MINISTRY OF HEALTH OF UKRAINE
ODESSA NATIONAL MEDICAL UNIVERSITY
DEPARTMENT OF GENERAL AND CLINICAL PHARMACOLOGY AND PHARMACOGNOSY

METHODICAL INSTRUCTIONS

FOR THE PRACTICAL CLASSES IN PHARMACOLOGY FOR THE THIRD YEAR STUDENTS OF MEDICAL FACULTY

Odesa 2023

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PREFACE

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
ACE	– angiotensin converting enzyme
Ampul. (amp.)	– ampoule
AR/SE	– adverse reaction / side effect
Bot.	– bottle
Caps.	– capsule
CCB	– calcium channel blockers
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 reuptake inhibitor
Supp.	– suppository
Syn.	– synonyms
Tab.	– tablet (s)
TCA	– tricyclic antidepressants
TS	– therapeutic systems
TTS	– transdermal therapeutic system

SECTION I. MEDICAL PRESCRIPTION

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 pharmaceutist 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.

The training objectives. *To know*: medical formulation, calculation rules and prescribing in different dosage forms. To be able to: prescribe any drug.

***Intersubject* integration**. Latin language.

Unit 1. MEDICAL PRESCRIPTION. STRUCTURE OF PRESCRIPTION. SOLID MEDICINAL FORMS

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.

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: Dose = a · b / 20 or Dose = a · m / 70, where a – an adult dose, b – the child's age, m – weight (kg).

SOLID DOSAGE FORM

1. The powders for oral administration. Their types (simple and complex). Massing and flavoring substances used for powders. Discharging rules for main and officinal powders.

2. Capsules, tablets and dragee. Their characteristics and types (simple, complex and patented). Discharging rules.

List of practical works. Write prescriptions:

1) 30 powder, containing Tetracyclini hydrochloridum (*Tetracycline hydrochloride*), SD – 0,25, in capsules. One capsule 4 times daily.
2) 10 powder, containing Papaverini hydrochloridum (*Papaverine hydrochloride*), SD – 0,02. One powder 3 times daily.
3) 10 powder, containing Paracetamolum (*Paracetamol*) and Acidum acetylsalicylicum (*Acetylsalicylic acid)* equally SD – 0,02. One powder 3 times daily.
4) 20 capsules, containing Oxacillini natrium (*Oxacillin sodium*), SD – 0,25. Two capsules 4 times daily.
5) 40 tablets of Nitroglycerinum (*Nitroglycerin*), SD – 0,0005. One tablet sublingually.
6) 50 tablets, containing Analginum SD – 0,25, Diabazolum and Phenobarbitalum (*Phenobarbital*) equally SD – 0,02. One tablet at night.
7) 25 patented tablets of Cephalginum. One tablet 3 times daily.
8) 100 dragee of Aminazinum (*Chlorpromazine*), SD – 0,025. One dragee 2 times daily.

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) What has been the dose solid and granular substances?
13) According to what rules are written magistral and the main officinal powders for oral?
14) What rules are written officinal capsules, tablets and dragee?
15) What features of writing out complex and patented capsules, tablets and dragee?

II. Original practical work in class

1. To view the collection of drugs in solid dosage forms.
2. To write prescriptions:

1) Ferric sulfate (*Ferri sulfas*), SD – 0,5 in powder, tablets, dragee and capsules.
2) Ascorbic acid (*Acidum ascorbibicum*), SD – 0,05, in powder and tablets.
3) 20 powders containing Pyridoxine hydrochloride (*Pyridoxini hydrochloridum*) SD – 0,002 and Acidum nicotinicum (*Nicotinic acid)*SD – 0,025.
4) 30 capsules containing Lipase (*Lipasa*), Amylase (*Amylasa*) equally SD – 25000 units, and Protease (*Proteasa*) SD – 1200 units.
5) 30 tablets of Pentalgine (*Pentalginum).*
6) 100 dragee of Festal.

Unit 2. LIQUID DOSED MEDICINAL FORMS

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.

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.

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

Unit 3. **LIQUID DOSED MEDICINAL FORMS (II)**

I. Individual work

Control questions

1. Sol.s for inner use. Rules of calculation and prescription main and officinalsol.s. Features of prescribing spirit and oil sol.s.
2. Concept about drops for inner use, as versions of sol.s for inner use. Officinal and main prescriptions. Rules of calculation.
3. Suspensions for inner use. The characteristic and differences from sol.s. Rules of prescription.
4. Dosage aerosols. Characteristic and rules of prescription.
5. 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.
6. Features of prescribing of patented and New Galen’s dosage sol.s.

List of practical works. Write prescriptions:

1) 200 ml. 10% of sol. Calcii chloridum (*Calci chloride*). 1 table spoon 3 times a day. Calculate an SD for Calcii chloridum.
2) Dioninum, drops for inner use. SD – 0,01 20 drops 3 times a day for 10 days. Write in developed and short form.
3) 10 ml. of 5% spirit sol. Iodum (Iodine). 5 drops at milk 2 times a day after meal for 30 days.
4) Suspension “Maalox”, vial for 250 ml. 1 table spoon 4 times a day
5) Aerosol ‘Berotek’ 15 ml. One inhalation 3 times a day.
6) 10 ampoules, containing 1 ml. 0,1% sol. Atropini sulfas, injection S.C. 1 ml., account SD.
7) 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.
8) 500 ml. of sterile isotonic 0,9% sol. Natrii chloridum (*Sodium chloride*). Prescribe 500 ml. I.V.
9) 10 ampoules, containing 1 ml. 1% oil sol. Progesteronum (*Progesterone*). I.M. injection, 1 ml.
10) 6 vials, containing 5 ml. 2,5% suspension Hydrocortisoni acetas (*Hydrocortisone acetate*). For injection in the cavity of affected joint; 3 ml. 1 time a week.

Tasks for self-control. Answer the following questions:

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

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.

Unit 4. SOFT DOSED MEDICIINAL FORMS. NON-DOSED MEDICINAL FORMS. CHECKING OF PRACTICAL SKILLS ON "MEDICAL PRESCRIPTION"

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. Solid non – dosed drug forms (powders). Rules of prescribing simple and complex powders. Constitutional substances for powders.
5. 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.
6. Non – dosed sol.s. Drops (eye, ear, dental and nasal), lotions, gargles, syringes. Rules of prescribing.
7. Suspensions, emulsions and aerosols for external use. 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 of powders, ointment, paste, containing 2% Amycazolum.
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.
10) 100 ml. 0,02% sol. of Furacilinum. For irrigating wound.
11) 100 ml. 10% oil sol. of Camphora (Camphor) for rubbing.
12) 10 ml. 0,1 % sol. Naphthysinum. For dropping in the nose.
13) Aerosol 'Amprovisolum' 50 ml. for external use. Place at the staggered surface for 5 sec.

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 constituens used to prepare the magistral powders, ointments, liniments, pastes? 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 powder, tablets, drops for inner use, sol. for injections (ampoules 1 ml. for I.M.), rectal suppositories.
2) 20 vaginal suppositories, containing Metronidazolum 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 powder, ointment, liniment, pastes containing 5.0 Streptocidum.
6) 10.0 ointment containing 1% Tetracyclini hydrochloridum. Lubricate the skin surface.
7) 50.0 powders, ointments, pastes containing 1% of salicylic acid (Acidum salicylicum), 3% boric acid (Acidum boricum) and 15% zinc oxide (Zinci oxydum).
8) 50 ml. of a 1% aqueous and alcoholic sol. of brilliant green (Viride nitens). Lubricate the skin surface.
9) 5 ml. of eye – drops in the form of a 5% suspension of hydrocortisone acetate (Hydrocortisoni acetas). 2 drops into the conjunctival sac.
10) 5 ml. of eye drops containing Sofradeks (Sofradeks).
11) Aerosol "Ingalipt» (Inhalyptum), 80 ml. bot.. Apply to the affected mucosa of the mouth.
12) 50 powders, tablets containing Platyphyllini hydrotartras, RD – 0.005 and Papaverini hydrochloridum, RD – 0.02.
13) Mixture, containing infusion of herbs cooked in Thermopsis (herba Thermopsidis), RD – 0.05, with the addition of ammonia – anise drops (Liquor ammonii anisatus), RD – 10 drops and sodium bicarbonate (Natrii hydrocarbonas), RD – 0.2.
14) Marshmallow extract (Althaea) liquid, RD – 20 drops.
15) 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.
16) Solutan (Solutan), a bot. of 50 ml. 20 drops three times a day.

SECTION II. GENERAL PHARMACOLOGY

Actuality of the unit. 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*: 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*: 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 5. 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: placentare, 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 (T1 / 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).

Unit 6. **GENERAL PHARMACOLOGY. PHARMACODYNAMICS.**

I. Individual work

Control questions

1. PHARMACODYNAMICS of the drugs:
   1. 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.
   2. 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.
   3. 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."
   4. 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.

5. 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.
6. 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").
7. Drugs interaction: addition, potentiation, antagonism and its types. Information about polypragmasy;
8. Incompatibility of drugs: physical, chemical, pharmacological. Use in medical practice.

