use*: aminoglycosides (Neomycin, Monomycin), polymyxins, Synthomycin, Bacitracin, Geliomycin, Gramicidin.

7. *Anti – Pseudomonal* antibiotics: cephalosporins of the 3rd, 4th generation, aminoglycosides 2nd and 3rd generations, polymyxins, carbenicillin, and others.

List of practical works. Prescribe drugs with their application (*separately from the prescription!*):

№	Name of the drug	Drug form
1.	Erythromycin (<i>Erythromycinum</i>)	Tab. 0,1; 0,25 capsules 0,1
2.	Azithromycin (<i>Azithromycinum</i>) syn.: Sumamed	Tab. 0,125, 0,5; caps. 0,5.
3.	Lincomycin hydrochloride (<i>Lyncomycini hydrochloridum</i>)	Amp. 30 % 1 ml.; caps. 0,25; ointment 2 % 15,0
4.	Tetracycline (<i>Tetracyclinum</i>)	Tab. 0,05, 0,1, 0,25
5.	Doxycycline hydrochloride (<i>Doxycyclini hydrochloridum</i>)	Caps. 0,05 and 0,01
6.	Laevomycetin (<i>Laevomycetinum</i>) syn.: Chloramphenicol	Tab 0,25 and 0,5; caps 0,1; 0,25 and 0,5; vials 10 ml. of 0,25 % sol., eye drops
7.	Gentamicin sulfate (<i>Gentamycini sulfas</i>)	Vials 0,08; amp. 4 % 1 – 2 ml.; ointment 0,1 %.
8.	Amikacin sulfate (<i>Amykacini sulfas</i>)	Vials 0,1, 0,25 and 0,5; amp. 5, 12,5 and 25 % 2 ml.
9.	Polymyxin B sulfate (<i>Polymyxini B sulfas</i>)	Tab. 500000 IU; 0,025 vials (250000 IU), 0,05 (500000 IU).
10.	Synthomycin (<i>Synthomycinum</i>)	Emulsion, liniment in Bot. 25,0

Tasks for self-control. Choose the correct answers:

1. *What is the mechanism of antimicrobial action of tetracycline?*

- A. Contributes to the loss of amino acids and nucleotides
- B. Inhibits murein synthesis
- S. Violates the synthesis of nucleic acids
- D. Binds to divalent cations
- E. Suppresses protein synthesis in cells of sensitive microorganisms

2. *Which of the listed drugs can be prescribed to a patient who suffers from chronic otitis media and had hepatitis six months ago?*

- A. Tetracycline
- B. Methacycline
- S. Gentamicin
- D. Ampioks
- E. Doxycycline

3. *Specify an antibiotic that can cause severe suppression of hematopoiesis, dyspepsia, "gray" syndrome of newborns:*

- A. Tetracycline
- B. Lincomycin
- S. Ceftriaxone
- D. Neomycin sulfate

E. Levomycetin

4. A patient with pneumonia has a history of anaphylactic shock to penicillins. What antibiotic can be prescribed in this case?

- A. Ceftriaxone
- B. Azithromycin
- S. Levomycetin
- D. Tetracycline
- E. Polymyxin B

5. Specify a semi-synthetic antibiotic that undergoes pronounced entero-intestinal recirculation:

- A. Benzylpenicillin
- B. Doxycycline
- S. Tetracycline
- D. Cefazolin
- E. Oxacillin

II. Original practical work in class

1. To view the collection of drugs.
2. Work with the tests (Krok-1).
3. Prescribe and ground the choice of drug:

- 1) biosynthetic antibiotic to treat urinary tract infections;
- 2) bacteriostatic antibiotic against meningococcal infection;
- 3) semi – synthetic broad – spectrum antibiotic for the treatment of bacillary dysentery;
- 4) drug for the treatment of Chlamydia pneumoniae;
- 5) oto – and nephrotoxic antibiotic;
- 6) in case of purulent wounds;
- 7) preparation with myelotoxicity;
- 8) osteotropic antibiotic;
- 9) semi – synthetic antibiotic that affect the formation of tooth enamel.
- 10) antibiotic - azalide;
- 11) aminoglycoside of 2nd generation;
- 12) semi-synthetic penicillin;
- 13) the drug replacement Metatsiklin;
- 14) antibiotic from the group of polymyxins;
- 15) antibiotics, which used for special indications;
- 16) hepatotoxic antibiotics;
- 17) aminoglycoside of 3rd generation;
- 18) antibiotic with a primary effect on gram-negative microflora;
- 19) antibiotic that inhibits protein synthesis of microorganisms;
- 20) an antibiotic that inhibits the ability to live Pseudomonas aeruginosa.

Unit 45. ADVERSE EFFECTS OF ANTIBIOTICS

Actuality of theme. Basically, antibiotics are low-toxic substances for humans. However, in the course of treatment, they can have side effects on the patient's body. The occurrence of adverse reactions to antibiotics is a complex pathophysiological process, in the development of which a number of factors are involved. On the one hand, the risk of causing adverse reactions is determined by the properties of the antibiotic itself, and on the other hand, by the reaction of the patient's body to it. The occurrence of side effects during antibiotic therapy depends on many factors: properties of the antibiotic itself; individual properties of the macroorganism; doses of the medicinal product; duration of treatment; medicinal form.

1. COMPLICATIONS OF ANTIBIOTIC THERAPY:

- 1) development of resistance of microorganisms (biological, species, secondary, persistent, cross);

2) development of allergic reactions (anaphylactic shock, Quincke's edema, urticaria, rhinitis, conjunctivitis, dermatitis, etc.);

1. Immediate (up to 30 minutes): severe - anaphylactic shock, Quincke's edema, bronchospasm; moderate - urticaria.

2. Rapid (1-48 hours): severe - Quincke's edema, bronchospasm; moderate - urticaria, skin itching, erythema, rhinitis.

3. Delayed (> 48 h): the most severe - blood dyscrasia, Stevens-Johnson syndrome, Lyell's syndrome, serum sickness; moderate - urticaria, erythema, arthritis, hemolytic anemia, eosinophilia, thrombocytopenia, leukopenia, agranulocytosis, interstitial nephritis, vasculitis, lupus-like syndrome, fever

To determine hypersensitivity use:

1. Intradermal test - AB solution is injected under the skin on the forearm in a volume of 0.1 ml. The result is taken into account after 20 minutes by the diameter of the erythema zone (papule) at the injection site. The reaction is positive if the size of the papule is more than 1 cm

2. Sublingual method - 1/8 tablet is placed under the tongue. The result is considered positive if allergic manifestations are observed after 20 minutes.

3. Immunoblotting is a highly sensitive method, which is based on detected antibodies to individual antigens on nitrocellulose membranes, on which precipitation is determined using labeled antiglobulin serums. A positive reaction is considered when a dark strip appears.

4. Enzyme immunoassay is a quantitative method of detecting the presence of IgE to an allergen in the wells of the tablet. After combining the antigen with the enzyme-labeled immune serum, the substrate/chromogen is added to the mixture. The substrate is split by an enzyme and the color of the reaction product changes; the intensity of staining is directly proportional to the number of bound antigen molecules and labeled antibodies. With a positive result, the color of the chromogen changes.

3) the development of superinfection against the background of treatment of the primary disease (candidomycosis, staphylococcus, hypovitaminosis);

4) direct organotoxic effects (neuro-, hepato-, nephro-, myelotoxicity, gastrointestinal disorders, etc.);

5) development of an exacerbation reaction (endotoxic shock);

6) mutagenic, teratogenic, embryotoxic effect.

Give examples. Methods of preventing complications.

Pharmacosafety and interchangeability of drugs.

Tasks for self-control. Choose the correct answers.

1. What is the mechanism of antimicrobial activity of tetracycline?

- A. Promotes loss of amino acids and nucleotides
- B. Inhibits the synthesis of murein
- C. Violates the synthesis of nucleic acids
- D. Bound to divalent cations
- E. Inhibits protein synthesis in cells of susceptible organisms

2. Which of the following drugs can be assigned to patient who is suffering from chronic otitis, and six months ago had hepatitis?

- A. Tetracycline
- B. Metacyclin
- C. Gentamicin
- D. Ampiox
- E. Doxycycline

3. Specify an antibiotic that can cause severe depression of hematopoiesis, dyspepsia, "grey baby" syndrome:

- A. Tetracycline
- B. Lincomycin
- C. Ceftriaxone
- D. Neomycin sulfate
- E. Laevomycetin

4. The patient with pneumonia and anaphylaxis to penicillin. What antibiotic can be assigned to in this case?

- A. Ceftriaxone
- B. Azithromycin
- C. Laevomycesin
- D. Tetracycline
- E. Polymyxin B

5. Specify a semisynthetic antibiotic, undergoing significant entero – hepatic recirculation:

- A. Penicillin
- B. Doxycycline
- C. Tetracycline
- D. Cefazolin
- E. Oxacillin

II. Original practical work in class

1. To view the collection of drugs.
2. Work with the tests (Krok-1).
3. Prescribe and ground the choice of drug:

- 1) myelotoxic antibiotic;
- 2) this is a nephrotoxic antibiotic;
- 3) to treat a purulent wound;
- 4) an antibiotic with high osteotropy;
- 5) a semi-synthetic antibiotic that disrupts the formation of tooth enamel;
- 6) an antibiotic that causes an endotoxic reaction;
- 7) an antibiotic that causes an allergic reaction of the immediate type;
- 8) an antibiotic that causes an allergic reaction of the delayed type;
- 9) an antibiotic that causes a muscle relaxant effect.

Unit 46. SULFONAMIDES.

Actuality of the unit. Sulfonamides were the first highly effective antibacterial agents. They have been used since 1935. At present, more than 20 sulfonamides are used in medical practice. All sulfonamides have got the wide spectrum of antimicrobial activity, the same mechanism of bacteriostatic action, and the difference is only in their pharmacokinetic properties. They are not as active as antibiotics, but the difference between them is that the sulfonamides do not have toxic effect on the cells of organism, as the antibiotics do; sulfonamides cause the secondary infections more seldom. At the current time the interest to sulfonamides has highly increased due to their relative safety, introduction of sulfonamides with prolonged terms of activity, but mainly due to the synergistic combination of *sulfamethoxazole* with *trimethoprim* (generic name, *co – trimoxazole*).

Widely used as antibacterial agents received derivatives of 8-hydroxyquinoline, imidazole, quinoxaline. Detected a high chemotherapeutic activity of the 4-quinolone. Today, all over the world are widely used fluoroquinolones. Their distinguishes from other himioterapeutics drugs a broader spectrum of activity. Today, the choice of antibiotic individual patient due not only to the sensitivity of the pathogen, but also side effects of the substance.

I. Individual work

Control questions

SULFONAMIDES

1. General characteristics, history of discovery.
 2. Mechanism and spectrum of antibacterial activity.
 3. Pharmacokinetics of sulfonamides.
 4. Classification of sulfonamides:
- A) Preparations, well absorbed from gastrointestinal system, with resorptive action:

- a) short – acting – Streptocide (Sulfanilamide), Norsulfazolum (Sulfathiazole), Sulfacyl – natrium, Aethazolum (Sulfaethidole);
- b) long – acting – Sulfapyridazinum, Sulfadimethoxine (Madribon);
- c) ultralong – acting – Sulfalene.

B. Preparations, poorly absorbed from gastrointestinal system, used for the treatment of intestinal infections – Phthalazolum (Phthalylsulfathiazole).

C. Combined preparations:

- a) with Salicylic acid for the treatment of non – specific ulcerative colitis – Salazopyridazinum, Salazosulphapyridine;
- b) with Trimethoprim – Co – trimoxazole (Biseptol, Bactrim).

D. Preparations for local usage – Streptocide, Sulfacyl – natrium and other sodium salts of sulfonamides.

5. Principles of the rational sulfonamide therapy.

6. Usage of sulfonamides for the therapy of different infection diseases.

7. Undesirable effects of sulfonamides, prevention and treatment.

8. Interaction of sulfonamides and other drugs (anticoagulants, Diphenin, antidiabetic, Hexamethylenetetramine, antibiotics and other antimicrobial drugs).

List of practical works. Prescribe drugs with their application (*separately from the prescription!*):

№	Name of the drug	Drug form
1.	Sulfalen (<i>Sulfalenum</i>)	Tab. 0,2 and 0,5
2.	Ftalazol (<i>Phthalazolum</i>)	Tab. 0,5
3.	Biseptol (<i>Biseptol</i>) syn.: Co-trimoxazole, Bactrim	Biseptol (co – trimoxazole), patented tab. – for adults: Biseptol – 480; for children: Biseptol – 120; oral suspension Bot. 100 ml.
4.	Sodium sulfatsil (<i>Sulfacylum – natrium</i>) syn.: Albucidum	Eye drops 30 % 10 ml.

Tasks for self-control. Choose the correct answers:

1. Why can blood disorders (anemia, leukopenia, agranulocytosis) occur when taking sulfonamide drugs?

- A. Violation of vitamin synthesis
- B. activation of lipolysis
- C. Destruction of the cell membrane
- D. Inhibition of glycolysis
- E. catabolic disorders

2. Why, when prescribing sulfonamides, does the doctor direct the patient to monitor diuresis and consume 1.5-2 liters of alkaline mineral water per day?

- A. To prolong the action
- B. To reduce the irritating effect on the stomach
- S. To neutralize the acid of gastric juice
- D. To shift the blood pH in the alkaline direction
- E. For the prevention of crystallization of acetyl derivatives of the drug in renal tubules

3. Sulfanilamides are widely used as bacteriostatic agents. The mechanism of antimicrobial action of sulfonamide drugs is based on their structural similarity with:

- And antibiotics
- B Glutamic acid
- C Folic acid
- D Nucleic acid
- E Para-aminobenzoic acid

4. Specify sulfanilamide, which is poorly absorbed in the gastrointestinal tract:

- A. Streptocide
- B. Co-trimoxazole
- S. Ciprofloxacin

- D. Sulfadimezin
- E. Phthalazole
- 5. *What combined sulfonamides do you use?*
- A. Ampioks
- B. Sulfalen
- S. Furadonin
- D. Cotrimoxazole
- E. Ciprofloxacin

II. Original practical work in class

1. To view the collection of drugs.
2. Work with the tests (Krok-1).
3. Prescribe and ground the choice of drug:
 - 1) sulfanilamide with a long half – life;
 - 2) sulfonamide in case of acute enterocolitis;
 - 3) sulfonamide in case of conjunctivitis;
 - 4) sulfanilamide drug with bactericidal action;
 - 5) antimicrobial with immunosuppressive action.
- 14) sulfanilamide drug that bad absorbed from the gastrointestinal tract;
- 16) sulfanilamide drug for topical application.

Unit 47. ANTIMICROBIAL PREPARATION OF A DIFFERENT CHEMICAL STRUCTURE.

Actuality of the unit: Derivatives of 8-oxyquinoline, imidazole, and quinoxaline are widely used as antimicrobial agents. High chemotherapeutic activity of 4-quinolone derivatives was revealed. Today, fluoroquinolones are widely used all over the world. They are advantageously distinguished from other chemotherapeutics by a wider spectrum of action. Today, the choice of an antibacterial drug for a specific patient is determined not only by the sensitivity of the pathogenic microorganism, but also by the undesirable effects of the substance.

1. QUINOLONES AND FLUOROQUINOLONES. General characteristics. Classification:

- *non – fluorinated quinolones* — Nalidixic acid, Oxolinic acid;
- I generation of fluoroquinolones — *Gram – negative*: Ciprofloxacin, Ofloxacin /Phlox, Tarivid, Zanotsin/ Pefloxacin (Abaktal), Norfloxacin (Norilet et al.), Lomefloxacin (Lomadey, Maxavin);
- II generation — *respiratory*: Levofloxacin (Tavanik), Sparfloxacin and others;
- III generation — *respiratory – anaerobic*: Moxifloxacin (Avelox), Gatifloxacin, Trovafloxacin, and others.

The mechanism and a spectrum of antibacterial action. Comparative characteristics of the generations. Indications for use. Undesirable effects.

2. The mechanism and a spectrum of antibacterial action of 8 – OXYQUINOLONE DERIVATIVES (Nitroxolin, Chlorquinaldon, Qiniofon, Intetrix). Indications for use. Undesirable effects.

3. The mechanism of action and of antibacterial spectrum of NITROFURAN DERIVATIVES (Furacilin, Nifuroxazide, Furazolidone, Furadonin, Furagin). Indications for use. Undesirable effects. Application of acidotic agents (Ammonium chloride, Ascorbic acid, etc.) in the case urinary tract infections.

4. The mechanism and a spectrum of antibacterial action of IMIDAZOLE DERIVATIVES (Metronidazole, Tinidazole). Indications for use. Undesirable effects.

5. The mechanism of action and antibacterial spectrum of OXAZOLIDINONE (Linezolid). Indications for use. Undesirable effects.

6. The mechanism and spectrum of antibacterial action of QUINAZOLINE DERIVATIVES (Dioxidine, Quinoxidin). Indications for use. Undesirable effects.

7. Pharmacology safety and the combined use of drugs.

List of practical works. Prescribe drugs with their application (*separately from the prescription!*):

№	Name of the drug	Drug form
1.	Chlorquinaldol (<i>Chlorchinaldolum</i>)	Tab 0,1 (for adults) and 0,03 (for children)
2.	Nitroxoline (<i>Nitroxolinum</i>) syn.: 5 – NOK	Tab 0,05
3.	Furazolidon (<i>Furazolidonum</i>)	Tab 0,05
4.	Furadonin (<i>Furadoninum</i>) syn.: Nitrofurantoin	Tab 0,05 and 0,1
5.	Ciprofloxacin (<i>Ciprofloxacinum</i>) syn.: Tsiprobay, Tsiprinol, Tsifran	Tab. 0,25; 0,5, 0,75; amp. 1 % 10 ml.; vials 0,2 % 50, 100 ml.
6.	Moxifloxacin (<i>Moxifloxacinum</i>) syn.: Aveloks	Tab,4; vials 400 mg sol of 250 ml. for infusions
7.	Dioxidin (<i>Dioxydinum</i>)	Amp. 1 % 10 ml.; 0,5 % 10 and 20 ml.; ointment 5 % 25,0 or 50,0

Tasks for self-control. Choose the correct answers.

1. *What preparations cause a mutagenic effect?*

- A. Ampioks
- B. Sulfalen
- S. Dioxidin
- D. Metronidazole
- E. Ciprofloxacin

2. *Which preparations belong to fluoroquinolones?*

- A. Furadonin
- B. Co-trimoxazole
- S. Ciprofloxacin
- D. Sulfadimezin
- E. Nitroxoline

acetyl derivatives of the drug in renal tubules

3. *What is the mechanism of antimicrobial action of fluoroquinolones?*

- A. Inhibition of peptidoglycan synthesis
- B. Inhibition of DNA gyrase
- C. Increasing the permeability of the bacterial wall
- D. Inhibition of RNA polymerase
- E. Antagonism with PABA

4. *Specify the drug that slows down the formation of cartilage tissue:*

- A. Furadonin
- B. Co-trimoxazole
- S. Ciprofloxacin
- D. Sulfadimezin
- E. Nitroxoline

5. *What antimicrobials have a disulfiram-like effect?*

- A. Ampioks
- B. Sulfalen
- S. Furadonin
- D. Metronidazole
- E. Ciprofloxacin

II. Original practical work in class

1. To view the collection of drugs.

2. Work with the tests (Krok-1).

3. Prescribe and ground the choice of drug:

- 1) nitrofurantoin derivative in case of acute cystitis;
- 2) nitrofurantoin derivative in case of enterocolitis;
- 3) 8 – oxyquinolone derivative in case of acute pyelonephritis;
- 4) naphthylidene derivative in pyelonephritis;
- 5) fluoroquinolone for the treatment of sepsis;
- 6) fluoroquinolone with anti – anaerobic activity;
- 7) quinazoline derivative in case of purulent pleurisy;
- 8) antimicrobial with immunosuppressive action.
- 13) a drug that inhibits DNA-hydrolyzing bacteria;
- 14) anaerobic respiratory fluoroquinolone;
- 17) a derivative of imidazole.

Unit 48. ANTITUBERCULOSIS, ANTISPIROCHETAL, ANTIPROTOZOAL DRUGS

Actuality of the unit. Until 1940, there was no effective chemotherapeutic agents for the treatment of tuberculosis. The first step in the development of TB chemotherapy was the opening in 1941, PAS. However, the main role in the transformation of the terrible scourge of tuberculosis in humanity curable disease played an antibiotic-streptococcal mitsin and simple chemical compound - isonicotinic acid hydrazide (INH), opened respectively in 1942 and 1954. Subsequently arsenal replenished several anti-TB drugs (rifampicin, ethambutol, some fluoroquinolones, etc.). However this does not solve the problem of medical treatment of the disease. The main reason for reducing the effectiveness of treatment for tuberculosis is the development of poly- and multidrug in mycobacteria, to overcome the anti-TB drugs that are administered in combination. At the beginning of the treatment to the simultaneous use of 3 preparations, for example, rifampicin, streptomycin and isoniazid. The social importance of TB diagnosis requires vigilance doctor in any specialty and knowledge of anti-TB drugs and their interactions with other drugs.

Syphilis is also a social disease. When treated with penicillin, it lasts for years and decades. The first tool for the treatment of syphilis (mercury compounds and mercury ointment) proposed the famous Paracelsus. Later they began to be used salts of arsenic and bismuth, which are now virtually out of the medical applications in connection with the appearance of a large arsenal of highly effective and much less toxic antibiotics. But, nevertheless, some bismuth preparations (bismuth) still have application in cases of spirochete infections resistant to antibiotics.

Pathogenic protozoa cause protozoan disease. In our country, the most common giardiasis, toxoplasmosis, trichomoniasis, chlamydia. In some regions still are cases of malaria, amebiasis, balantidiasis, leishmaniasis. The world's annual deaths due to malaria is about 1-2 million people. Therefore, the social significance of these diseases is important in the health of our country.

I. Individual work

Control questions

ANTITUBERCULAR DRUGS

1. General characteristics. History of discovery of basic drugs.

2. Classification:

Group A — drugs *most effective*:

- antibiotics — Rifampicin, Ethambutol;
- synthetic drugs — derivatives INH (Isoniazid);

Group B — drugs *with intermediate efficiency*:

- antibiotics — Streptomycin, Kanamycin, Capreomycin, Viomycin, Cycloserine;
- synthetic drugs — Ethambutol, Ethionamide, Protionamid, Pyrazinamide, fluoroquinolone (Ofloxacin, Lomefloxacin, and others.).

Group C — *drugs with low efficiency*:

- synthetic drugs — Sodium PASA, Thiacetazone (Tibon).
 3. Characteristics of the main groups. Comparative effectiveness. Adverse reactions.
 4. General principles of chemotherapy for tuberculosis.
- ANTISYPHILITIC DRUGS. General characteristics. Classification:
- *antibiotics*: first choice — penicillins; alternative — cephalosporins, macrolides, tetracyclines.
 - *bismuth* preparations (Biyohinol, Bismoverol).

Mechanism of antimicrobial activity of separate groups. Intoxication with Bismuth preparations, treatment.

ANTIPROTOZOAL DRUGS. General characteristics.

A. **Antimalarial drugs**. Classification:

1. Haematoschizontropic (blood schizontocides) — drugs effective against erythrocytic forms: Chloroquine, Chloridin (Pyrimethamine), Mefloquine, Acrichinum (Mepacrine), Quinine, sulphonamides. They are used for relief of acute attacks of malaria;
2. Histoschizontropic (tissue schizonticides) drugs:
 - influencing on the pre – erythrocytic (primary exoerythrocytic) forms: Primaquine, Chloridin (Pyrimethamine). Used for prevention or treatment of early relapses of the illness;
 - influencing on the paraerythrocytic (secondary exoerythrocytic) forms: Primaquine, Quinocide. Used for prevention of late relapses.
3. Gamontotropic drugs (influencing on the sexual forms of plasmodia):
 - Gamontocides — Primaquine, Chinocide;
 - Sporocides — Chloridin (Pyrimethamine)
4. Combined preparations — Fansidar, Metakelfin.

The mechanism of action of individual groups of drugs. The principles and steps for using antimalarials: individual and collective prevention of disease; relief of acute attacks; treatment and prevention of tissue forms of malaria relapses.

B. **Antiamebic drugs**. Classification:

- *drugs influencing on amebas in all sites of their localization* — Metronidazole, Tinidazole;
- *drugs influencing on amebas in the lumen* — Quiniofon, Intetrix, Chlorquinaldol, Etofamide;
- *drugs influencing on amebas in the lumen and intestinal wall* — Tetracycline;
- *drugs influencing mostly on the tissue forms of amebas in the intestinal wall and in the liver* — Emetine;
- *drugs influencing mostly on the tissue forms of amebas in the liver* — Chloroquine.

C. **Antilambliasis drugs**: Metronidazole, Furazolidone, Chloroquine.

D. Drugs for chemotherapy of the **toxoplasmosis**: Chloridin, Chloroquine, Tetracycline, sulfonamides, macrolides.

E. **Antitrichomoniasis drugs**: Metronidazole, Tinidazole, Osarsol, Trichomonacide. Mechanism of Metronidazole activity.

F. Drugs for chemotherapy of the **chlamydiosis**: Doxycycline, macrolides, Metronidazole, fluoroquinolones.

G. **Antileishmaniasis drugs**: antimony drugs (Meglumine), Neomycin, Metronidazole, Quinacrine.

H. Drugs for chemotherapy of the **balantidiasis**: Quiniofon; Mexaform, Tetracycline, Monomycin, Aminarsonum.

General characteristics. The mechanism of action. Pharmacology safety and the combined use of drugs.