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

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?

SECTION III. SPECIAL PHARMACOLOGY

DRUGS INFLUENCING THE PERIPHERAL INNERVATION

DRUGS INFLUENCING THE 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.

The training objectives. *To know* : the pharmacology of drugs that affect on the efferent part of the nervous system. *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.

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

Unit 7. CHOLINERGIC AGENTS. 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** – Armine[1]

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 – HOLINOMIMETICS direct and indirect (anticholinesterase substance) action. Mechanisms of action. Pharmacological effects. Pharmacokinetics. Comparative characteristics of preparations. Indications for use. Undesirable effects.
8. Poisonings with OPS. First Aid (reaktivator cholinesterase: Dipiroksim, Alloksim, Isonitrozin).

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

№	Name of the drug	Drug form
1.	**Pilocarpine** *(Pilocarpini hydrochloridum)*	Vial 5 ml. 1 % sol., eye drops
2.	**Neostigmine** (*Proserinum)*	Tab. 0,015; amp. 0,05 % sol. 1 ml.

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

3.	**Cyciton** *(Cytitonum)*	Amp. 1 ml.
4.	**Galanthamine** *(Galanthamini hydrobromidum)*	Amp. 1 % sol. 1 ml.
5.	**Pyridostigmine** *(Pyridostigmini bromidum)*	Tab. and dragee 0,06;amp. 0,5 % sol. 1 ml.
6.	**Alloxim** *(Alloximum)*	Amp. 0,075 lyophilic powder

Tasks for self-control. Choose the correct answers.

1. What effects cause M – cholinomimetics?

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;

Unit 8. 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 – holinergic blockers ─ atropine, belladonna preparations, scopolamine, homatropine, platifillin, metacin, ipratropium, gastrotsepin etc .;
   2) N – holinergic blockers :

– ganglionic blockers ─ gigrony, pentamin, benzogeksony, pahikarpin, pyrylium;
– myorelaxants ─ tubocurarine, diplatsin, pipekuroniyu, vecuronium, atracurium, dithylin;

   3) M, N – holinergic 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. Theraputic use. Undesirable effects. Treatment in cases of overdose.

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
1	2	3
1.	**Atropine** *(Atropini sulfas)*	Amp. 0,1 % sol., 1 ml.; eye drops – vial 1 % sol. 5 ml.
2.	**Platifilline** *(Platyphyllini hydrotartras)*	Amp. 0,2 % with 0,2 % sol. 1 ml.
3.	**Scopolamine** *(Scopolamini hydrobromidum)*	Amp. with 0,05 % sol. 1 ml.
4.	**Metacin** *(Methacinum)*	Tab. 0,002; amp. 0,1 % sol. 1ml.
5.	**Homatropine hydrobromide** *(Homatropini hydrobromidum)*	Vial of 0,25 % sol., eye drops, 5 ml.
6.	**Ipratropium** *(Ipratropium bromidum)* 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** *(Pirenzepi)* syn.: Gastrozepin	Tab. by 0,025; 0,05
8.	**Cyclodol** *(Cyclodolum)*	Tab. by 0,002
9.	**Pachicarpin** *(Pachycarpini hydroiodidum)*	Amp. 3 % sol. 2 ml.
10.	**Pentaminum** *(Pentaminum)*	Amp. 5 % sol. 1; 2 ml.

11.	**Tubocurarine** *(Tubocurarinum chloridum)*	Amp. by 1,5 ml. (1 ml. — 0,01)
12.	**Dithylinum** ***(****Dithylinum)*	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.

Unit 9. PREPARATIONS INFLUENCING ON TRANSMISSION OF NEURAL IMPULSE IN ADRENERGIC SYNAPSE. 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: there types, locflisation 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 t* – Dopamine*, Ephedrine;
2) *α-adrenergic agonists* – Noradrenaline, Mesatonum, Naphthyzinum, Halazolinum(Xelomethazoline)

Central α2-adrenomimetics Clophelinum(Clonidine), Methyldopa, Guanfacine**;

3) β – adrenergic agonists:
   – Non – selective (β1-+β2) – Isadrinum, Alupent (Orciprenalinum)***;
   – Cardioselective (β1) – Dobutamine;

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

**Central α2-adrenoceptor agonists are discussed in topic № 25

*** Ortsiprenalin stimulates predominantly β 2-adrenergic receptors.

– β2-selective:

- *– short-acting (3-8h)*

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

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

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** *(Adrenalini hydrochloridum)*	Amp.0,1 % sol., 1 ml.
2.	**Dopamine** *(Dofaminum)*	Amp. 4 % sol., 5 ml.
3.	**Ephedrine** *(Ephedrini hydrochloridum)*	Amp. 5 % sol.,1 ml.; tab. 0,025
4.	**Noradrenaline** (*Noradrenalini hydrotartras)*	Amp. 0,2 % sol., 1 ml.
5.	**Mesatonum** *(Mesatonum)* syn.: Phenylephrine	Amp. 1 % sol.1 мл, tab. 0,01
6.	**Halazolinum** *(Halazolinum)* syn.: Xylomethazoline	VIAL 0,05 and 0,1 % sol., nasal drops
7.	**Isadrinum** *(Isadrinum)* syn.: Isoproterenol, Novodrin	Tab. by 0,005; vial 0,5 % sol. f/inh. by 25, 100 ml.
8.	**Dobutamine** *(Dobutaminum)*	Amp. 5 % sol., 5 ml.
9.	**Salbutamol** *(Salbutamolum)* syn.: Ventolin	Aer. f/inh. 0,1 mg/dose, balloon 10 ml.; tab. 0,002, 0,004
10.	**Fenoterol** *(Fenoterolum)* syn.: Berotec, Partusisten	Aerosol f/inh. 0,2 mg/dose, 15 ml.; tab. 0,005; (*Partusisten)* – 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 ß-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 preasure
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;

Unit 10. **ADRENONEGATIVE PREPARATIONS**

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). Adrenolitics are the leading drugs in the treatment of the most common diseases of the cardiovascular system: hypertension, tachyarrhythmias, ischemic heart disease (angina, myocardial infarction, cardiosclerosis), 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, Tropaphenum, Aminazinum, Pyrroxanum;
   - Selective (α_1) – Prazosin, Doxazosin, Terazosin
3) β – adrenergic antagonists:
   - *Nonselective* ($\beta 1_{+2}$) – Propranolol (Anaprilinum), Oxprenolol*, Pindolol*, Timolol
   - *Selective* (β1) – 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.

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.

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

№	Name of the drug	Drug form
1.	**Dihydroergotamine**	Amp. 0,1 % sol. 1 ml., tab. 0,0025

	(Dihydroergotaminum)	
2.	**Phentolamine** *(Phentolamini hydrochloridum)*	Tab. 0,025
3.	**Prazosin** *(Prazosinum)* syn.: Minipress	Tab. 0,001, 0,005
4.	**Doxazosin** *(Doxazosinum)*	Tab. 0,002, 0,004
5.	**Anaprilinum** *(Anaprilinum)* syn.: propranolol, inderal, obzidan	Tab. 0,01 and 0,04
6.	**Pindolol** *(Pindololum)*	Tab. 0,005; ampl. 0,02 % sol. 5 ml.
7.	**Timolol** *(Timololum)*	Tab. 0,005, 0,01; vial 0,25; 0,5 % sol. 5 ml. (eye drops).
8.	**Metoprolol** *(Metoprololum)* syn.: spesicor, lopresol	Tab. 0,05 and 0,1; amp. 1 % by 5 ml.
9.	**Atenolol** *(Atenololum)*	Tab. 0,05, 0,025 и 0,1
10.	**Carvedilol** *(Carvedilolum)*	Tab. 0,0625, 0,0125, 0,025
11.	**Reserpine** *(Reserpinum)*	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 ß-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 ß-blockers:

A. Bradyarrhythmia
B. Arterial hypertension
C. Angina pectoris
D. Bronchial asthma
E. Atherosclerosis

5. Adverse effects of ß-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) the drug on the base of ergot alkaloids;
5) antianginal, requiring careful use in hypothyroidism, diabetes, etc.;
6) for treatment of glaucoma;
7) ß-blocker is not recommended during pregnancy;
8) amophilic β-adrenoblocker;
9) for treatment of hypertonic disease with the expressed displays of an atherosclerosis;
10) the preparation, which effect develops after 7 – 14 days of reception.

DRUGS INFLUENCING THE AFFERENT INNERVATION

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 agents affecting the re – receptors of the skin and mucous membranes. *Be able*: to solve the test tasks, situations – tional and pharmacotherapeutic problems, prescribe and analyze prescriptions on preparations in this section.

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

Unit 11. PREPARATIONS IRRITATING RECEPTORS

Actuality of the unit. Expectorant, laxative, choleretic 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 Thermopsidis, root of istoda, mukaltin, Pertussin, Terpin hydrate;

direct action – herb thyme, marshmallow root, rhizome cyanosis, plantain leaves, potassium iodide;

b) *mucolytics* (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 appetiteful, 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.