List of practical works. Prescribe drugs with their application (*separately from the prescription!*):

№	Name of the drug	Drug form
1.	Isoniazid (<i>Isoniazidum</i>)	Tab 0,3; amp 10 % sol 5 ml.
2.	Rifampicin (<i>Rifampicinum</i>)	Caps 0,15, 0,3, 0,45; amp 0,15

3.	Sodium para – aminosalicylate (<i>Natrii para – aminosalicylas</i>) syn.: PASA	Tab 0,25 and 0,5
4.	Ekstentsillin (<i>Extencilline</i>) syn.: Bicillin 1, Benzyl penicillin benzathine	Vials 1 200 000 and 2 400 000 IU
5.	Biyohinol (<i>Biiochinolum</i>)	Vials 100 ml.
6.	Chloroquine (<i>Chloroquinum</i>) syn.: Quingamin, Delagil	Tab 0,25; amp 5 % sol 5 ml.
7.	Hloridin <i>Chloridinum</i> syn.: Pyrimethamine	Tab 0,005 and 0,01
8.	Quinine sulfate (<i>Chinini sulfas</i>)	Tab. 0,25 and 0,5
9.	Metronidazole (<i>Metronidazolium</i>)	Tab. 0,25 and 0,5; vaginal supp. 0,5; amp. 0,5 % sol. 10 and 20 ml.; vials 0,5 % 100 ml.

Tasks for self-control. Choose the correct answers.

1. Specify antitubercular drug effective in the intracellular location of the mycobacterium:
 - A. Sodium pair aminosalicylate
 - B. Isoniazid
 - S. Ethambutol
 - D. Streptomycin
 - E. Ethionamide
2. On the third day after syphilis treatment by benzylpenicillin such symptoms as fever, enlarged lymph nodes appeared. What is the reason?
 - A. Inefficiency the drug
 - B. Endotoxin reaction
 - C. Superinfection
 - D. Idiosyncrasy
 - E. Cumulation
3. Which drug causes hypersalivation, dark staining on the gingival edge, gingivitis, stomatitis, nephropathy, polyneuritis?
 - A. Primaquine
 - B. Metronidazole
 - S. Biiochinol
 - B. Chloroquine
 - E. Rifampicin
4. Specify the antiprotozoal drug, possessing immunosuppressive, anti – inflammatory, anti – arrhythmic action:
 - A. Primaquine
 - B. Fansidar
 - C. Tetracycline
 - D. Chloroquine
 - E. Metronidazole
5. Which drug should be appointed at the multi – organ localization of amebiasis (intestinal lesions, liver, lungs)?
 - A. Chloroquine
 - B. Furazolidon
 - I. Metronidazole
 - D. Tetracycline
 - E. Emetine hydrochloride

II. Original practical work in class

1. To view the collection of drugs.
2. Work with the tests (Krok-1).
3. Prescribe and ground the choice of drug:
 - 1) antituberculosis drug, which is the mechanism of action similar to sulfonamides;
 - 2) antituberculosis agents – antagonist of vitamin B₆;
 - 3) antituberculosis antibiotic that causes red discoloration of urine;

- 4) metal – containing drug for the treatment of syphilis;
- 5) anti-tuberculosis drug - a derivative of HINA;
- 6) drug for removal of acute malaria fit;
- 7) for prophylaxis of malaria;
- 8) drug for treatment of intestinal amebiasis;
- 9) drug with anti – amebial, anti – lamblial and anti – toxoplasma activity;
- 10) antibiotic for toxoplasmosis treatment;
- 11) drug for the treatment of chlamydia.
- 12) antichlamydial drug - DNA gyrase inhibitor;
- 13) hematoschizotropic drug;
- 14) sporontocidal agent;
- 15) anti-leishmaniasis agent;
- 16) preparation that acts on amoebae in the lumen and intestinal wall;
- 17) preparation for the treatment of balantidiasis;
- 18) a drug that inhibits DNA-dependent RNA polymerase and inhibits mycolic acid synthesis.

Unit 49. ANTHELMINTIC AND ANTIFUNGAL PREPARATIONS

Actuality of the unit. Pathogenetic fungi and viruses cause diseases, which are wide spread. Adequate choice of therapy depends on the knowledge of pharmacokinetics and toxic parameters. Few anti – viral agents directly affect viruses in the extra – cell period of life. That is why it is very hard to find the preparations with the specific effect on viral corpse and with no effect on the human (host) cells. The problem of anthelmintic agents is also very important. While living in human organism helminths are using the tissue liquor as nutrition, they disturb the mechanism of metabolism. Also a physician due to wide spreading of dermatomycosis, systemic mycosis and candidamycosis should now numerous modern antimycotic agents. As the rule candidamycosis develop as aggravation of chemotherapy of inflectional diseases.

I. Individual work

Control questions

ANTHELMINTIC DRUGS

1. General characteristics, history of usage.
2. Classification:
 - A. Drugs for the treatment of intestinal **nematodiasis** (*ascariasis, enterobiasis, necatoriasis, trichocephaliasis, ankylostomiasis*):
 - destroying the helminthes metabolic processes — Albendazole (Zentel), Mebendazole (Vermoxum), Levamisole (Dekaris), Naftamon, Pirviny pamoate;
 - paralytic action — Pyrantel (Combantrin), Piperazine adipate, Ethylene tetrachloride;
 - B. Drugs for the treatment of intestinal **cestodiasis** (*diphyllobothriasis, teniasis, teniarinchosis*):
 - paralytic action — Praziquantel, Fenasal, Dichlorophen, Filixan, Pumpkin seeds;
 - destroying the helminthes metabolic processes — Aminoacriqinum.
 - C. Drugs for the treatment of **systemic helminthoses**:
 - **trematodoses** (*opistorhoze, fascioliasis, clonorchiasis, paragonimiasis, schistosomiasis*) — Praziquantel, Hloksil, Antimony sodium tartrate;
 - **nematodoses** (*trichinosis, filariasis*) — Ivermectin, Ditrazin, Mebendazole;
 - **cestodiasis** (*echinococcosis, cysticercosis*) — Albendazole, Mebendazole, Praziquantel.
3. Mechanisms of action for separate groups. Special features, adverse effects.

ANTIFUNGAL DRUGS

1. General characteristics.
2. Classification:
 - A. Drugs for the treatment of **dermatomycosis**:

- *azoles*: for local usage — Clotrimazole, Miconazole; for systemic – Ketoconazole, Itraconazole etc.;
- *antibiotics* — Griseofulvin etc;
- *acids* — Salicylic, Benzoic;
- *dyes* — Brilliant green, Methylene blue;
- *Iodine preparations* — Spirituous sol. of iodide, Kalium iodide;
- *preparations from different chemical groups* — Undecine, Zincundane, Mycoheptinum, Nitrofungin, Naftifine, Ciclopirox, Terbinafine, Tolnaftate.

B. Drugs for the treatment of candidamycosis:

- *azoles*: for local usage — Clotrimazole, Miconazole; for systemic – Ketoconazole, Intraconazole etc.;
- *polyene antibiotics* — Nystatin, Levorin, Mycoheptinum, Amphotericin B;
- *antiseptics* — Dekamin, Ciclopirox, Vagotil et al.

C. Drugs for the treatment of systemic mycosis: *polyene antibiotics* (Amphotericin B, Amphoglucaminum, Mycoheptinum), *azoles* for systemic usage (Ketoconazole, Fluconazole, Itraconazole).

3. Classification of the AZOLES:

1) *imidazole* derivatives*:

- 1st generation (only for local usage 2 – 3 times per day, course – 2 – 6 weeks): Clotrimazole, Miconazole, Isoconazole, Amikazole, Bifonazole;
- 2nd generation (locally, course – 2 – 3 days): Econazole, Tioconazole;
- 3^d generation (for local and systemic therapy, 1 time per day): Ketoconazole, Sulconazole, Oxiconazole;

2) *triazole* derivatives: Fluconazole, Itraconazole, Terconazole.

4. Mechanisms of action of the separate groups. Adverse effects.

List of practical works. Prescribe drugs with their application (*separately from the prescription!*):

№	Name of the drug	Drug form
1.	Mebendazole (<i>Mebendazolium</i>) syn.: Vermoxum	Tab. 0,1
2.	Pyrantel (<i>Pyrantelum</i>)	Tab. 0,25; susp. in Bot. 15 ml. (50 mg/1ml.)
3.	Fenasal (<i>Phenasalum</i>)	Tab. 0,25
4.	Praziquantel (<i>Praziquantel</i>)	Tab. 0,6
5.	Amphotericin B (<i>Amphotericinum B</i>)	Vials 50.000 units
6.	Nystatin (<i>Nystatinum</i>)	Tab. 250000 and 500000 units; vaginal supp. 250000 units; ointment in tubes 15,0 (1 g – 100.000 units)
7.	Griseofulvin (<i>Griseofulvinum</i>)	Tab. 0,125; susp. in Bot. 100 ml.
8.	Clotrimazole (<i>Clotrimazole</i>)	Intravaginal tab. 0,1; cream 1% 20,0; sol. 1% 15 ml.
9.	Fluconazole (<i>Fluconazole</i>) syn.: Diflucan	Sol. in vial 0,2 %; caps. 0,05; 0,1; 0,15 and 0,2

Tasks for self-control. Choose the correct answers.

1. Name the antihelminthic agent that has immunomodulatory properties:

- A. Piperazine
- B. Mebendazole
- C. Pyrantel

* К производным имидазола относятся и препараты, обладающие антибактериальным, антипротозойным и противогельминтозным спектрами действия (метронидазол, тинидазол, мебендазол и др.).

- D. Levamisole
E. Naftamon
2. *What preparation is advisable to appoint at the mixed intestinal and extra – intestinal helminthic invasion?*
A. Praziquantel
B. Levamisole
C. Pyrantel
D. Chloxil
E. Piperazine adipate
3. *For the treatment of systemic mycosis amphotericin B is appointed. What is TRUE about this drug?*
A. Appointed only in systemic mycosis
B. Well absorbed in the digestive tract
C. It inhibits the synthesis of the cell wall polymers
D. Has fungistatic activity
E. Cause severe hepato, nephrotoxic, myelotoxic effects
4. *What drug should be prescribed for intestinal nematodes?*
A. Acyclovir
B. Azidothymidine
C. Abendazole
D. Bonafton
E. Ganciclovir
5. *For which disease is fluconazole prescribed?*
A. Influenza
B. Chickenpox
C. Viral hepatitis
D. Candidomycosis
E. Shingles

II. Original practical work in class

1. To view the collection of drugs.
2. Work with the tests (Krok-1).
3. Prescribe and ground the choice of drug:
 - 1) drug for the treatment of enterobiosis with metabolic action;
 - 2) a medicine for the treatment of teniarinosis;
 - 3) a drug in the treatment of teniasis;
 - 4) for local treatment of candidamycosis;
 - 5) imidazole derivative for the treatment of dermatomycosis;
 - 6) antibiotic for treatment of systemic mycosis;
 - 7) at extraintestinal trematodosis;
 - 8) at extraintestinal cestodiasis;
 - 9) antimikoznoe agent from the group of polyene antibiotics;
 - 10) for treating tinea dyes from the group;
 - 11) triazole;
 - 12) preparation of replacing itraconazole.

Unit 50. ANTIVIRAL PREPARATIONS

Actuality of theme. Viruses cause diseases that are widespread and of current social importance (viral hepatitis, influenza, herpes, AIDS). Knowledge of pharmacokinetic and toxicity parameters is of great importance for an adequate selection of drugs. Only certain drugs have a direct harmful effect on viruses in the extracellular period of life, which is due to the peculiarities of the biology of viruses. In this regard, it is extremely difficult to find selectively acting means that would affect viruses without damaging the cells of the "host".

I. Independent work**control questions****ANTIVIRAL DRUGS**

1. General characteristics.

2. Classification *according to origin*:– **Interferons** (Interferon, Interlock, Reaferon, Alferon, Betaferon) and **interferon inducers** (Poludan, Amixin, Arbidol);– **Synthetic drugs**:

- amantadine derivatives — Remantadine, Midantanum;
- analogs of nucleosides — Idoxuridine, Acyclovir, Ribavirin, Gancyclovir, for AIDS treatment – Zidovudine (Azidothymidine), Lamivudine etc.;
- from different groups — Bonafton, Oxolin, Florenalum, Tebrophen etc

3. Classification *according to indications*:– Influencing the **DNA – containing viruses**:

- herpesviruses: *herpes simplex* — Acyclovir, Foscarnet, Vidarabine, Trifluridine; *herpes zoster and chicken pox, cytomegalovirus* — Acyclovir, Ganciclovir, Foscarnet;
- *smallpox virus* — Metisazon;
- *hepatitis virus B and C* — Interferons, Amixin.

– Influencing the **RNA – containing viruses**:

- *HIV (antiretroviral)* — HIV reverse transcriptase inhibitors (Azidothymidin, Lamivudine, Didanosine, Nevirapine), HIV protease inhibitors (Saquinavir, Indinavir, and others.);
- *influenza virus type A* — Amantadine, Amiksin;
- *influenza virus types A and B* — neuraminidase inhibitors (Zanamivir, Oseltamivir), Arbidol;
- *Respiratory syncytial virus* — Ribavirin.

4. Classification of antiviral drugs by mechanism of action:

- inhibit the virus adsorption to the cell and its penetration into the cell, as well as the process of releasing the viral genome - midantan and rimantadine;
- inhibit the synthesis of early proteins of the virus - guanidine;
- inhibit the synthesis of nucleic acids - zidovudine, acyclovir, vidarabine, idoxuridine;
- oppress "assembly" virions - metisazon;
- cells increase resistance to the virus - interferons.

5. INTERFERONS. Classification by *types and origin*:

- **natural** (culture of human leukocyte cells stimulated by viruses): α – *interferon* (human leukocyte interferon, Egiferon, Velferon), β – *interferons* (Torayferon);
- **recombinant** (by genetic engineering): *interferons* α – 2A (Reaferon, viferon, Roferon, Pegasys), *interferons* α – 2B (Laferon, Intron – A, Inreko), α – 2C (Berofer), β – *interferons* (Betaferon, Fron), γ – *interferons* (Gammaferon, Immukin, Immunoferon).

5. Pharmacological characteristics of the main representatives of antiretrovirals, antinflu, antiherpetic drugs. Undesirable effects. Pharmacology safety and the combined use of drugs.

6.

List of practical works. Prescribe drugs with their application (*separately from the prescription!*):

№	Name of the drug	Drug form
1.	Rimantadine (<i>Remantadinum</i>)	Tab. 0,05
2.	Laferon (<i>Laferonum</i>) syn.: interferon alfa – 2b recombinant	Vial by 1000000 IU
3.	Pegasys (<i>Pegasys</i>) syn.: peginterferon alfa – 2a	Vial by 0,5 and 1 ml. (0,18 and 0,135)
4.	Acyclovir (<i>Aciclovir</i>)	Tab. 0,2; ophthalmic ointment 3 %, creme in tubes 5 % 5,0
5.	Azidothymidine (<i>Azidotimidin</i>) syn.:	Caps. 0,1 and 0,25; sol. for infusion in vial

Zidovudine	2% 20 ml.
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Tasks for self-control. Choose the correct answers:

1. Name an antiviral agent that has immunomodulatory properties:

- A. Piperazine
- B. Mebendazole
- C. Viferon
- D. Levamisole
- E. Naphtamon

2. What drug should be prescribed for chicken pox?

- A. Praziquantel
- B. Acyclovir
- C. Pyrantel
- D. Khloxyol
- E. Piperazine adipinate

3. What drugs suppress the adsorption of the virus on the cell and its penetration into the cell?

- A. Praziquantel
- B. Midantan
- C. Rimantadine
- D. Khloxyol
- E. Piperazine adipinate

4. What drug must be prescribed for the prevention of influenza A?

- A. Acyclovir
- B. Azidothymidine
- C. Rimantadine
- D. Bonafton
- E. Ganciclovir

5. For which disease is zidovudine prescribed?

- A. Influenza
- B. Chickenpox
- C. Viral hepatitis
- D. HIV infection
- E. Shingles

II. Original practical work in class

1. To view the collection of drugs.
2. Work with the tests (Krok-1).
3. Prescribe and ground the choice of drug:
 - 1) recombinant drug with antiviral and antitumor activity;
 - 2) an antiretroviral drug that is a nucleotide analogue;
 - 3) an antiviral agent - an amantadine derivative;
 - 4) antiviral agent - analogue of nucleosides;
 - 5) for the treatment of viral hepatitis B and C;
 - 6) when infected with cytomegalovirus;
 - 7) itraconazole replacement drug.

Unit 51. CHECKING OF PRACTICAL SKILLS ON “ANTIMICROBIAL, ANTIVIRAL AND ANTI-PARASITIC AGENTS”

CONTENT MODULE VII. DRUGS AFFECTING ORGAN SYSTEMS, THERAPY OF EMERGENCY CONDITIONS, PHARMACOTOXICODYNAMICS.

Actuality of section. The section devoted to drugs for the pharmacotherapy of the pathology of individual systems summarizes and repeats many groups of drugs that were studied in previous topics ("Agents affecting the afferent and efferent nervous system", "Agents affecting the CNS " etc). In addition, a clinical approach to the selection of drug groups in the case of disorders of the gastrointestinal tract, breathing, and reproductive activity is being formed, which determines the importance of this section.

FIRST AID is a set of medical measures aimed at providing medical assistance in emergency situations that occur at work, in everyday life, during traffic accidents, catastrophes, man-made accidents and acute neurological, therapeutic, surgical and terminal conditions. Failure to provide first aid in the event of accidents, sudden acute illnesses of a person leads to serious consequences, up to death. Timely first aid. plays an important role in the further treatment of victims and patients, contributes to shortening the terms of their medical and labor rehabilitation.

The side effect of drugs is becoming an increasingly urgent medical and social problem. According to various authors, adverse drug reactions are observed in 10-30% of the population, in 3% of cases they are the reason for consulting a doctor, in 5% - the reason for hospitalization, in 3% - the reason for intensive therapy, in 12% lead to a significant increase in the length of stay of patients in the hospital, and in 1% of patients in general can be the cause of fatal consequences. In Ukraine, this problem is also becoming more and more relevant.

Learning objectives. Know: the pharmacology of drugs that affect the functions of the gastrointestinal tract, breathing, and reproductive activity. Pharmacotherapy of emergency conditions and acute poisonings, the risk of developing toxic effects of drugs and its prevention.

Be able to: justify the choice and prescribe the drugs of this section in different dosage forms, solve test tasks, situational and pharmacotherapeutic tasks.

Interdisciplinary integration. Normal and pathological anatomy, physiology, pathological physiology, biochemistry of the digestive, respiratory and reproductive systems.

Unit 52-53. DRUGS AFFECTING ON THE GASTROINTESTINAL SYSTEM

Actuality of the unit. Agents that affect the function of digestive organs - one of the important sections of pharmacology, which includes groups of substances that ensure the normalization of various components of the digestive process - appetite, secretory function of the stomach, pancreas, liver, as well as motility of the gastrointestinal tract . Currently, infectious and toxic hepatitis, peptic ulcer disease of the stomach and duodenum, appetite disorders and, as a result, excess body weight or body weight deficiency are increasingly common. Therefore, the doctor should be aware of modern groups of drugs used to correct disorders of the gastrointestinal tract.

I. Individual work

Control questions

1. Classification of drugs affecting the digestive system:
 - 1) affecting the *appetite and digestive function*:
 - stimulating (orexigenic);
 - inhibiting appetite (anorexigenic);
 - 2) affecting the function *of the salivary glands*;
 - 3) used at disturbances *of gastric secretory function*:
 - stimulating;
 - inhibiting;
 - gastroprotectives;

- agents improving regeneration mucosa of stomach and duodenum;
- 4) *emetic drugs, antiemetic*;
- 5) affecting *the motility of the gastrointestinal tract*:
 - enhancing motility and laxatives;
 - reducing motility and anti – diarrheals.
- 6) *hepatotropic*;
- 7) regulating *the function of pancreas*.
 1. Drugs STIMULATING of APPETITE:
 - reflector stimulators: a) bitters (infusions and tinctures of bitter plants); b) flavoring and extracted substances (cinnamon, pepper, garlic, broths, decoctions of vegetables);
 - central stimulators: Peritol.

Mechanisms of action. The indications to application. Undesirable effects.
 3. Drugs, DECREASING of APPETITE (anorexic)*:
 - serotoninomimics ** – Mazindol, Sibutramine, Fenfluramine;
 - adrenomimetics, dofaminomimetics – phenylalkylamines derivatives (Phepranon, Dezopimon),
 - dofaminomimetics – Bromocriptine.

Mechanisms of action. Indications for use. Undesirable effects.
 4. Pharmacological regulating secretion of SALIVARY GLANDS: stimulators — M – cholinomimetics, anticholinesterase; inhibitors — M – cholinoblockers
 5. Drugs STIMULATING SECRETION function of the stomach: *for diagnostics* — Pentagastrin, Histamine; *for replacement therapy* — Gastric juice natural, Acidin – pepsin, Abomin, Panzinorm forte, carbonated mineral water. Indications for use.
 6. Drugs SUPPRESSING SECRETION function of stomach (antiulcer):
 - 1) Inhibitors of H⁺, K⁺, ATP – ase (proton pump): 1 generation — Omeprazole; 2 generation — Pantoprazole, Rabeprazole (Pariet, Kontrolok), Esomeprazole, Lansoprazole, and others.;
 - 2) blockers of H₂ – histaminoreceptors: 1 generation — Cimetidine ***; 2 generation — Ranitidine, 3 generation — Famotidine, Nizatidine, Roxatidine etc.;
 - 3) M₁ – cholinoblockers — Gastrocepin;
 - 4) drugs diminishing excitement of vagal endings – antacids, adsorbents, coating demulcents, astringents, local anaesthetics (see unit 13);
 - 5) substances regulating intensity of excitation of CNS and vegetative centers – tranquilizers, psychosedatives, antidepressants;
 - 6) adjuvant therapy (for special reasons):
 - ✓ antihelicobacter agents — antibiotics (semisynthetic penicillins, macrolides, tetracycline) synthetic antimicrobials (Metronidazole, bismuth preparations);
 - ✓ gastroprotectors and agents that improve regeneration of the stomach mucous;
 - ✓ normalizing gastric motility and duodenum — spasmolytics, prokinetics.

Pharmacodynamics, pharmacokinetics proton pump inhibitors, H₂ – histamine blockers. Differences between generations, advantages and disadvantages. Undesirable effects. Application. Modern approaches to the treatment of peptic ulcer.
 7. GASTROPROTECTORS. Classification:
 - providing mechanical protection of the mucous membrane — Sucralfate, colloidal bismuth preparations (bismuth subcitrate colloidal /De – nol/);
 - increasing mucosal resistance to damaging factors — Dalargin, prostaglandin analogues (Misoprostol).

Pharmacological characteristics.
 8. Drugs IMPROVING REGENERATION of the mucous membrane of the stomach and duodenum — steroid anabolics (Nerobol, Retabolil), non – steroid anabolics (Methyluracil, Riboxin,

* To anorexigenic also belong agents that decrease lipids absorption (orlistat) and carbohydrates (biguanides) in GI tract

** SSRI antidepressants also possess anorexigenic action (unit №19)

*** Excluded from medical practice because of significant toxicity

Potassium orotate) vitamin U (Methylmethionine), DOXA, Gastrofarm, Sodium oxyferrous carbon, Dalargin. Mechanisms of action. Indications to application.

9. Emetic drugs (see unit 12).

10. ANTI – EMETIC drugs:

- Central – acting — neuroleptics (Aminazinum, Etaperazine), antiserotonin (Granisetron, Ondansetron, Tropisetron); dopamine – blockers (Domperidone, Metoclopramide), M – cholinoblockers (Atropine, Scopolamine, Aeron), antihistamine (Diprazin, Dimedrolum);
- Peripheral – acting – drugs diminishing excitement of vagal endings – Anaesthesin, Tincture of mint, Menthol, coating demulcents, astringents). Indications to application.
- Anti – regurgitants — Cisapride.

Indications to application.

11. Drugs STRENGTHENING PERISTALSIS of gastrointestinal tract tract:

- enhancing efferent innervation — M – cholinomimetics, anticholinesterase agents, serotonin and dopamine – blockers (Metoclopramide, Domperidone, Cisapride), sodium chloride, etc.;
- laxatives (see unit 12);

12. Drugs REDUCING PERISTALSIS of gastrointestinal tract tract:

- reducing efferent innervation: M – cholinoblockers, myotropic spasmolytics
- antidiarrheals:
 - *symptomatic agents*: enveloping, astringents, absorbent (Lignosorb, Attapulgit, Smectite), spasmolytics, M – cholinoblockers agonists of opiate receptors of the intestine – Loperamide (Imodium), etc.;
 - *for diarrhea caused by infectious process*: antimicrobials (Phtalazol, Tetracycline, Chloramphenicol, Intetrix, Enterosediv et al.), drugs that regulate intestinal biocenosis (probiotics – Biphydumbacterin, Bactisubtil, Linex, Hilak et al.)

Mechanisms of action. Indications for use.

13. HEPATOTROPIC. Basic principles of treatment of liver disease: causal treatment (antivirals, antimicrobials), pathogenetic (hepatoprotectors influencing the processes of tissue metabolism (antioxidants vitamins, amino acids and protein hydrolysates, etc.), adsorbents, antidotes, inhibitors and inducers of microsomal systems performing the metabolism of xenobiotics, immunomodulators, anti – inflammatory, cholelitholytic (Henofalk, Ursafalk), choleric).

Classification of *hepatoprotectors*:

- based on flavonoids — milk thistle (Gepabene, Legalon, Carsil, Gepatofalk – plantations, Silibor); other plants – Hofitol, Cathergen (Cianidanol), Liv – 52 (Gepaliv);
- organopreparations of animal origin — Syrepar, Hepatosan;
- containing essential phospholipids — Essentiale, Phosphogliv, Essliver;
- drugs of different groups — Boehmite, Ademetionine (Heptral), lipoic acid (Thioctacid, Valium), Hepa – Merz (Ornithine), etc.