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***(Tinctura Amara)*	Vial 25 ml.
2.	Patented medicinal forms, containing Menthol: ointment **"Menovazine"**, **"Efcamone"**, tabl. **"Pectusinum"**, aerosolum **"Camfomen"** etc.	
3.	**Acetylcysteine** *(Acetylcysteinum)*	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 **Thermopsidis grass** (herba Termopsidis), SD – 0,05 and **Ammonia anise drops** (Liquorum ammonii anisatus), SD – 10 drops	
5.	**Mucaltin** *(Mucaltinum)*	Tab. 0,05
6.	**Ambroxole** *(Ambroxolum)* syn.: Lasolvan	Tab. 0,03; amp. 0,015 % sol. 2 ml. for injections; vial. 0,75 % sol. 100 ml. for peroral intake and inhalations

7.	**Castor oil** *(Oleum Ricini)*	Vial 30 ml., caps. 0,5 and 1,0.
8.	**Decoction of bark Frangula** *(cortex Frangulae)*, SD – 2,5	
9.	**Bisacodyl** *(Bisacodylum)*	Dragee 0,005; suppositories 0,01
10.	**Magnesium sulfate** *(Magnesii sulfas)*	SD – 25,0.
11.	**Allohol** *(Allocholum)*	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. Terpine
E. Acetylcysteine

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

A. Bromhexine
B. Acetylcysteine
C. Mucaltin
D. Terpine
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 case of oral poisoning;
5) laxative in the decoction form;
6) synthetic laxative, causing chemical irritation of the intestinal mucous membrane receptors;
7) laxative for chronic constipation, acting mainly in the small intestine;
8) drug, stimulating bile secretion;
9) choleretic comprising a bile acid;
10) bile expelling preparations from spasmolytic group;
11) drug in case of myositis.

Unit 12. DRUGS PROTECTING THE RECEPTORS. CHECKING OF PRACTICAL SKILLS ON "AGENTS INFLUENCING ON AFFERENT AND EFFERENT INNERVATIONS".

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
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.

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

№	Name of the drug	Drug form
1.	**Anaesthesin** *(Anaesthesinum)*	Tab. 0,3; 5 % ointment
2.	Patented preparations on the basis of Anaesthesinum: **Bellasthesinum''**, **Pavesthesinum**", suppositories Anaesthesolum, ointment Menovazinum, Sledianum	
3.	**Novocain** *(Novocainum)* syn.:Procaine	Amp. 0,25% sol. (for infiltration anesthesia); 1 – 2 % sol. (for conductive anesthesia) 10 ml.
4.	**Lidocaine** *(Lidocainum)*	Amp. 1 % sol. 10 and 20 ml.; 10 % 2 ml.; 2 % 2 and 10 ml.
5.	**Trimekain** *(Tetracainum)* syn.: Dicain	Amp. 0,5 %; 1 %, 2 % and 3 % sol.s 5 ml.
6.	**Ultrakain** (*Ultracainum)*	Amp. 1 % and 2 % sol. 1 ml.
7.	**Zinc sulfate** (*Zinci sulfa)s*	Eye drops 0,1 %, 0,25 %, 0,5 % sol. 10 ml.

8.	**Maalox** *(Maalox)*	Patented tab., suspension in vial 250 ml.
9.	**Enterosgel** *(Enterosgelum)*	Pack with gel by 45, 135, 225, 450, 650 and 900 g.

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) shot-acting local anaesthetic for infiltration anaesthesia;
2) local anaesthetic used in ophthalmology;
3) local anesthetic for conductive anaesthesia;
4) local anesthetic in suppositories;

5) local anesthetic as antiarrhythmic;
6) astringent in eye drops;
7) prevents the absorption of poison in case of poisonings;
8) for treatment of peptic ulcer.

DRUGS ACTING ON 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;
- nootrops, 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 13. GENERAL ANESTHETICS. 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 – Ether[3], 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.
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 disulfiraml.ike 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** *(Propofolum)* syn.: Diprivan	Amp. 1 % emulsion by 20 ml.
2.	**Propanidid** *(Propanididum)* syn .: Sombrevin	Amp. 5 % sol. 10 ml.
3.	**Ketamine hydrochloride** *(Ketamini hydrochloridum)* syn.: Kalipsol, Ketalar, Ketanest	Vial 1 % sol. 20 ml. and 5 % sol. 10 ml.
4.	**Thiopental-sodium** *(Thiopenthalum-natrium)*	Vial 0,5 and 1,0
5.	**Sodium oxybutyrate** *(Natrii oxybutyras)*	Amp. 20 % sol. 10 ml.
6.	**Ethanol** *(Spiritus aethylicus)*	40 %, 70 %, 95 % sol.
7.	**Teturam** *(Teturamum)* syn.: Disulfiram	Tab. 0,15 and 0,25

Tasks for self-control. Choose the correct answers.

[3] Currently is not used practically.

1. What preparation is most often causes damage to the liver:
A. Nitrous oxide
B. Halothane
C. Hexsenal
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) non-inhalation 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 a patient with complaints of vomiting, headache, severe pain in the stomach and in the calf muscles, flickering flies in front of the eyes was delivered. He drank alcohol on the eve. What caused the poisoning? What is the antidote?

Unit 14. 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 – gistaminoreceptors (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. Theraputic 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, daazepam etc .;

– Hydantoin derivatives – phenytoin (Diphenin), etc .;

– Fatty acid derivatives – valproate (Depakine) and sodium valproate, gamma – aminobutyric acid (sodium oxibutirate, Aminalon), 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 oppressing his 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.

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

№	Name of the drug	Drug form
1)	**Phenobarbital** *(Phenobarbitalum)*	Tab. 0,05 ;0,1 and 0,005 for children
2)	**Nitrazepam** *(Nitrazepamum)* syn.: Radedorm	Tab. 0,005 and 0,01
3)	**Doxylamine** *(Doxylamine)* 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** *(Dipheninum)* syn.: Phenytoin	Patented tab.
8)	**Depakene** *(Depakinum)* syn.: Sodium valproate, Konvulex	Tab. 0,3; syrup in vial 150 ml.; amp. 0,4 f/inj.
9)	**Carbamazepine** *(Carbamazepinum)* syn.: Finlepsin, Tegretol	Tab. 0,1; 0,2 и 0,4
10)	**Ethosuximide** *(Ethosuximidum)* syn.: Suksilep	Caps. by 0,25
11)	**Levodopa** *(Levodopa)*	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 "emotional" form of insomnia;
2) hypnotic – inducer of liver microsomal oxidation;
3) hypnotic, almost not causing apnea during sleep;
4) with the expressed phenomenon "after-action" (“hangover”);
5) hypnotic don`t do anxiolytic, anticonvulsant and muscle relaxant effects;
6) anticonvulsant with spasmolytic, hypotensive, tocolytic effects;
7) for prevention of petit mal (absence) attacks;
8) for prevention of grand mal (tonic-clonic) attacks;
9) in status epilepticus;
10) antiepileptic agent – Na^+-channel blocker with anti-arrhythmic activity;
11) antiepileptic agent – NMDA-receptor blocker;
12) antiepileptic agent at neuralgia of trigeminal nerves;
13) dopaminergic antiparkinsonian agent;
14) cholinergic drug for treatment Parkinson’s syndrome.

Unit 15. PHARMACOLOGY OF NON-NARCOTIC ANALGESICS. 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 irritional use of serious undesirable – governmental actions (ultserogenic, 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 polling 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 preperations: Arthrotec® (Diclofenac + Misoprostol), Dolaren (Diclofenac + Paracetamol), Coldrecs (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** *(Acidum acetylsalicyllicum*) syn.: Aspirin, Aspirin-cardio	Tab. 0,1; 0,25; 0,325; 0,5
2.	**Analgin** (*Analginum)* syn.: Methamizole	Tab. 0,5; amp. 25 and 50 % sol. 1 and 2 ml.
3.	**Baralgin** *(Baralgin)* syn.: Spazmalgon, Maksigan, Trigan	Tab. patented; amp. by 5 ml.; supp. rect.
4.	**Paracetamol** *(Paracetamolum)* 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
5.	**Ibuprofen** (*Ibuprofenum)* syn.: Brufen	Tab. 0,2; 0,4 и 0,6; syrup 2 % sol. 100 ml.; ointment 5 %; gel 10 % by30,0
6.	***Diclophenac-sodium*** *(Diclophenac-natrium)* syn.: Ortophen, Voltaren	Tab. 0,025; supp. rect. 0,05; amp. 2,5 % sol. 3 ml.; ointment 2 % by 30.
7.	**Indomethacin** *(Indometacinum)* syn.: Metyldole	Tab. 0,025, 0,0075, 0,01, 0,1; supp. rect. 0,05; ointment 10 % 40,0.
8.	**Naproxen** *(Naproxenum)* syn.: Bonifen	Tab. 0,25 and 0,5; supp. rect. by 0,25 and 0,5
9.	**Meloxicam** *(Meloxicamum)* syn.: Movalis	Tab. 0,0075 and 0,015; rectal supp. by 0,015
10.	**Nimesulide** *(Nimesulide)*	Tab. 0,1 and 0,2; gel 1 % by 20,0

	syn.: Nimesil, Nimulid, Nice	
11.	**Celecoxib** *(Celecoxib)* syn.: Celebrex	Caps. by 0,1 and 0,2
12.	**Ketorolak** *(Ketorolak)* syn.: Ketanov	Tab. 0,01, amp. 3 % sol. 1 ml.
13.	**Dimexid** (*Dimexidum)*	100 ml bottle
14.	**Benzydamine** (*Benzydamine*) syn.: tantum	

Tasks for self-control. Choose the correct answers.