Mechanisms of action of the main groups. Indications for use. Undesirable effects.

14. Drugs regulating function of PANCREAS:

- stimulators — bitters, acids;
- inhibitors — proteolysis inhibitors: aprotinin (Contrycal, Gordoks), phytopreparations;
- for replacement therapy — Pancreatin, Mezym – forte, Festal, Panzitratt, Panzynom, Betaine. Preparations inhibiting the function of pancreas – inhibitors of proteolysis (Contrykal), phyto – preparations.

Mechanisms of action of the main groups. Indications for use. Undesirable effects.

Pharmacology safety and the combined use of drugs.

List of practical works. Prescribe drugs with their application (*separately from the prescription!*):

№	Name of the drug	Drug form
1.	Ranitidine (<i>Ranitidine</i>)	Tab. 0,15, 0,3
2.	Famotidine (<i>Famotidine</i>)	Tab. 0,02, 0,04

3.	Omeprazole (<i>Omeprazole</i>)	Tab. 0,02
4.	Rabeprazole (<i>Rabeprazole</i>) syn.: Pariet, Controlok	Tab. 0,02
5.	Peritol (<i>Peritol</i>) syn.: Cyproheptadine	Tab. 0,004
6.	Fenfluramine hydrochloride (<i>Fenfluramine hydrochloridum</i>)	Caps. 0,06
7.	Riboxinum (<i>Riboxinum</i>) syn.: Inosine	Tab. 0,2, amp. 2 % sol. 10 ml.
8.	Metoclopramide (<i>Metoclopramide</i>) syn.: Cerucalum	Tab. 0,01, amp. 2 ml.
9.	Essentiale (<i>Essentiale</i>)	Amp. 10 ml.; caps. patented.
10.	Silibor (<i>Silibor</i>)	Tab. 0,04
11.	Geptral (<i>Heptral</i>)	Tab. and vial 0,4
12.	Loperamide (<i>Loperamide</i>) syn.: Imodium	Caps. 0,002; vials 0,002 % 100 ml.
13.	Linex (<i>Linex</i>)	Caps. patented

Tasks for self-control. Choose the correct answers.

- Point out drug that reduce gastric secretion and causes anti-androgenic effect:
 - Ranitidine
 - Rabeprazole
 - Gastrocepin
 - Almagel
 - Helicocin
- Patients with diarrhea appointed drug regulating intestinal biocenosis. Identify drug.
 - Loperamide
 - Intetrix
 - Phtalazol
 - Smecta
 - Linex
- A patient with chronic constipation was appointed synthetic laxative with predominant effect on the colon. Find out it.
 - Castor oil
 - Bisacodyl
 - Magnesium sulfate
 - Decoction of Frangula bark
 - Forlax
- To the obese patient doctor prescribed an anorexigenic agent with antiparkinsonian action. Specify the drug.
 - Bromocriptine
 - Fenfluramine
 - Phepranon
 - Metformin
 - Mazindol
- For the symptomatic treatment of diarrhea was appointed antidiarrheal drug – opioid receptor agonist. Specify the drug.
 - Intetrix
 - Metoclopramide
 - Ftalazol
 - Loperamide
 - Linex

II. Original practical work in class

- To view the collection of drugs.
- Work with the tests (Krok-1).
- Prescribe and ground the choice of drug:
 - at alimentary obesity;
 - H₁ – histamine blockers at an anorexia;

- 3) at hypersalivation;
- 4) to prevent vomiting;
- 5) antisecretory drug – inhibitor of microsomal liver oxidation;
- 6) antisecretory drug with additional antihelicobacter effect;
- 7) for the symptomatic treatment of gastritis hyperacid;
- 8) for acceleration of healing of the stomach's ulcer;
- 9) at disbacteriosis;
- 10) at acute diarrhea;
- 11) derivative ademetonine by toxic hepatitis;
- 12) in acute pancreatitis.
- 13) laxative that improves motor function mainly of the small intestine;
- 14) gepatoprotektor based flavonoids;
- 15) inhibitors of H⁺, K⁺ ATP-PS 2nd generation;
- 16) antihelicobacter drug;
- 17) the central stimulant of appetite;
- 18) agonist of intestinal opioid receptor;
- 19) the drug replacement pantoprazole;
- 20) the drug replacement bifidumbacterin.

Unit 54. DRUGS AFFECTING ON THE RESPIRATORY SYSTEM

Actuality of the unit. Drugs can be delivered to the lungs by inhalation, oral or parenteral routes. Inhalation is often preferred because the drug is delivered directly to the target tissue – the airways – and is effective in doses that do not cause significant systemic side effects. Clinically useful drugs act by various mechanisms, for example, by relaxing bronchial smooth muscle, or by modulating the inflammatory response. Commonly encountered respiratory disorders are asthma, rhinitis, chronic obstructive pulmonary disease, and cough.

I. Individual work

Control questions

1. STIMULANTS OF BREATHING (analeptics) – see unit 23).
2. EXPECTORANTS – see unit 14.
3. ANTITUSSIVES. Classification:
 - 1) Non – narcotic antitussives:
 - centrally acting — glaucine, tusuprex, combined — bronholytin (glaucine + ephedrine + oil basil ordinary);
 - peripherally acting — Libexin, Falimint.
 - 2) Narcotic antitussives — Codeine, Ethylmorphine hydrochloride, Estocine.
Mechanisms of action. Indications and contraindications for use. Undesirable effects.
 4. Drugs used IN PULMONARY EDEMA (acute left ventricular heart failure):
 - abortion of "breathing panic" — narcotic analgesics (Morphine);
 - decreasing of the preload and the pressure in the pulmonary artery – diuretics (Furosemide), Nitrates, Morphine;
 - afterload reduction — nitrates and other vasodilators;
 - inotropic cardiac stimulation — cardiotonic: cardiac glycosides (Digoxin), non – glycoside (Dobutamine, Dopamine);
 - anti – foam — ethyl alcohol pairs, synthetic antifoams;
 - oxygen therapy, mechanical ventilation;
 - symptomatic therapy — antiarrhythmics etc.
 5. Drugs used at ASTHMA and BRONCHOSPASTIC CONDITION. Classification:

I. Bronchodilators (broncholytics):

- adrenomimetics — Salbutamol, Fenoterol, Isadrinum, Ephedrine etc.;
- M – cholinoblockers – Ipratropium, Troventol.
- myotropic spasmolytic drugs – Theophylline, Aminophylline, No – spa;
- combined – Ditek, Berodual, Broncholytin, Solutan.

II. Antiallergic and desensitizing:

- glucocorticosteroids – Prednisolone, Beclomethasone, Budesonide etc.;
- stabilizers of mast cells – Cromolyn sodium /Intal/, Ketotifen;
- blockers of H₁ – histaminoreceptors – Dimedrolum, Suprastin, Tavegil, Histadine etc.;
- antagonists of leukotriene receptors – Zafirlukast, Montelukast.

Mechanisms of action. Indications and contraindications to application.

List of practical works. Prescribe drugs with their application (*separately from the prescription!*):

№	Drug name	Drug form
1.	Codeine phosphate (<i>Codeini phosphas</i>)	Tab. 0,015
2.	Glaucine (<i>Glaucine</i>)	Dragee 0,01 and 0,04
3.	Bronholytin (<i>Broncholytin</i>)	Syrup bot. by 125 ml.
4.	Acetylcysteine (<i>Acetylcysteinum</i>)	Powder 0,1, 0,2; amp. 20 % sol. 5 and 10 ml. for inhalation
5.	Salbutamol (<i>Salbutamolum</i>)	Aerosol 0,1 mg/dose, 10 ml. bot.; Tab. 0.002, 0.004
6.	Tiotropium bromide (<i>Tiotropium bromide</i>) syn.: Spiriva	Powder. for/ing. in caps. 18 mcg
7.	Theophylline (<i>Theophyllinum</i>) syn.: Neofillin	Tab. 0,1 and 0,3
8.	Ethymizol (<i>Aethimizolum</i>)	Tab. 0,1; amp. 1 % or 1,5 % sol. 3 and 5 ml.
9.	Ketotifen (<i>Ketotifenum</i>) syn.: Zaditen	Tab. 0,001
10.	Beclomethasone dipropionate (<i>Beclometasonum dipropionas</i>)	Aerosol 50, 100, 200 mcg/dose

Tasks for self-control. Choose the correct answers.

1. Which drug should be assigned in chronic bronchitis with thick sputum of purulent character?
 - A. Salbutamol
 - B. Codeine phosphate
 - C. Ipratropium
 - D. Glaucine hydrochloride
 - E. Acetylcysteine
2. The patient suffers from bronchial asthma. Concomitant disease – coronary heart disease. What adrenoagonists necessary to assign to remove bronchospasm?
 - A. Ephedrine
 - B. Izadrin
 - C. Adrenaline
 - D. Formoterol
 - E. Orsiprenalina sulfate
3. Patient for decreasing of bronchial asthma attack was appointed antiallergic drug, which action develops in 2 – 4 weeks reception. Specify the medication:
 - A. Cetirizine
 - B. Tiotropium bromide
 - C. Ketotifen
 - D. Beclomethasone
 - E. Ephedrine
4. The patient with bronchial asthma appointed drug montelukast. What is the mechanism of action of this drug?

- A. It stimulates mainly β_2 -adrenergic receptors
- B. Increases cAMP content in the smooth muscle of the bronchioles
- C. Blocks M – cholinergic receptors
- D. Blocks leukotriene receptors
- E. Blocks phospholipase A_2

5. Specify a drug that has anti – allergic, anti – inflammatory action, relaxes the smooth muscles of the bronchi and restores its sensitivity to adrenomimetics?

- A. Bronholitin
- B. Theophylline
- C. Suprastin
- D. Ketotifen
- E. Beclomethasone

II. Original practical work in class

1. To view the collection of drugs.
2. Work with the tests (Krok-1).
3. Prescribe and ground the choice of drug:

- 1) non – productive cough;
- 2) hormonal drug in the treatment of bronchial asthma;
- 3) to stimulate respiratory center after general anesthesia;
- 4) non – narcotic antitussive agent;
- 5) mucolytic agent – donator of SH – groups;
- 6) combined antitussive drug;
- 7) bronchodilator containing tea alkaloid;
- 8) bronchodilator in chronic obstructive pulmonary disease, which can cause glaucoma attack, urinary retention, tachycardia, dry mouth;
- 9) in case of acute bronchospasm.
- 10) antitussal drug, primarily inhibiting the central link of the cough reflex;
- 11) the drug replacement fenoterol;
- 12) bronchodilator in the aerosol.

Unit 55. DRUGS AFFECTING ON MYOMETRIUM. CONTRACEPTIVES.

Actuality of the unit. Disturbances of natural regulation of secretory and motor function of myometrium needs application of special medicines that can compensate deficit of natural metabolites, restore processes of inter – influence of sympathetic and parasympathetic systems as well as different biologically active substances. Information concerning medicines that influence on myometrium, remain important for maintainance of pregnancy, successful course of pregnancy, normalization of endocrinic system of women.

I. Individual work

Control questions

Drugs affecting the UTERUS. Classification:

A. Drugs stimulating uterine muscles (uterotonics):

- 1) Stimulating *parturition activity* (cause tonic contractions of the pregnant uterus):
 - biogenic preparations — Oxytocin (2 – 5 U), Pituitrinum, Estrone, Serotonine, Dinoprost, Dinoprostone, Prostenon, vitamin B₁, C;
 - preparations of plant origin — Pachycarpinum, Quinine, Castor oil;
 - synthetic preparations — Isoverine, Anaprilinum, Proserinum, Calcium salts.
- 2) *For stoppage of uterine bleeding* (cause tetanic contractions):
 - biogenic preparations — Oxytocin (10 IU);

- preparations of plant origin — Ergot alkaloids (Ergometrine, Ergotamine, Ergotal), and Spherofisin, barberries, shepherd's bag, water pepper etc.;
- synthetic preparations — Cotarnine chloride.

B. Drugs *weakening uterine muscles* (utero – , tocolytics):

1) directly applicable for *tocolysis*:

- beta – adrenomimetics – Partusisten, Ritodrine;
- myotropic (magnesium sulfate);
- oxytocin receptor blockers (atosiban);
- NSAIDs (indomethacin);
- calcium channel blockers (vasotropic).

2) *with tocolytic activity*: hormones (progesterone), tranquilizers, drugs for narcosis, inhibitors of the release of oxytocin (ethanol), donator of nitrogen oxide, potassium channel activators, H₁ – histamine blockers, α-blockers, anti – bradykinin agents, GABA – ergic, vitamin drugs (tocopherol acetate).

General characteristics. Indications for use.