1. What is the analgesic which doesn't have anti-inflammatory effects:

A. Aspirin
B. Paracetamol
C. Nimesulide
D. Analgin
E. Voltaren

2. Specify the pharmacological effects of non – narcotic analgesics

A. Analgesic
B. Psychostimulant
C. Antipyretic
D. Anticonvulsive
E. Anti-inflammatory

3. Choose combined preparations of non – narcotic analgesics

A. Indomethacin
B. Spazmalgon
C. Nimesulide
D. Meloxicam
E. Baralgin

4. Ways of easing ulcerogenic action of NSAIDs

A. Take with coating demulcents
B. Use selective COX-2 inhibitors
C. Combine with β-blockers
D. 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) in case of arthralgia with gastric ulcer;
12) NSAID for local usage with fibrinolytic and antiseptic actions, good penetrated through tissue barriers;
13) for mouth gargling in case of inflammation with pain syndrome

Unit 16. PHARMACOLOGY OF NARCOTIC ANALGESICS

Actuality of the unit. Narcotic analgesics are substances that capable with resorptive action to suppress intracentral 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. OPIUM ALKALOIDS. Classification:

a) derivatives of *phenanthrene* (Morphine, Codeine);

b) derivatives of *isoquinolin* (papaverine).

5. 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;

6. Opioid receptors. Endorphins and enkephalins.

7. 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);

8. Morphine's pharmacodynamics and pharmacokinetics.

9. Comparative characteristics of narcotic analgesics.

10. Indications and contraindications. Adverse effects.

11. 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!):*

№	Name of the drug	Drug form
1.	**Morphine hydrochloride** *(Morphini hydrochloridum)*	Amp. 1 % sol. 1 ml.; tab. 0,01
2.	**Omnoponum** *(Omnoponum)* syn.: Pantopon	Amp. 1 and 2 % sol. 1 ml.
3.	**Codeine phosphate** *(Codeini phosphas)*	Tab. 0,015
4.	**Ethylmorphine hydrochloride** *(Aethylmorphinum hydrochloridum)* syn.: Dionin	Tab. 0,015; (*Dioninum*), 1 – 2 % sol., eye drops
5.	**Promedolum** *(Promedolum)* syn.: Trimeperidine	Tab. 0,025; amp. 1%, 2% sol. 1 ml.
6.	**Fentanyl** *(Phentanylum)*	Amp. 0,005% sol. 1, 2 and 10 ml.

	syn.: Fentanest	
7.	**Pentazocine** *(Pentazocinum)* syn.: Elixir, Fortre	Tab., supp. by 0,05; amp. 3 % sol. 1 – 2 ml.
8.	**Tramadol** *(Tramadolum)* 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** *(Buprenorphinum)*	Tab. 0,0002; amp. 0,03 % sol. 1 and 2 ml.
10.	**Naloxone** *(Naloxonum)*	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. Spasmolitic
- 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.

Unit 17. 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*[4] (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.
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 trancquilizers. 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 (T1 / 2 to 6 hours) – Triazolam, Midazolam.
- medium – acting (6 – 24 h) – Lorazepam, Nozepam, Flunitrazepam and others.
- long – acting (T1 / 2 more than 24 hours) – Nitrazepam, Phenazepam, Diazepam, Phenazepam, Flurazepam (prodrug, T1 / 2 ≈ 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 – mezapam, gidazepam, buspirone, mebicar.

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

PSYCHOSEDATIVES.

1. General characteristic. Classification:

[4] It is used in gastroenterology

- 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 + Barbital – sodium), etc.
- 3. 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** *(Aminasinum)* syn.: Chlorpromazine	Dragee 0,025, 0,05 и 0,1; amp. 2.5% sol. 1, 2, 5, 10 ml.; tab by0,01;
2.	**Aethaperazine** *(Aethaperazinum)*	Tab. 0,004; 0,006 and 0,01
3.	**Haloperidol** *(Haloperidolum)*	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** *(Droperidolum)*	Amp. 0,25% sol. 2, 5 and 10 ml.
5.	**Talamonal** *(Thalamonal)*	Amp. by 2ml.
7.	**Flushpirilen** (*Fluspirilenum*)	Amp. by 2 ml. suspension (1 ml. – 0,002).
6.	**Sulpiride** *(Sulpiridum)* syn.: Eglonil	Caps. 0,05
8.	**Azaleptine** (*Azaleptinum)* syn.: Clozapine, Leponeks	Tab. 0,025 and 0,05; amp. 2,5% sol. 2 ml.
9.	**Chlozepide** *(Chlozepidum)* syn.: Chlordiazepoxide, Elenium	Tab., dragee, caps. 0,005, 0,01 and 0,025
10.	**Diazepam** *(Diazepam)* syn.: Seduksen, Sibazon, Relanium, Valium	Tab. 0,0001; 0,002 and 0,005; amp. 0,5% sol. 2 ml.
11.	**Phenazepam** *(Phenazepamum)*	Tab. 0,0005; 0,01 and 0,0025; amp. 0,3% sol. 1 ml.
12.	**Gidazepam** *(Gidazepamum)*	Tab. 0,02 and 0,05
13.	**Tinct. Leonuri** *(T-ra Leonuri)*	Vial 50 ml.
14.	Mixture of **Tinct**. **radix Valerian** (Valeriana), SD – 0,5, and **Sodium bromide** (Natrii bromidum**)**, SD – 0,3	
15.	**Valocordin** *(Valocordin)*	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. Extrapyramidal 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.

Unit 18. ANTIDEPRESSANTS. PSYCHOSTIMULATORS. NORMOTHYMICS

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, increases 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:
   - *nonselective 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 α2-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: Antidepresive activity also possess drugs of other pharmacological groups: anxiolytics (alprazolam, buspirone), antiparkinsonian drugs (midantan), antiepileptics (karbamazepin), low – dose of neuroleptics (Thioridazine, Levomepromazine,Clozapine), gepatoprotektors – Heptral etc. .

2. Pharmacokinetics of antidepressants.

3. Pharmacodynamics. The conception of the thymeretics, sedatic and "balanced" action of antidepressants. Comparative characteristics of preparations from different groups. Classification depending on clinical effect.

4. Indications and special features of clinical usage.

5. Adverse effects. Contraindications for usage.

NORMOTHYMICS

1. *Lithium* preparations (Lithium carbonate / Lithionitum – 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) phenylalkilamines – Amphetamine[5] (Phenaminum);

2) sydnonimines – Sydnocarbum;

3) *purine* derivatives (xanthines)[6] – Caffeine, Caffeine – benzoate sodium.

4) *piperidine* derivatives – meridil

2. Pharmacokinetics, pharmacodynamics of phenylalkilamines. Adverse effects, clinical usage. Rules of application. Formation of dependence. Features of Sydnokarbum and Meridil destination.

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

Conception of ACTOPROTECTORS (bemethyl).

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

№	Name of the drug	Drug form
1.	**Pirazidol** (*Pyrazidolum)*	Tab. 0,025 and 0,05
2.	**Amitriptyline** *(Amitriptylinum)*	Tab. 0,025; amp. 1 % sol. 2 ml.

[5] In medical practice, are not used

[6]Complete classification of xanthine, see the topic number 23.

3.	**Imizine** *(Imizinum)* syn.: Imipramine	Tab. 0,025; amp. 1,25 % sol. 2 ml.
4.	**Maprotiline** *(Maprotiline)*	Tab. 0,025
5.	**Fluoxetine** *(Fluoxetinum)* syn.: Prozac	Tab., caps. 0,01 and 0,02
6.	**Bupropion** *(Bupropion)*	Tab. 0,15
7.	**Mirtazapine** *(Mirtazapine)*	Tab. 0,03
8.	**Coaxil** *(Coaxil)* syn.: Tianeptine	Tab. 0,125
9.	**Lithium carbonate** (*Lithii carbonas)*	Tab. 0,3
10	**Sydnocarb** (*Sydnocarbum)*	Tab. 0,005; 0,01 and 0,025
11.	**Caffeine-sodium benzoate** *(Coffeinum-natrii bensoas)*	Tab. 0,1 and 0,2; amp. 10% and 20% sol. 1 and 2 ml.

Tasks for self-control. Choose the correct answers.

1. Thymeretics effect of antidepressants is due to:

A Blockade of central α_2-adrenoceptor
B. Blockade of central H_1 histaminoreceptors
S. Central M – cholinomimetic effect
D. Blockade of central $5HT_2$-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 thymeretic 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).

Unit 19. NOOTROPS. ADAPTOGENS. ANALEPTICS

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 (pshychometabolic stimulators, cerebroprotectores)

1. General characteristics. Classification:

– substances with predominantly *cholinomimetic action:*

- *racetam* (pyrrolidone derivatives) – piracetam (nootropil), aniracetam, etiratsetam 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, Corazolum, Aethymisolum;
- drugs with the mixed mechanism of action – Camphora, Sulfocamphocainum, Cordiaminum.

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

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

№	Name of the drug	Drug form
1.	**Piracetam** (*Pyracetamum)* syn.: Nootropil	Tab. 0,4; 0,8 and 1,2; vials 20 and 33 % sol.
2.	**Aminalon** *(Aminalonum)*	Tab. 0,25
3.	**Cavintone** *(Cavinton)* syn .: Vinpocetine	Tab. 0,005; amp. 0,5 % sol. 2 ml.
4.	**Tinct. Ginseng** *(Tinctura Ginsengum)*	Vial 50 ml.
5.	**Liquid extr. Echinacea** *(Extractum*	Vial 50 ml.

	Echinacea fluidum)	
6.	**Pancrotin** *(Pancrotinum)*	Tab. 0,15; amp. 1 ml.; vials 50 ml.
7.	**Cordiamine** *(Cordiaminum)*	Amp. 1 and 2 ml.; amp. 1 ml.; vial by 15 ml. for inner use
8.	**Bemegride** *(Bemegridum)*	Amp. 0,5% sol. 10ml.
9.	**Aethymizole** *(Aethymizolum)*	Tab. 0,1; amp. 1% and 1,5% sol. 3 and 5 ml.
10.	**Sulfocamfocain** *(Sulfocamfocainum)*	Amp. 10 % sol. 2 ml.
11.	**Camphor** *(Camphora)*	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.

1. Specify what will be after prolong administration of nootropcs:

A. Cerebroprotective action
B. Pro – oxidant action
C. Causes euphoria, dependence
D. Improve cerebral blood flow
E. Improve brain function

2. Which nootropic drug has the additional psychostimulant effect

A. Sulbutiamine
B. Lucidril
C. Aminalon
D. Pyritinol
E. Piracetam

3. Which adaptogen is known as "golden root"?

A. Ginseng
B. Schisandra
C. Rhodiola rosea
D. Leuzea
E. Eleutherococcus

4. Which analeptik do we use with an overdose of anesthetic and hypnotic drugs:

A. Caffeine
B. Bemegride
C. Sulfokamfokain
D. Kordiamin
E. Etimizol

5. What will be in overdose of analeptics?

A. Collaps
B. Acidosis
C. Cardiac arrest
D. Seizures
E. 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) analeptic, topically used as an antiseptic and irritant;
4) adaptogen with nootropic activity;
5) in case of faint, acute vasal insufficiency;
6) analeptic – derivative of nicotinic acid;
7) in case of respiratory center depression with symptoms of cardial failure;
8) for increasing of vitality tonus and immune resistance;
9) in rehabilitation period after cerebro – cranial trauma.

Unit 20. PREPARATIONS CAUSING ABUSE. CHECKING OF PRACTICAL SKILLS ON "DRUGS ACTING ON THE CNS".

DRUGS OF ABUSE[7]: hallucinogens, opioids, amphetamines, Cocaine, Caffeine, antidepressants, Cannabis, barbiturates, barbiturates, tranquilizers, alcohol, nicotine etc.

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

DRUGS AFFECTING THE CARDIOVASCULAR SYSTEM

The training objectives. *To know:* pharmacology of drugs affecting the cardiovascular system. *Be able to:* solve the test tasks, situational and pharmacological tasks, to prescribe and analyze recipes for preparations of this section.

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

Unit 21. CARDIOTONICS. CARDIAC GLYCOSIDES. NON-GLYCOSIDES CARDIOTONICS

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

[7] 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 sudstances lead to dependence.

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 cardiotonic 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** (*Digitoxinum*)	Tab. 0,0001; rectal suppositories 0,00015
2.	**Digoxin** (Digoxinum)	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** *(Herba Adonis vernalis)*, MD – 0,5	
5.	**Strophanthin** (*Strophanthinum)*	Amp. 0,05 % sol. 1 ml.
6.	**Corglyconum**	Amp. 0,06 % sol. 1 ml.
7.	**Cardiovalenum**	Bot. 15 ml.
8.	**Unithiol** (*Unithiolum)*	Amp. 5 % sol., 10 ml.
9.	**Panangin** (*Panangin)* syn.: asparkam	Patented dragee and amp. 10 ml.
10.	**Trilon B** syn .: disodium edetate	Amp. 5 % sol. 5 and 10 ml.
11.	**Dobutamine (***Dobutaminum)*	Amp. 5 % sol. 5 ml.
12.	**Milrinone** (*Milrinonum)*	Amp. 0,1 % sol. 1 ml.

Tasks for self-control. Choose the correct answers.

1. What is the reason of cardiotonic 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 QRST complex and increasing of R wave. As a result of what effect did this happen?

A. «+» tonotropic
B. «+» inotropic
C. « – » chronotropic
D. « – » dromotropic
E. «+» bathmotropic

4. Patient with chronic heart failure who received Digitoxin appeared headache, nausea, xanthopsia. Which drug may reduce the symptoms of intoxication?

A. Naloxone
B. Dipyroxim
C. Bemegride
D. Unitiol
E. Atropine sulfate

5. The patient with cardiogenic shock received cardiotonic 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) cardiotonic from group of stimulators of β1 adrenoreceptors.
9) cardiotonic – a phosphodiesterase inhibitor.

Unit 22. 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. Ethiopathogenic 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* — dihydropiridine derivatives:
- 1st generation — Nifedipine (Fenigidin, Corinfar);
- 2nd generation — Nifedipine – GITS, Aml.odipine, 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 affects.

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 (***Novocainamidum)* syn.: Procainamide	Tab. 0,25, amp. 10% sol. 5ml.
2.	**Diphenin** (*Dipheninum*) syn.: Phenytoin	Tab. patented.
3.	**Lidocaine hydrochloride** *(Lidocainum hydrochloridum*)	Amp. 2 % sol. 2 and 10 ml.; amp. 10 % sol. 2 ml.
4.	**Propafenone** *(Propafenone*) syn.: Ritmonorm	Tab. 0,15 and 0,3; amp. 0,35 % sol. 10 and 20 ml.
5.	**Anaprilin** *(Anaprilinum)* syn.: Propranolol	Tab. 0,01 and 0,04.
6.	**Atenolol** *(Atenololum)*	Tab. 0,05, 0,025 and 0,1
7.	**Acebutolol** *(Acebutololum)*	Tab. 0,2 and 0,4
8.	**Amiodarone** (*Amiodaronum)* syn.: Cordarone	Tab. 0,2, 0,05, amp. 5 % sol. 3 ml.
9.	**Verapamil** (*Verapamilum)* syn.: Izoptin, Finoptinum	Tab. 0,04, 0,08 and 0,12; amp. 0,25 % sol. 2 ml.
10.	**Tincture of Hawthorn** *(Grataegus)*	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. Aml.odipine
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 overdosage by cardiac glycosides;
9) antiarrhythmic of plant origin.

Unit 23. ANTIANGINAL DRUGS. 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 throung 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 If – channels of the sinus node controlling spontaneous diastolic depolarization (Ivabradine), and others.

I. Individual work

Control questions

ANTIANGINAL DRUGS

1. Ethiopathologic 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) ACE inhibitors – ramipril, perindopril;

d) 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.**;

b) selective blockers of If-channels (ivabradin).

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. Pecularities 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:
  - alkaloids: Caffeine (1,3,7 – trimethylxanthine), Theobromine (3,7 – dimethylxanthine), Theophylline (1,3 – dimethylxanthine);
  - semisynthetic: Aminophylline /Eufillin/, Diprofillin, Pentoxifylline /Trental, Agapurin/ etc.***;

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

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

*** Xanthines are rarely used as antianginal agents.

- mixed mechanism of action — Apressin, Dibazolum, 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, β2-adrenergic agonists increase the inhibitory effect through presynaptic β2-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), cardiotonic (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!):*

№	Name of the drug	Drug form
1.	**Nitroglycerine** (*Nitroglycerinum)*	Tab. 0,0005; caps. 0,0005; Bot. 1% spirit sol. 10 ml.; aerosols in balloons

		12,0 and 30,0
2.	**Sustak** (*Sustac)*	Tab. 0,0026 (– mite) and 0,0064 (– forte)
3.	**Isosorbide mononitrate** *(Isosorbidum mononitratum)*	Tab. 0,02 and 0,04; in ampoules with 1% sol. 1 ml.
4.	**Isosorbide dinitrate** *(Isosorbidum dinitratum)* syn.: Nitrosorbid	Tab. 0,005, 0.01 and 0,02; in ampoules with 1% sol. 10 ml.; caps 0,02 , 0,04 , 0,06
5.	**Molsidomine (***Molsidomin)* syn.: Corvaton	Tab. 0,002 and 0,004
6.	**Trimetazidine** *(Trimetazidinum)* syn.: Preduktal	Tab. 0,02
7.	**Dipyridamole** (*Dipyridamolum)* syn.: Curantylum	Tab. 0,025, in amp. 0,5 % sol. 2 ml.
8.	**ATP – long** *(Adenosinum phosphatum)*	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.