CONTRACEPTIVE DRUGS. Classification:

- combined *estrogen – progestin preparations*:
 - monophasic — Rigevidon, Non – ovlon, Miniziston, Diane – 35 and others.;
 - biphasic — Anteovin, Neo – eunomin;
 - three – phase — Trisiston, Tricvilar and others.;
- monocomponent — *small doses of progestogens* (mini – pill): Continuin, Norgestrel, Microlut and others.;
- *postcoital progestin contraceptives*: Levonorgestrel (Postinor);
- *depot contraceptives*: injected (Depo – Provera /Medroxyprogesterone acetate/), implant (Levonorgestrel /Norplant/);
- *vaginal contraceptives* (spermicides): Benzalkonium chloride /Eroteks/, Nonoxynol etc.

Mechanisms of action of each group. Pharmacological effects. Comparative characteristic of preparations. Indications and contraindications to prescription. Undesirable effects.

Male contraception – Gossypol. Undesirable effects.

List of practical works. Prescribe drugs with their application (*separately from the prescription!*):

№	Name of the drug	Drug form
1.	Oxytocin (<i>Oxytocinum</i>)	Amp. 1 and 2 ml. (5 and 10 IU)
2.	Dinoprostone (<i>Dinoproston</i>)	Tab. 0,0005
3.	Ergometrine maleate (<i>Ergometrini maleas</i>)	Amp. 0,05 % 1 ml., tab. 0,001
4.	Partusisten (<i>Partusisten</i>) syn.: Fenoterol	Tab. 0,005; amp. 0,005 % 10 ml.
5.	Triziston (<i>Trisiston</i>)	Dragee No. 21. From 1 st till 6 th day of menstrual cycle – 1 dragee of violet colour; from 7 th till 12 th day – on 1 dragee of pink colour; from 13 th till 21 st day – on 1 dragee of orange colour, then break for 7 days.

Tasks for self-control. Choose the correct answers.

1. Which drug is necessary to appoint a woman in childbirth, if it is observed labors, and the cervix is not opened yet?

- A. Partusisten
- B. Dinoprostone
- C. Oxytocin
- D. No – spa
- E. Magnesium sulfate

2. Female 25 years old was admitted to the department of pathology of pregnancy with threatened miscarriage. What hormonal drug it is expedient to appoint?
- Estrone
 - Progesterone
 - Retabolil
 - Menopausal gonadotropin
 - Estradiol
3. Select uterotonic from ganglionic blockers group:
- Propranolol
 - Neostigmine
 - Terlipressin
 - Ergometrine
 - Pachycarpin
4. What are the undesirable effects of contraceptives require a change of drug or dose reduction?
- Breast tenderness
 - Vaginal infection, urethral extension
 - Hyperpigmentation
 - Profuse bleeding
 - Amenorrhea
5. What component of oral contraceptives can cause development of venous thromboembolism?
- Gestagen
 - Oxytocin
 - Estrogen
 - Vasopressin
 - Androgen

II. Original practical work in class

- To view the collection of drugs.
- Work with the tests (Krok-1).
- Prescribe and ground the choice of drug:
 - plant-origin drug to reduce postpartum uterine bleeding;
 - uterotonic from prostaglandin drugs;
 - hormonal drug for induce labor;
 - adrenergic tocolytic drug;
 - three-phasic oral contraceptive.
 - tocolytic;
 - uterotonic of synaptic action;
 - vitamin preparation with tocolytic activity;
 - synthetic drug stimulating the generic activities;
 - myotropic tocolytics.

Unit 56-57. PHARMACOTHERAPY OF ACUTE DRUG POISONING AND EMERGENCY STATES

Actuality of the unit. Poisoning is especially acute and complex process which requires the emergency qualified medical care. The outcome of the poisoning depends on the effectiveness of the aid. In most cases timely aid done in full volume can save the life of the person who had taken even the lethal dose. Untimely or irrational therapy is ineffective, in less severe poisoning serious complications may develops. Effectiveness of the urgent care in case of poisoning depends in turn on the nature of the poison, which should be diagnosed by a doctor. He can use the special antidote. Also it is important to distinguish between syndromes, which play a serious role in pathogenesis. This will help to select preparations for pathogenic therapy.

I. Individual work

Control questions

ACUTE POISONINGS

1. Classification of toxins. Factors determining their toxicity: the physico – chemical properties; concentration, path and speed of penetration of the toxin into the body; poisoned species, age, sex, weight, individual features and others. The phases of toxins action.

2. General aid measures in acute poisoning:

1) **Prevention of further entering of poison into the organism** (removal of the poison that is not sucked) in cases of poisoning by: a) the lungs; b) skin and conjunctiva; c) the stomach. Neutralization reaction non – absorbed poison in the gastrointestinal tract: adsorption, oxidation, neutralization, binding, precipitation.

2) **Accelerate removal of poison from the body:**

- *unabsorbed*— laxatives, cleansing enemas, etc.;
- *absorbed* — forced diuresis, alteration in the acid – base balance of urine, hemosorption, hemodialysis, gastrointestinal, peritoneal dialysis, blood transfusions and others.

3) **Antidote therapy.** Classification of antidotes mechanism of action:

- a) physico – chemical — adsorbents;
- б) chemical — complexons, donators of SH – groups, protamine sulfate;
- в) physiological (functional) — atropine, naloxone, etc.;
- г) immunological — antitoxic serums.

Application of specific antidotes:

- ✓ indirect anticoagulants – vicasol;
- ✓ direct anticoagulants – protamine sulfate;
- ✓ atropine – physostigmine;
- ✓ barbiturates and narcosis – bemegride;
- ✓ benzodiazepines – flumazenil;
- ✓ bromide, lithium – sodium chloride;
- ✓ isoniazid – pyridoxine hydrochloride;
- ✓ paracetamol, dichloroethane – acetylcysteine;
- ✓ magnesium sulfate – calcium chloride;
- ✓ methanol, ethylene glycol – ethyl alcohol;
- ✓ non – depolarizing muscle relaxants – neostigmine;
- ✓ muscarine – atropine;
- ✓ opioids – naloxone;
- ✓ iron – containing agents – deferoxamine;
- ✓ cardiac glycosides – unitiol, acetylcysteine, complexons (EDTA, etc.), potassium supplements (Pananginum);
- ✓ salts of heavy metals – unitiol, acetylcysteine, complexons (EDTA, penicillamine, sodium thiosulfate, and others.);
- ✓ POC – cholinesterase re – activators (dipyroxim, alloxim), atropine;
- ✓ cyanide – EDTA, sodium nitrite, sodium thiosulfate, methylene blue (hromosmon), ascorbic acid, vitamin B₁₂.

4) **Symptomatic therapy** of functional disorders:

- in case of respiratory disorder of various ethnology: suppressing of breathing center, obturation of respiratory tracts, edema of the larynx and lungs, blocking of the respiratory muscles;
- in case of vascular tone disorder: blood pressure decreasing (poisoning with hypnotics, ganglionic blockers, sympatholytic and adrenolytic agents, drugs with myotropic action), increasing of blood pressure (poisonings with vasoconstrictive preparations, analeptics, phenaminum);
- in case of disorder in heart activity: myocardium dysfunction, cardiac arrhythmia, cardiac arrest;
- renal function;
- in case of convulsion syndromes (poisoning with analeptics, N – cholinomimetics agents, phenothiazine derivatives, insulin, strychnine and other poisons, resulting in seizures);

- body temperature (hyperthermia: poisoning of tranquilizers, barbiturates, H₁ – histamine blockers, hypothermia: poisoning of antipsychotics, opioids, alcohol);
- metabolic disorders (acidosis, alkalosis, electrolyte imbalance);
- dehydration;
- sharp pain;
- agitation;
- hypoxia of various etiologies (violation of breathing and blood circulation, hemolysis, the blockade of the respiratory enzymes, changes in hemoglobin).

EMERGENCY STATES. Basic drugs:

1. In case of acute decompensation of chronic *congestive heart failure*:

- with a congestive type of hemodynamics:
 - right ventricular heart failure — elimination of the underlying cause (pulmonary embolism, asthmatic status, etc.), reducing hypoxia effect on blood flow in the pulmonary artery;
 - left ventricular heart failure (pulmonary edema, cardiac asthma) — see unit № 41: respiratory support, anti – foaming agents, vasodilators (nitrates), narcotic analgesics (morphine), diuretics (furosemide), cardiotonic glycoside and nonglycoside cardiotonic (dopamine).
- with hypokinetic hemodynamics type (cardiogenic shock): stabilization of hemodynamics; antiarrhythmic; narcotic analgesics, non – glycoside cardiotonics, vasodilators.

2. *Myocardial infarction* (see unit № 23).

3. *Acute vascular insufficiency* — hypertensive: adrenergic agonists, glucocorticoids, analeptics (see unit № 25).

4. *Hypertensive crisis* — antihypertensive agents (see unit № 25).

5. *Spasms of smooth muscles of the abdominal organs (kidney, liver, intestinal colic)* — cholinolytics, myotropic spasmolytics, non – narcotic and narcotic analgesics.

6. *Anaphylactic shock* — adrenaline, glucocorticoids in large doses, calcium chloride, H₁ – histamine blockers and others.

7. *Hyperglycemic (diabetic) coma* — correction of acidosis, dehydration using liquids (sodium bicarbonate, saline), insulin ultra short and short action depending on the level of hyperglycemia, cocarboxylase, potassium salt.

8. *Hypoglycemic coma* — hypertonic sol.s of glucose, adrenaline, glucocorticoids.

List of practical works. Prescribe drugs with their application (*separately from the prescription!*):

№	Name of the drug	Drug form
1.	Corglycon (<i>Corglyconum</i>)	Amp. 0,06 % 1 ml.
2.	Epinephrine hydrochloride (<i>Adrenalini hydrochloridum</i>)	Amp. 0,1 % 1 ml.
3.	Dopamine (<i>Dopaminum</i>)	Amp. 4 % sol. 5 ml.
4.	Mezaton (<i>Mesatonum</i>) syn.: Phenylephrine	Amp. 1 % 1 ml.
5.	Diazepam (<i>Diazepamum</i>) syn.: Sibazon, Relanium	Amp 0,5 % sol. 2 ml.
6.	Furosemide (<i>Furosemidum</i>) syn.: Lasix	Amp. 1 % 2 ml.
7.	Proserin (<i>Proserinum</i>) syn.: Neostigmine	Amp. 0,05 % 1 ml.
8.	Naloxone (<i>Naloxonum</i>)	Amp. 1 ml. (1 ml. — 0,0004 g)
9.	Unithiol (<i>Unithiolum</i>)	Amp. 5 % 5 ml.
10.	Flumazenil (<i>Flumazenilum</i>) syn.: Anexat	Amp. 0,01 % sol. 5 ml.
11.	Deferoxamine (<i>Deferoxaminum</i>) syn.: Desferal	Vials 0,5
12.	Enterogel (<i>Enterogelum</i>)	A package with gel 45, 135, 225, 450, 650 and 900 g

Tasks for self-control. Choose the correct answers.

1. *Specify the drug effective in cases of poisoning of insecticide from the group POC:*
 - A. Strychnine
 - B. Unithiol
 - C. Spironolactone
 - D. Proserin
 - E. Dipyroxim

2. *Select a substance that can cause methemoglobinemia and at the same time used as an antidote to cyanide poisoning?*
 - A. Sodium nitrite
 - B. Sodium thiosulfate
 - C. Phenol
 - D. Dichloroethane
 - E. Acetic acid

3. *After administration of dithylin the muscular tonus has not recovered. What kind of assistance is necessary to provide the patient?*
 - A. Hemodialysis
 - B. Blood transfusion
 - C. Hemosorption
 - D. Forced diuresis
 - E. Peritoneal dialysis

4. *In the intensive care unit the patient with diabetic coma entered. What kind of insulin should be given?*
 - A. Protafan NM
 - B. Actrapid HM
 - C. Humulin N
 - D. Ultratard HM
 - E. Humulin M30

5. *In the student headache in the occipital part, tinnitus, facial flushing abruptly appeared in the class. At measuring the blood pressure increased upto 140/90 mm hg. Select drugs for first aid:*
 - A. Captopril sublingually
 - B. Diazepam orally
 - C. Magnesium sulfate orally
 - D. Propranolol sublingual
 - E. Furosemide orally

II. Original practical work in class

1. To view the collection of drugs.
2. Work with the tests (Krok-1).
3. Prescribe and ground the choice of drug:
 - 1) for forced diuresis;
 - 2) inotropic agent for congestive heart failure;
 - 3) at an acute vascular insufficiency;
 - 4) for the relief of seizures as a symptom;
 - 5) absorbed after oral poisoning;
 - 6) for poisoning by heavy metal and cardiac glycosides;
 - 7) the antidote of muscarine;
 - 8) specific antidote of morphine;
 - 9) antidote for overdosage of non – depolarizing myorelaxants;
 - 10) benzodiazepines antidote;
 - 11) an antidote of heparin;
 - 12) methyl alcohol antidote;
 - 13) for the treatment of hemosiderosis;
 - 14) for hypertensive crisis for sublingual use;
 - 15) at asthmaticus status;
 - 16) at renal colic;

- 17) pulmonary edema;
- 18) at malignant hyperthermia;
- 19) at manic excitation;
- 20) at anaphylactic shock.