Unit 20. DIURETIC DRUGS. COMPLEX THERAPY OF CHRONIC HEART FAILURE. ANTI-GOUT DRUGS

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 electrolites 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. Knowledges of rational and safe use of diuretics contribute to successful treatment of various diseases, including heart failure.

I. Individual work

Control questions

DIURETICS

1. Ethiopathogenesis 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/, Bufenox /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;
- acidificating — 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;
- 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;

* Termin saluretics mean primarly inhibitors of Na^+ and Cl^- reabsorption.

- 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 (Aml.odipine);
- ***additional*** (in certain clinical situations): vasodilators (nitrates, calcium channel blockers), antiarrhythmic, non – glycoside cardiotonic, 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).

ANTI-GOUT 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.

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

№	Name of the drug	Drug form
1	2	3
1.	**Mannit** *(Mannitum)* syn.: mannitol	Bot. 500 ml., containing 30 g of substance; amp. 15% sol. 200, 400, 500 ml. each
2.	**Aminophylline** *(Aminophyllinum)* syn.: Euphyllin	Tab. 0,15; ampoules 2,4% – 10 ml. and 24% – 1 ml.
3.	**Diacarb** *(Diacarbum)* syn.: Acetazolamid	Tab. 0,25
4.	**Dorzolamidum**	Vial 2 % sol. 5 ml
5.	**Hydrochlorothiazide** *(Hydrochlorthiazidum)* syn.: Dihlotiazid, Hydrochlorothiazide	Tab. 0,025 and 0,1
6.	**Clopamide** *(Clopamidum)* syn.: Brinaldix	Tab. 0,02

7.	**Furosemide** *(Furosemidum)* syn.: Lasix	Tab. 0,04; amp. 1% 2 ml. *(Lasix)*
8.	**Torasemide** *(Torasemidum)* syn.: Trifas	Tab. 0,005, 0,02, 0,2
9.	**Ethacrynic acid** *(Acidum etacrynicum)* syn.: Uregei	Tab. 0,05
10.	**Triamterene (***Triamterenum)*	Caps. 0,05
11.	**Spironolactone** *(Spironolactonum)* syn.: veroshpiron	Tab. 0,025
12.	**Triampur** *(Triampur)*	Patented tab.
13.	**Amiloride** (*Amiloridum)*	Tab. 0,005
14.	**Allopurinol** (*Allopurinolum)*	Tab. 0,1

Tasks for self-control. Choose the correct answers.

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

D. Ural
E. Phytolysinum

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) 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 course treatment of gout;
10) agent for the treatment of acute attack of gout.

Unit 25. AGENTS THAT REGULATE BLOOD PRESSURE. ANTIHYPERTENSIVE AND HYPERTENSIVE PREPARATIONS

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. Ethiology of hypertension. Mechanisms for blood pressure contol.
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 α2-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; α1-Adrenergic blockers — Prazosin, Doxazosin;
   - α and β – blockers — Labetalol, Carvedilol, Proxodolol;
   - sympatholytic drugs — Reserpine, Raunatin, Octadin;
   - ganglioblockers — Benzohexony, 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/, Dibazolum, nicotinic acid and its derivatives (Ksantinola Nicotinate /Komplamin/, Nikoshpan) and others.

2) selective:
   - Calcium channel blockers — Verapamil, Nifedipine, Aml.odipine, Diltiazem **;
   - Potassium channel activators — Minoxidil, Diazoxide;
   - nitric oxide donators — Sodium nitroprusside and others.***

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

1) diuretics;
2) inhibitors of renin-angiotensin system
   a) ACE – inhibitors containing:
   - sulfhydryl group — Captopril, Alacepril, Zofenopril etc;
   - carboxyl group — Lisinopril, Enalapril, Perindopril, Ramipril, Trandolapril, and others;
   - phosphoryl group – Fosinopril, Ceronapril;

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* Full classification of miotropic agents is given in unit № 23.
** Classificaton of calcium channel blockers is given in unti № 22.
*** From clinical view, peripheral vasodilators are classified into: arteriolar (calcium channel blockers, potassium channel blockers, hydralazin /apressin/ etc.); arteriolar and venous (α-adrenoblockers, ganglionic blockers, nitrovasodilators (nitroglycerin, sodium nitroprusside), no-spa, papaverin etc.).

– hydroxame group — Idrapril.

b) antagonists of angiotensin II receptors:

- competitive (with quick reversible blockage – replaced by excess of angiotensin II - Losartan, Eprosartan;

- non-competitive (with slow reversible blockage) - Valsartan, Candesartan, Irbesartan, Telmisartan.

c) direct rennin inhibitors – aliskerin.

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

VI. *Combined* drugs — Adelphanum (Reserpine+Dihydralazine+Hydrochlorothiazide), Sinepres (Reserpine+Dihydroergotoxin+Hydrochlorothiazide), Kristepin (Reserpine+Dihydroergocristine+Clopamide), Kapozid (Captopril+Hydrochlorothiazide), Co – Renitek (Enalapril+Hydrochlorothiazide), Papazol (Papaverine+ Dibazolum) 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 — Corazolum, Cordiaminum, Caffeine, Camphora;
– Drugs acting on angiotensin system — Angiotensinamide;
– 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** (*Clophelinum)*	Tab. 0,000075, 0,00015, amp. 0,01 % sol. 1 ml.
2.	**Bisoprolol** *(Bisoprolol)* syn.: Concor	Tab. 0,005, 0,01
3.	**Nifedipine** (Niphedipinum) syn.: Fenigidin	Tab. 0,01 and 0,02
4.	**Aml.odipine** (*Aml.odipin)* syn.: Norvasc	Tab. 0,005, 0,01
5.	**Dibazol (***Dibazolum)* syn.: Bendazol	Tab. 0,004 and 0,02, amp. 0,5 and 1 % sol. 1, 2, 5 ml.
6.	**No-spa** (*Nospanum)* syn.: drotaverine	Tab. 0,04, amp. 2 % sol. 2 ml.
7.	**Papaverini hydrochloridum** *(Papaverini hydrochloridum)*	Tab. on 0,04; amp. 2 % sol. 2 ml.; rectal suppositories 0,02

8.	**Magnesii sulfas** (*Magnesii sulfas)*	Amp. 20 % sol. 5 ml., 25 % sol. 10 and 20 ml.
9.	**Xantinoli nicotinas** *(Xantinoli nicotinas)*	Tab. 0,15, amp. 15 % sol. 2 and 10 ml.
10.	**Captopril** *(Captoprilum)*	Tab. 0,025, 0,05, 0,1
11.	**Enalapril** (*Enalaprilum)*	Tab. 0,005, 0,01, 0,02
12.	**Lisinopril (Lisinopril)**	Tabl. 0,01 and 0,02
13.	**Fosinopril** *(Fosinopril)* syn.: Monopril	Tab. 0,01, 0,02
14.	**Losartan (***Losartanum)*	Tab. 0,05

Tasks for self-control. Choose the correct answers.

1. Which hypotensive drug is characterized by analgesic, hypothermic, sedative, nootropic, M – anticholinergic effects?

A. Captopril
B. Nifedipine
C. Dibazol
D. Metoprolol
E. Clonidine

2. Note the effects typical to calcium channel blockers?

A. Spasmolytic effect
B. Uterotonic effects (increased uterine contractions)
C. Atherogenic effect
D. Nephroprotective, diuretic effect
E. Antiaggregant effect

3. Choose a calcium channel blocker, causing reflex tachycardia

A. Verapamil
B. Nifedipine
C. Aml.odipine
D. Cinnarizine
E. Nimodipine

4. What adverse effects can occur during the use of ACE inhibitors?

A. Dry cough
B. Hypokalemia
C. Violations of renal function
D. Violations of vision
E. Violation of sexual function

5. The aldosterone receptor antagonists unlike ACE inhibitors:

A. Reduce the hypertrophy of the left ventricle of the heart
B. Do not change the level of potassium in the blood
C. Affects the level of bradykinin, prostaglandins, prostacyclin in the blood
D. 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) ACE inhibitor that is a lipophilic pro-drug;
10) long-acting ACE inhibitor that almost doesn't undergo metabolism;
11) hypotensive – antagonist of angiotensin – II receptors;
12) in case of acute hypotension.

Unit 26. AGENTS ACTING ON MICROCIRCULATION AND BLOODFLOW

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* A_2: 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. Ethiopathogenesis. 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 /Sermyon/, Dihydroergotamine, Dihydroergotoxine etc.;
- *calcium channel blockers* — Nimodipine, Cinnarizine, Flunarizine;
- *antagonists of serotonin* — Methysergide, Peritol, Pyzotiphen /Sandomygran/ etc.;
- *drugs that improve metabolic processes* — nootrops (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: Ethiopathogenic factors. Classification of drugs:

– *for a treatment of migraine attacks*:
  - specific (anti – migraine) action: alpha – adrenoblockers (ergotamine, dihydroergotamine) and 5 – HT_1 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 – HT_2 receptor antagonists (Methysergide, Pyzotiphen, 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:

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

Concept about VEINOTONIC DRUGS: endotheliotropic, drugs and other ergot alkaloids. Indications and contra – indications.

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

№	Name of the drug	Drug form
1.	**Fenofibrate** *(Phenofibrate)*	Caps. 0,1
2.	**Lovastatin** *(Lovastatinum)*	Tab. 0,1; 0,2; 0,4
3.	**Cinnarizine** *(Cinnarizine)* syn.: Stugeron	Tab. 0,025; caps. 0,075
4.	**Nimodipine** *(Nimodipine)*	Tab. 0,03; Bot. 0,02 % sol.
5.	**Cavinton** *(Cavinton)* syn.: Vinpocetine	Tab. 0,005; amp. 0,5 % 2 ml.
6.	**Sumatriptan** *(Sumatriptan)* syn.: Imigran	Tab. 0,05; 0,1
7.	**Dihydroergotamine** *(Dihydroergotaminum)*	Tab. 0,0025; amp. 0,1 % sol. 1 ml.
8.	**Troxevasin** *(Troxevasin)* syn.: Troxerutin, Venoruton	Caps. 0,3, amp. 10 % sol. 3 ml.
9.	**Pentoxifylline** *(Pentoxyphylline)* 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) xanthine derivatives for the treatment of diabetic angiopathy;
7) a drug for the complex treatment of varicose veins that stabilize hyaluronic acid with a P – vitamin activity;
8) for relief of migraine.

Unit 27. CHECKING OF PRACTICAL SKILLS ON "DRUGS ACTING ON CARDIOVASCULAR SYSTEM"

DRUGS AFFECTING METABOLISM

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 28. HORMONAL PREPARATIONS OF POLYPEPTIDE AND AMINOACID STRUCTURE. ANTI-HORMONAL DRUGS

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*, s*timulating*, *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 lutheinizing 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 PITUITRAY 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, gensulin 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** *(Corticotropinum)*	Vials 10 – 20 – 30 – 40 U
2.	**Octreotide** *(Corticotropinum),* syn.: Sandostatin	Amp. 1 ml. (1 ml. – 0,0001 and 0,0005)
3.	**Pituitrin** *(Pituitrinum)*	Amp. 1 ml. (1 ml. – 5 U).
4.	**Desmopressin** *(Desmopressinum)* syn.: Diprivan	Vials 1 ml. (1 ml. – 0,0001) for nasal application
5.	**Oxytocin** (*Oxytocinum*)	Amp. 1 and 2 ml. (5 and 10 U)
6.	**Levothyroxine** (*Levothyroxinum sodium*)	Tab. 0,000025; 0,00005 and 0,0001
7.	**Potassium iodide** (*Kalii iodidum*)	Tab. 0,04; 0,125; 0,25 and 0,5; vials 3 % sol 200 ml.
8.	**Merkazolil** (*Mercazolilum*)	Tab. 0,005
9.	**Calcitrin** (*Calcitrinum)*	Vials 10 and 15 IU
10.	**Actrapid HM** (*Aktrapid HM*)	Vials 10 ml. (1 ml. – 40 and 100 IU)
11.	**Protafan HM** (*Protaphan Insulinum NM*)	Vials 3 ml. (1 ml. — 100 U)
12.	**Glibenclamide** (*Glibenclamide*) syn.: Maninil	Tab. 0,005

13.	**Glimepiride** (*Glimepiridum*) syn.: Amaryl	Tab. 0,001; 0,002; 0,003; 0,004; 0,006
14.	**Metformin** (*Metforminumm*)	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.

Unit 29. HORMONAL PREPARATIONS OF STEROID STRUCTURE

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 it's 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.

5. 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, Sigetin etc.

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

C) *Combined* (estrogen – progestin, estrogen – progestogen – 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 № 42). 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!):*

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

	Bekotid, Beklomet	doses
8.	**Sinaflan** (*Synaflanum*)	0,025 % ointment in tubes on 10 and 15 gms
9.	**Estrone** (*Oestronum*) syn.: Folliculin	Amp. 0,05 % and 0,1 % oil sol. 1 ml.
10.	**Sinestrol** (*Synoestrolum*) syn.: Estronal	Tab. 0,001; in ampoules 0,1 % and 2 % oil sol. 1 ml.
11.	**Progesterone** (*Progesteronum*) syn.: Lutein	Amp. 1 and 2,5 % oil sol. 1 ml.
12.	**Rigevidon** (*Rigevidon*)	Tab. patented.
13.	**Testosterone propionate** (*Testosteroni propionas*) syn.: androfort	Amp. 1 – 5 % oil sol. 1 ml.
14.	**Retabolil** (*Retabolilum*) 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 spontenousmiscarriage. 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) in case of Addison's disease;
2) for treatment of collagenosis;
3) at allergic bronchospasm;
4) at anaphylactic shock;
5) for local treatment of allergic dermatitis;
6) for treatment of a malignant tumour of prostrate gland;
7) for treatment of a breast cancer in 35 – year – old woman;
8) for climacteric syndrome;
9) oral contraceptives;
10) in the period of reconvalescence (recovery).

Unit 30. WATER-SOLUBLE VITAMINS

Actuality of the unit. Biosynthesis of vitamins basically is fulfilled outside the human organism. Endogen biosynthesis of some vitamins by the microbes of human intestine can not cover up the requirements of the whole organism. That is why human is supplied with vitamins basically with dietary. Vitamins are not the energy supply or plastic elements, but they are essential for all life processes and are biologically active in small doses. Insufficient income of vitamins into the organism or breaking of their bioavailability leads to the development of pathological processes, such as hypo or avitaminosis. In increased doses vitamins are widely used in medical purposes as powerful non – specific pharmacodynamic agents. Due to their wide use every physician should know the pharmacology of vitamins for their rational and safe prescribing.

I. Individual work

Control questions

1. The role of vitamins in the tissue metabolism. Concept about vitamers.
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 B_1)*[**] ─ thiamine chloride, thiamine bromide, cocarboxilase; vitamers — benfotiamine, and others. Pharmacodynamics. Undesirable effects. Application.
2) *Riboflavin (vitamin B_2)*[**]─ riboflavin, riboflavin mononucleotide. Pharmacodynamics. Indications and contra – indications.
3) *Nicotinic acid (vitamin PP, B_3)*[**] ─ 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 (Nicotinates potassium and magnesium, Xantinole nicotinate, Lithonit).
4) *Pyridoxine (vitamin B_6)*[**] ─ pyridoxine hydrochloride and combined preparations – Milgamma, Magne B_6 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 B_5)*[**] ─ calcium pantothenate, panthenol. The biological role. Indications for use.
8) *Pangamic acid (vitamin B_{15})* ─ 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.

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

№	Name of the drug	Drug form
1.	**Thiamine chloride** (*Thiamini chloridum*) syn.: aneurine	Tab. 0,002, 0,005 and 0,01; amp. 2,5 and 5 % sol. 1 ml.
2.	**Cocarboxylase hydrochloride** (*Cocarboxylasi hydrochloridum*)	Amp. 0,05 of lyophilized powder
3.	**Riboflavin mononucleotide** (*Riboflavinum – mononucleotidum*)	Amp. 1 % sol. 1 ml.
4.	**Pyridoxine hydrochloride** (*Pyridoxini hydrochloridum*)	Tab. 0,005 and0,01; amp. 1% and 5 % sol. 1 ml.
5.	**Nicotinic acid** *(Acidum nicotinicum*)	Tab. 0,05; in amp. 1 % sol. 1 ml.
6.	**Ascorbic acid** *(Acidum ascorbinicum*)	Tab., powder 0,05 and 0,1; amp. 5%

[*] Cyanocobolamine (vitamin B_{12}), folic acid (vitamin B_c, B_9) are discussed in unit № 31.
[**] Coenxyme-composing.

		and 10% sol. 1 ml.
7.	**Ascorutin** *(Ascorutinum*)	Patented tab.
8.	**Panthenol** *(Panthenol*) syn.: Dexpanthenol	Aerosol 140 g

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 B_6 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 healing of a burn wound.

Unit 31. LIPID-SOLUBLE VITAMINS. ENZYME PREPARATIONS. DRUGS ACTION OF CALCIUM-PHOSPHORUS BALANCE

Actuality of the unit. On metabolism may influence hormones, vitamins and other substances. Some of them have antioxidant and anti – hypoxic action, others can activate or normalize metabolic processes in cells, stimulate regeneration. For example, in medicine enzymes drugs and their inhibitors are widely used (for necrotic processes, thrombosis, thromboembolism, digestion disorders, cancer, etc.). It is perspective to develop a group of immobilizing enzymes chemically and physically associated with the carrier matrix, which stabilizes active agent, prolong its action. Created enzyme preparations placed in liposomes, which are used for entering the targeted cell. Also in modern pharmacology amino acids, some of which have independent use as drugs (Methionine, Glycine, Cerebrolysinum et al.) occupy a significant role. Occupy an important place mixtures of amino acids and their combinations with micro – and macroelements used as agents for parenteral nutrition.