Unit 58. PHARMACOTOXYCODYNAMICS.

Actuality of the unit. WHO apply the following requirements to modern medications the: high efficiency, safety, availability and acceptability for a patient. The problem of safety of application of medications becomes more actual. It is known that at every 20th patient medications intake is accompanied by undesirable effects. It is linked, foremost that the amount of medicinal preparations with high biological activity increases in medical practice, low quality of preclinical and clinical researches of drugs. Task of doctor – to do everything from him depending, to guarantee maximally safety of patient. Knowledges of pharmacotoxicodynamics (section of pharmacology about the undesirable effects of drugs), ability correctly to pick up preparation, to estimate it's efficiency and safety are needed for this purpose. The strict control of safety drugs application is inalienable part of state policy in industry of medications practically entire countries of world.

I. Individual work

Control questions

1. Historical stages of pharmacotherapy: empirical, ethiopathogenetical, evidentiary. The concept of evidence – based medicine.
2. The principles of rational pharmacotherapy. Requirements for modern medicines.
3. Types of adverse reaction / action: An unknown and unexpected, serious, foresight, and possible etc.
4. The classification of adverse reactions by pathogenetic principle:
 - I) *Dose – dependent, organotoxic* (type A):
 - related to pharmacological activity;
 - at the absolute or relative drug overdose;
 - at the drug interaction.
 - II) *Unrelated with a dose* (type B, or unpredictable, or dose – independent):
 - immunological reactions (allergic, violations of immunological properties of organism);
 - pseudoallergic reactions;
 - pharmacological changeability (idiosyncrasy);
 - at local application.
 - III) *At the prolonged application*:
 - adaptive changes;
 - at the drug cancelation («rebound» and «withdrawal» phenomenon);
 - organotoxic action.
 - IV) *Delayed action*:
 - blastomogenic (carcinogenic);
 - action related to the reproductive function (lowered fertility, mutagenic, teratogenic, embryotoxic, fetotoxic actions, penetration in the milk).
3. Ethiopathogenetic mechanisms of side reactions in every group.
4. Factors affecting to the drugs side reactions:
 - unrelated with medicine (features of patient's organism, therapy conducted by a doctor etc.);
 - related to the clinic – pharmacological description of a drug;
 - related to a quality of preparations (substandard and falsified).
5. The concept of causation adverse reaction to medication. The degree of reliability due to the effect of adverse reactions of drugs: definite, probable, possible, conditional, doubtful.

6. Basic ways of decision of medical treatment safety. System of pharmacological supervision in world and Ukraine. Medico – juridical and organizational aspects. Role of doctor in the exposure of adverse reactions of drugs.

7. Methods of exposure and collection of information about the adverse reactions of medications. Cards of spontaneous reports (form 137/o).

8. The concept of the formulary system. Formularies medicines (national, regional, hospital).

List of practical works

1. Give examples of organotoxic, blastomogenic and carcinogenic, mutagenic, teratogenic, and embryonic fetotoxic actions of drugs.

2. Find examples of drugs that can cause tolerance, idiosyncrasy, the phenomenon of "rebound", "withdrawal".

3. Make a list of drugs that have a narrow breadth of therapeutic action.

Tasks for self-control. Choose the correct answers.

1. *Specify an antibiotic that may cause adverse effects such as myorelaxant, ototoxicity, teratogenic, mutagenic:*

- A. Gentamicin
- B. Penicillin
- C. Tetracycline
- D. Chloramphenicol
- E. Dicloxacillin

2. *Action dithylin lasted over an hour. What enzyme genetic deficiency could be a reason of abnormally long action of the drug?*

- A. Butyrylcholinesterase
- B. Glucose – 6 – phosphate dehydrogenase
- C. Peroxidases
- D. Acetyltransferase
- E. Amylase

3. *The 59 years – old patient during treatment with isadrin started to complain on chest pain in heart region. What is a putative reason of this complication?*

- A. Stimulation of M – cholinergic receptors
- B. Inhibition of β 1-adrenoceptors
- C. Stimulation of α 1-adrenoceptors
- D. Inhibition of α 1-adrenoceptors
- E. Stimulation β 1-adrenoceptors

4. *What adverse reaction of medications belongs to a dose – dependent type?*

- A. Pseudoallergic reaction
- B. Immediate hypersensitivity
- C. The potentiation of action in pharmacodynamic interaction
- D. Idiosyncrasy
- E. Delayed type hypersensitivity

5. *What is the relationship of side effects if the side effects of the development coincides with the action of the drug, side effect is predictable and the abolition of the drug causes disappearance of side effect?*

- A. Definitions
- B. Probable
- C. Possible
- D. Conditional
- E. Doubtful

II. Original practical work in class

1. To view the collection of drugs.
2. Work with the tests (Krok-1).
3. To write recipes and justify the choice of drug:
 - 1) drug that causes idiosyncrasy;
 - 2) a drug that causes organotoxyc action;

- 3) a drug having the phenomenon of "return";
- 4) a drug having the phenomenon of "cancellation";
- 5) drug causes adaptive changes;
- 6) the drug that causes blastomogenic action;
- 7) a drug that affects the reproductive function;
- 8) preparation with a teratogenic effect.

Unit 59. PEDIATRIC PHARMACOLOGY AND PHARMACOLOGY OF AGED PATIENTS. PHARMACOTHERAPY DURING BREAST-FEEDING.

Actuality of the unit. Pharmacotherapy in children's age differs fundamentally from the treatment adult people is not only quantitatively but also qualitatively. In appointing the drug necessity to take into account particularities to different periods of development, pharmaceutical, pharmacokinetic, pharmacodynamic, therapeutic and toxic factors. Particular attention pay to the particularities dosage of drugs.

The topical of the development and improvement of pharmacotherapy in elderly and senile age cause by tendency of demographic aging. The level of disease of elderly persons is twice higher than level of disease of persons under 40 years of age. For the elderly is characteristic a combination of diseases of various origins, chronic flow of pathological processes. Features of pharmacotherapy in the elderly and senile age are caused with the aging of the organism. In many cells reduces the oxygen consumption, decrease activity respiratory enzymes, chance phospholipid composition of the membrane. These factors should be considered when appointment drugs.

Pharmacotherapy of infant age differs considerably from the treatment is not only quantitatively but also qualitatively. . In appointing the drug, must be taken into account features of the different periods of development, pharmaceutical, pharmacokinetic, farmakodinamic, therapeutic and toxic factors. Particular attention is drawn to the features of dosage preparations.

The relevance of the development and improvement of pharmacotherapy in elderly and senile age caused by the tendency of demographic aging. The incidence of elderly persons about twice higher than that of people younger than 40 years old. For elderly people are typical a combination of diseases of various origins, chronic pathological processes. Features of pharmacotherapy in the elderly and old age are associated with the aging of the organism. Wherein, in many cells reduces the oxygen consumption activity decreased respiratory enzymes varies phospholipid composition of the membrane. These factors should be considered in prescribing.

Features of pharmacotherapy for pregnant women is largely determined by the prediction of drug effects on the developing fetus. The placental barrier is permeable to varying degrees, for the vast majority of medicines. Getting into the blood and fetal tissue, the preparation may determine: the pharmacological effect; fetotoxic effect, violation of fetal development, teratogenic action. Features of pharmacotherapy in nursing mothers reduced to decreasing the danger of undesirable action of drugs taken by the mother on the baby. The drugs enter into the organism while feeding the baby and can be toxic.

I. Individual work.

Control questions.

PEDIATRIC PHARMACOLOGY AND PHARMACOLOGY OF AGED PATIENTS

1. The general principles of perinatal and pediatric pharmacology.
2. Medicines and pregnancy. Pharmacokinetics and pharmacodynamics particularities. Possible unwanted effects of drugs for the mother and fetus.
3. Use of drugs during lactation.
4. The drugs permitted for use in the treatment of neonates.
5. Drugs contraindicated for neonates.

6. Pharmacokinetics and pharmacodynamics particularities of drugs at children. Adverse effects and drug interactions at children.
7. Dosage forms in pediatrics and particularities of dosing drugs for children. Methods for calculating dosages in pediatrics.

$$A = B \frac{a}{a + 12} ; \quad A = B \frac{4a + 20}{100} ; \quad A = B \frac{\delta}{70} ;$$

A – average therapeutic dose for the child;
 B - average therapeutic dose for an adult;
 a - the age (number of complete years);
 δ - weight (kg).

General principles of geriatric pharmacology.

1. Age-related changes that affect the pharmacokinetic and pharmacodynamic of drugs.
2. Possible unwanted effects of drugs used in geriatrics.
3. The main groups of drugs used in geriatric practice.

PHARMACOTHERAPY DURING BREAST-FEEDING.

I. General principles of perinatal pharmacology.

1. Medications and Pregnancy. Features of pharmacokinetics and pharmacodynamics of the medicines in pregnant women.
2. Possible undesirable effects of drugs on the mother and fetus.
3. Medicinal products allowed for use by pregnant women (antibiotics, antihypertensives, and others.)
4. Drugs, which are absolutely contraindicated in pregnancy period (Category X). The effects on the fetus by streptomycin, estrogens, androgens, iodine preparations, quinine and others.
5. Drugs having teratogenic action (category D). Impact on the fetus tranquilizers, antidepressants, analgesics, antihypertensives and others. Examples.
6. The use of drugs during lactation.

List of practical works

Solve situational problems.

1. Pregnant women after taking the drug emerged bleeding. Which groups of drugs can provoke it?
2. Pregnant woman asked the pharmacist with a request to recommend vitaminopreparaty. Which ones and why can be used during pregnancy?

List of practical works.

Solve situational problems.

1. The patient suffered a stroke. What drugs used in the post-stroke period?
2. The patient suffers from atherosclerotic encephalopathy. Recommend drug improving a cerebral circulation.
3. The patient 69 years have obesity. What anorexigenic drug rationally to appoint?
4. An elderly patient suffering from chronic pancreatitis. What enzymatic drug necessary for him?
5. The doctor diagnosed the child's scarlet fever. Recommend antibiotic, justify a decision. Which groups of antibiotics are contraindicative for children?
6. Newborn baby diagnosed with salmonella. Name the drug of choice. Which antibiotics are not prescribed for child?
7. Earlier from insomnia patient took phenobarbital. Answer the question, may to use this drug during pregnancy? Justify your answer.
8. Patient 78 years take treatment for pneumonia. Which antibiotics are not prescribe for elderly patients?

Tasks for self-control. Choose the correct answers.

PEDIATRIC PHARMACOLOGY AND PHARMACOLOGY OF AGED PATIENTS

1. *Specify an antibiotic that can cause children 'gray syndrome of newborn. "*

- A. Gentamicin
- B. Penicillin
- C. Tetracycline
- D. Levomycetinum
- E. Dicloxacillin

2. *Specify the hypnotic, which doesn't cause apnea to elderly patients.*

- A. Phenobarbital
- B. Zopiclone
- C. Reladorm
- D. Zolpidem
- E. Zaleplon

3. *What drugs is contraindicated for children?*

- A. Ampicillin
- B. Tetracycline
- C. Methicillin
- D. Ciprofloxacin
- E. Boric acid

4. *Why Aspirin is contraindicated in children?*

- A. Violate bone growth
- B. Causes allergic reactions
- C. Causes Reye's syndrome
- D. Violates the absorption of food
- E. Causes constipation

5. *Choose the drugs, which are contraindicated in gerontological practice.*

- A. Indomethacin
- B. Amitriptillin
- C. Diphenhydramine
- D. Suprastin
- E. Loratidine

PHARMACOTHERAPY DURING BREAST-FEEDING.

1. *What drugs should not be prescribed to pregnant women?*

- A. Lithium Drugs
- B. antithyroid drugs
- C. Penicillin
- D. Isoniazid
- E. Trichopolium

2. *A pregnant suffers from constipation. Choose a laxative.*

- A. Dufalak
- B. Castor oil
- C. Magnesium sulfate
- D. Potassium Sulfate
- E. Neostigmine

3. *Name the drug, which can be used in renal colic in pregnancy.*

- A. Atropine
- B. Noshpa
- C. Analgin
- D. Morphine
- E. Promedol

4. *Which drug causes preterm labor?*

- A. Partusisten
- B. Anaprillin
- C. Oxytocin
- D. Noshpa
- E. Dinoprostum

5. *Choose preparations which give rise to congenital defects.*

- A. Warfarin
- B. Methotrexate
- C. papaverine
- D. Phenytoin
- E. Iron sulfate

II. Original practical work in class

1. Work with the tests (Krok-1)
2. Prescribe and ground the choice of drug
 - 1) The patient has arteriosclerotic encephalopathy. Recommend drug improving a cerebral circulation.
 - 2) What anorexigenic drug rationally to prescribe for patient 69 years old with obesity?
 - 3) An elderly patient suffering from chronic pancreatitis. What enzymatic drug necessary for him?
 - 4) The doctor diagnosed the child's scarlet fever. Recommend antibiotic, justifying the choice. Which groups of antibiotics are contraindicated for children?
 - 5) Newborn baby diagnosed with salmonellosis. Name the drug of choice.
 - 6) Earlier from the insomnia patient took phenobarbital. Answer the question, may she to use this drug during pregnancy? Justify your answer.
 - 7) The patient 78 years take treatment for pneumonia. Which antibiotics aren't prescribed for elderly patients?

Unit 60. THE ROLE OF THE PHARMACIST IN THE PREVENTION OF NEGATIVE CONSEQUENCES OF USING DRUGS. **TEST CONTROL**

Actuality of the unit. Rational pharmacotherapy is one of the most important directions of development of modern medicine. In the appointment of therapy should be the interaction doctor, pharmacist and patient. A Pharmaceutical custody implies pharmacist participation in drug treatment, which may provide an explanation to the patient about the drug unwanted actions, correct reception in view of features of pharmacokinetics and pharmacodynamics.

Careful attention should be paid to elderly and senile age. For the elderly is characterized by a combination of diseases of various origins, chronic pathological processes. In addition, they forget how to take the drug and need additional explanation and reminder. Some drugs have a particular application - before a meal or after a meal, the shock and maintenance doses, and so on. Pharmacist must draw the patient's attention to these factors, since it affects the effectiveness of the therapy and the occurrence of undesirable effects.

Particular attention should be paid to drug treatment for pregnant women, taken into account the effect of the drug on the developing fetus. Features of pharmacotherapy in nursing mothers reduced to decreasing the danger of undesirable action of drugs taken by the mother on infant health. Cases of polypharmacy found in modern medicine. Often the combination of diseases of various origins, patients visit several doctors particular specialties and receive diverse destination. As a result, a appointments list contains five or more drugs simultaneously. In this case it is necessary to take into account the interaction of drugs to prevent the emergence of non-desirable effects.

Careful attention should be paid to the use of non-prescription medicines.

I. Individual work

Control questions

I. General principles of pharmaceutical care.

1. The definition of "pharmaceutical care". The role of the pharmacist.

2. The development of self-concept. Characteristics of the negative aspects of self-concept.
3. Nonprescription drugs. The criterias are on which the drug belongs to a prescription or OTC.
4. Symptomatic treatment of diseases, its negative sides.
5. The categories of patients requiring a pharmacist attention.
6. Brand and generic products, their features.
7. A pharmaceutical custody in the sale of OTC. a pharmacist action algorithm.
8. Compliance as a factor in the effectiveness of drug therapy.
9. Pharmaceutical care of patients with colds (sore throat, rhinitis, cough, fever). Evaluation of pharmacotherapy in terms of benefit / harm in the absence of clinical diagnosis. Product characteristics, features of application, adverse effects, contraindications.
10. Pharmaceutical care of patients with gastrointestinal disorders (obstipation, heartburn, diarrhea, flatulence, goiter). Evaluation of pharmacotherapy in terms of benefit / harm in the absence of clinical diagnosis. Product characteristics, features of application, adverse effects, contraindications.
11. The pharmaceutical care of patients with diseases of the nervous system (headache, anxiety, fatigue). Evaluation of pharmacotherapy in terms of benefit / harm in the absence of clinical diagnosis. Product characteristics, features of application, adverse effects, contraindications.
12. The pharmaceutical care of patients with skin diseases (herpes, acne, etc.). Evaluation of pharmacotherapy in terms of benefit / harm in the absence of clinical diagnosis. Characteristics of drugs, especially the use of undesirable effects contraindications.
13. The pharmaceutical care of patients with micro traumas (cuts, abrasions, scratches). Product characteristics, features of application, adverse effects, contraindications.
14. The pharmaceutical care of patients with burns and frostbite. Character, stick preparations, especially the application, adverse effects, contraindications.
15. The pharmaceutical care of patients with diseases of the joints and skeletal muscles. Evaluation of pharmacotherapy in terms of benefit / harm in the absence of clinical diagnosis. Product characteristics, features of application, adverse effects, contraindications.
16. The pharmaceutical care of patients with allergic diseases. Evaluation of pharmacotherapy in terms of benefit / harm in the absence of clinical diagnosis. Product characteristics, features of application, adverse effects, contraindications.
17. The pharmaceutical care of patients with iron deficiency anemia. Product characteristics, features of application, adverse effects, contraindications.
18. The principles of use of oral contraceptives. Product characteristics, features of application, adverse effects, contraindications.
19. Clinical and pharmaceutical aspects of the use of alcohol in medicine. Interaction of the alcohol with drugs. Examples.
20. The interaction of drugs with food. Examples.

List of practical works

Solve situational problems.

1. The patient post-traumatic arthritis. Which drug should be used? Specify features REFERENCE.
2. The patient is suffering from iron deficiency anemia. Recommend drug and specify features of the application.
3. The patient while taking bisacodyl reduce the effect of digitoxin. Explain why and give recommendations.
4. A child 2 years suffered from fever for the viral disease. What antipyretic?
5. The patient with pielitah appointed drug from the group of fluoroquinolones. What drug, specify features of the application?
6. To inspect the ocular fundus must be assigned mydriatic the patient with glaucoma. Specify the medication Explain the choice.
7. The doctor diagnosed pneumonia in a child. Recommend antibiotic, justifying the choice. Which groups of antibiotics are contraindicated for children?

8. With regard to insomnia patient received diazepam. Answer the question, is it possible to use said preparation in combined with caffeine therapy? Justify your answer.
9. The patient was 78 years old was treated with pneumonia. Soon she worsened hearing. Analyze the situation, which antibiotic could cause the above side effects?

Tasks for self-control. Choose the correct answers.

1. *What drugs contraindication for stomach ulcers?*

- A. Almagell
- B. Omeprazole
- C. Indomethacin
- D. Diclofenac sodium
- E. Pirenzepine

2. *The patient asked the pharmacist to the issue than the drink sulfadimetoksin. Choose the correct answer.*

- A. sour juice
- B. Sweet juice
- C. Simple water
- D. Alkaline water
- E. Milk

3. *Advise the patient how to take furadonin.*

- A. For 1 hour before meals
- B. During the 30 minutes before a meal
- C. During the meal
- D. After the meal
- E. For 2 hour before meals

4. *What kind of drug is not compatible with dairy products?*

- A. Tetracycline
- B. Ciprofloxacin
- C. Aspirin
- D. Indomethacin
- E. Diclofenac

5. *Patients with hypochromic anemia gets ferrogradumet. Which drug increases the absorption of iron?*

- A. Warfarin
- B. Ascorbic acid
- C. Diazepam
- D. Phenytoin
- E. Pyridoxine

II. Class work

1. Work with the tests (Krok-1)

Recommended literature

Basic:

1. Pharmacology: a textbook for students. medical and dental faculties of higher med. textbook institutions of Ukraine: ed. 4th correction. and reworked. / [I.C. Chekman, V.M. Bobyr'ov, V.J. Kresyun and others]. - Vinnytsia: New book, 2020. - 472 p.
2. Pharmacology: a textbook for the medical stud. of higher medical institutions of Ukraine: view. 4th edition corrected and reworked. / [I.C. Chekman, V.J. Kresyun, V.V. Godovan and others]. - Vinnitsa: The New Book, 2017. - 784 pp.
Pharmacology: textbook. for students. honey. f-tiv higher. honey. textbook institutions / ed. IS Chekman; IS Chekman, NO Gorchakova, LI Kazak and others. - 4 types. - Vinnytsia: Nova Kniga, 2017. - 783 p.
3. Drug formulation with general pharmacology: teach. manual: 2nd edition corrected and reworked / [V.J. Kresyun, V.V. Godovan]. - The Odessa National Medical University, 2017. - 280 p.
4. Pharmacology on pictures and schemes: textbook manual / V. V. Godovan ; ed. By V. I. Kresyun. Vinnitsa: The New Book, 2019. - 462 pp.

Additional literature:

1. Pharmacology: workshop: textbook. way. for students. higher honey. textbook institutions / VM Bobyrev, OM Vazhnych, TO Devyatkin and others. - Vinnytsia: New book, 2017. - 351 p
2. Kolot EG Drugs affecting the nervous and cardiovascular systems Kolot EG, Devyatkina NM - Poltava: LLC SPE "Ukrpromtorgservice", 2019. - 155 p.
3. Pharmacology in crossword puzzles: [textbook. way. for students. higher textbook institutions] / VM Bobyrev, EG Kolot, S. Yu. Chechotina, TO Devyatkina. - Poltava: Ukrpromtorgservice, 2018. - 150 p.
4. Pharmacology-Cito! (Pharmacological logic): textbook [for students. BH3] / HΦaY; for order. SM Drogovoz. - Kharkiv: Title, 2018. - 232 p.
5. Pharmacology: teaching method. way. for self-preparation of students for a single state. qual. exam (using the English-language database of test tasks Step-1) / H. I. Voloshchuk [etc.]; Vinnytsia. NMU. MI Pirogov. - Vinnytsia: Works, 2019. - 166 p.
6. Handbook of drug equivalence - Rx index® / auto-method. IA Zupanets [etc.]; for ed. : prof. IA Zupanets, acad. NAS of Ukraine, prof. VP Chernykh. - 3rd ed., Ext. and processing. - Kyiv: Pharmacist Practitioner, 2019. - 832 p.
7. Pharmacology by Rank and Dale: 9th edition: in 2 volumes. Volume 1 / James M. Ritter, Rod Flower, Graham Henderson, Young Kong Locke, David McEwen, Humphrey P. Rank
8. Pharmacology [Text]: manual-guide for preparation for LII "Step 1. General medical training" / II Zamorsky, SP Melnichuk, TG Kopchuk [etc.]. - Chernivtsi: Medical University, 2018. - 271 p. : ill., color. il. - Bibliogr. : p. 270.
9. Katzung and Trevor's Pharmacology [Text]: examination & board review / B. G. Katzung, M. Kruidering-Hall, A. J. Trevor. - 12th ed., International Edition. - New York; Chicago; San Francisco: McGraw Hill Education, 2019. - 585 p.
10. Pharmacology in Drawings and Schemes [Text] = Pharmacology in Drawings and Scyemes: for students. med., pharmac. universities III-IV years a. / VV Godovan; for order. V. Y. Kresyun; City of Health of Ukraine, Odessa. nat. honey. un-t. - Vinnytsia: Nova Kniga, 2020. - 464 p
11. USMLE: Step 1 [Text]: lecture notes 2020: Pharmacology / ed. S. R. Harris. - New York: Kaplan Medical, Inc., 2020. - 335 p.
13. Pharmacology [Text]: textbook / IV Nekoal, TV Kazanyuk. - 8th type. - Kyiv: Medicine, 2018. - 552 p. - Bibliogr. : p. 551.
12. Pharmacology [Text] = Pharmacology. Guide to essential drugs: a guide to basic drugs / II Zamorsky, TS Shchudrova, TG Kopchuk [etc.]. - Chernivtsi: Medical University, 2018. - 141 p.

15. Electronic information resources:

1. <http://moz.gov.ua>
2. "State Register of Medicines of Ukraine" - Access mode:

<https://moz.gov.ua/derzhavnij-reestr-likarskih-zasobiv-ukraini>

3. ATC-classification - Access mode: <https://compendium.com.ua/uk/atc/>

4. Online platform with protocols based on evidence-based medicine - Access mode: <http://guidelines.moz.gov.ua/>

5. Emergency medical care: pre-hospital stage. New clinical protocol / Order of the Ministry of Health of Ukraine 05.06.2019 No 1269 - Access mode:

https://moz.gov.ua/uploads/2/12737-dn_20190605_1269_dod.pdf

6. State form of medicines 12th issue, 2020: - Access mode: <https://www.dec.gov.ua/materials/chinnij-vipusk-derzhavnogo-formulyara-likarskih-zasobiv/>

7. State Expert Center of the Ministry of Health of Ukraine [http:// https://www.dec.gov.ua/](http://https://www.dec.gov.ua/)

8. State Enterprise "Ukrainian Scientific Pharmacopoeial Center for Quality of Medicines" <http://sphu.org/>

9. National Scientific Medical Library of Ukraine <http://library.gov.ua/>

10. National Library of Ukraine named after VI Vernadsky <http://www.nbu.gov.ua/>

11. Resource for predicting drug interactions (based on FDA instructions, in English)
URL: <http://www.drugs.com>

12. Resource-directory of medicines and forecasting of inter-drug interactions (in English).
URL: <http://www.medscape.org>

1. State Expert Center of Ministry of Health of Ukraine <http://www.dec.gov.ua/index.php/ua/>

2. Ukrainian Scientific Pharmacopoeial Center for Quality of Medicines <http://sphu.org/>

3. National Scientific Medical Library of Ukraine <http://library.gov.ua/>

4. National Library of Ukraine Vernadsky <http://www.nbu.gov.ua/>

5. Resource providing free, peer-reviewed, accurate and independent data on prescription drugs (<https://www.drugs.com>)

6. Resource with essential point-of-care drug (www.medscape.org)

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