I. Individual work

Control questions

1. FAT – SOLUBLE VITAMINS [*]:

1) Retinol *(vitamin A)* — Retinol acetate, Retinol palmitate, and others. Pharmacodynamics. Application. Hypo – and hypervitaminosis.
2) Tocopheroles *(vitamin E)* — Tocopherol acetate. The biological significance. Application.
3) Calciferoles *(vitamin D).* Drugs D_2 — Ergocalciferol, α – kaltsidol; D_3 — cholecalciferol; $25(OH)D_3$ — Calcifediol; $1,25(OH)_2D_3$ — Calcitriol (Osteotriol, Rokaltrol); Dihydrotahisterol. Pharmacodynamics. Application. Hypo – and hypervitaminosis.

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

⇒*suppress the bone resorption*:

- sexual hormones;
- calcitonins — Calcitonin, Miakaltsik;

[*] Vitamin K (nafthquinones) discussed in unit № 32.

- active metabolites of vitamin D [**] — Calcitriol, α – caltsidol;
- bisphosphonates [**] — Etidronate, Clodronate, Alendronate, Ibandronate;
- salts of calcium — Calcium chloride, Calcium carbonate and others.;
- ossein – hydroxyapatite (Osteogenon);

⇒ *increase bone mass:*

- fluorides — sodium ftuoride (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.

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

3. The interaction of vitamins among themselves and with other drugs.

4. Polyvitamins (Neurorubin, Milgamma, Neurovitan, vitamins in complexes with enzymes (Vitrum, Aevitum, Undevit, Unicap, Oligovit etc.). Indications and contraindications.

5. Plants with high contents of vitamins (sea buckthorn, wild rose, cranberries, currants, etc.).

6. Conception about avitaminosis.

7. 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.

8. 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, Panzynorm, Festal Mezym – forte etc.;
3) *Fibrinolytic* agents ─ Fibrinolysin, Streptokinase, Streptodecase, Urokinase, Alteplase etc.;
4) *different* preparations ─ Lydase, Cytochrome C, Penicillinase, Asparginase etc.

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

9. ENZYME INHIBITORS. Classification

[**] Activate remodeling of physiologic structure of osseal tissues.

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.

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

№	Name of the drug	Drug form
1.	**Tocopherol acetate** (*Tocopheroli acetas*)	Amp. 5 %, 10 %, 30 % oil sol.s 1 ml.; vials. 5, 10 and 30% sol.s 10, 20, 25 and 50 ml.
2.	**Retinol acetate** (*Retinoli acetas*)	Bot. 3.44% (100000 units in 1 ml.) oil sol., 10 ml.
3.	**Ergocalciferol** (*Ergocalciferolum*)	Bot. 0,125 % oil sol. or 0,5 % spirit sol. 10 ml.; dragee 500 IE; caps. 500 and 1000 IE
4.	**Osteotriol** *(Osteotriol)* syn.: Calcitriol	Caps. 0,00025 and 0,0005
5.	**Alendronate sodium** *(Alendronate sodium)*	Tab. 0,1
6.	**Calcium chloride** (*Calcii chloridum*)	Bot. 5 and 10 % sol.; amp. 2,5 % sol. 5 ml. and 10% soluion 10 ml.
7.	**Oleum Hippopheae** (*Oleum Hippopheae*)	Bot. 100 ml.
8.	**Vitrum** (*Vitrum*)	Tab. patented.
9.	**Trypsin crystalline** (*Trypsinum crystallisatum*)	Amp. and vials containing 0,005 and 0,01
10.	**Lidaza** (*Lydasum*)	Vials 64 units a lyophilized powder
11.	**Pancreatin** (*Pancreatin*)	Tab. patented.
12.	**Teraflex** *(Theraflex)*	Caps. patented.
13.	**Methionine** (*Methioninum*)	Tab. 0,25
14.	**Cerebrolysin** (*Cerebolysinum*)	Patented amp. 1, 5 and 10 ml.

Tasks for self-control. Choose the correct answers.

1. 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

2. Which of the following drugs are suitable these 4 definitions: growth vitamin, anti – infective, epithelial, and vitamin against xerophthalmia?

A. Ergocalciferol
B. Riboflavin
C. Retinol acetate
D. Tocopherol acetate
E. Vikasol

3. Patient with ischemic heart disease was appointed Tocopherol. What effect a doctor expected to get?

A. Spasmolytic
B. Antiatherosclerosis
C. Increase the delivery of oxygen to the myocardium
D. Antioxidant
E. Negative inotropic

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

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

5. In a patient with myocardial infarction and coronary artery thrombosis. Which of the drugs used for thrombolysis?

A. Streptokinase
B. Trypsin
C. Lidase
D. Pentoxyphyllin
E. Acetylsalicylic acid

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 menorrhea dysfunctions;
2) at myocardial dystrophy;
3) at hyperkeratosis;
4) for the treatment of rickets;
5) drug metabolite of vitamin D3 for osteoporosis in a postmenopause;
6) bisphosphonates for the treatment of deforming ostitis (Paget's disease);
7) in osteoarthritis to stimulate the regeneration of cartilage tissue;
8) at ulcer disease of stomach;
9) at postoperative scars;
10) at chronic pancreatitis;
11) for increasing of appetite;
12) at pneumonia for expectoration of sputum;
13) at post – stroke period;

14) at chronic hepatitis.

DRUGS INFLUENCING ON THE IMMUNE SYSTEM

Unit 31. ANTIALLERGIC AND IMMUNOTROPIC PREPARATIONS

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, Aminocapronic acid, gold preparations, Penicillamine, etc.

* Also used as anticancer (unit № 32).

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;

⇒ *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 (Dibazolum), 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* — Dibazolum, 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.

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* Classification of interferons is given in unit № 39.

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;
- *H_1 – 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.

Б. 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. H_1-HISTAMINE BLOCKERS [*]. General characteristics. Classification:

I generation — derivatives:

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

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

[*] Termin of «anti-histamins» regarding H_1-histamine blockers is oldfashion, cause it does not reflect all pharmacodynamics peculiarities of new drugs from that group.

[*] Banned in many countries because of fatal arrhythmia development.

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.

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

№	Name of the drug	Drug form
1.	**Thymalin** *(Tymalinum)*	Vials 0,01
2.	**Azathioprine** (*Azathioprinum*)	Tab. 0,05
3.	**Filgrastim** *(Filgrastimum)* syn.: Filstim	Vials 1 ml.(0,3 mg) a sol. for injections
4.	**Immunal** *(Immunal)*	Drops for intake in vials. 50 ml.; Tab. 0.08
5.	**Dimedrol** (*Dimedrolum*) 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** (*Diazolinum*)	Dragee and tab. 0,05 and 0,1
7.	**Diprazin** (*Diprazinum*) syn.: Pipolfen	Tab. 0,025, dragee 0,025 and 0,05, amp. 2,5 % 2 ml.
8.	**Suprastin** (*Suprastinum*)	Tab. 0,025, amp. 2 % 1 ml.
9.	**Loratadine** (*Loratidinum*)	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** *(Cetirizine)* syn.: Cetrin	Tab. 0.01; vials. 1% sol. of 10 and 20 ml. for oral use
11.	**Fexofenadine (**Fexofenadinum) syn.: Telfast	Tab. 0.12, 0.18
12.	**Cromolyn sodium** (*Cromolyn Sodium*) syn.: Intalum	Caps 0,02 for inhalation

Tasks for self-control. Choose the correct answers.

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 H_1 – 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) H_1 – histamine blockers with a strong hypnotic effect;
5) Anti – histamine agent with minimal hypnotic effect;
6) H_1 – histamine blockers, used to treat influenza;
7) H_1 – 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;
   adrenergic agonist for relieve of anaphylactic shock.

DRUGS AFFECTING THE BLOOD SYSTEM

Classification of drugs that affect the blood system:

1) affecting *hematopoiesis*:
- erythropoiesis ─ stimulants and suppressors;
- leucopoiesis ─ stimulants and suppressors;

2) 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;

3) 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 33. DRUGS AFFECTING THE LEUCOPOIESIS, BLOOD COAGULATION

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).

I. Individual work

Control questions

1. Agranulocytosis. Ethiopathogenesis. 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 efficcacy. Indications and contraindications for use.

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

1) *cytotoxic:*
   a) *alkylating* agents — Dopanum, Sarcolysine, 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 – molercular – 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, Streptodecase, 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.

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

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

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

15.	**Warfarin** *(Varfarinum)*	Tab. 0,002; 0,003; 0,005
16.	**Clopidogrel** (*Clopidogrel*) 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:

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. Aminocapronic 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.

Unit 34. PREPARATIONS AFFECTING 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*), Heamofer (*Ferrous chloride*), Maltofer (*Ferrous hydroxide polymaltose complex*);
- combined: Tardiferon, Ferroplex, *(+ascorbic acd*), 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 B_{12}) and its preparations — Cyanocobalamin, Hydroxycobalamin, Cobamamid (desoxyadenosilcobalamin) vitohepat. Folic acid (vitamin B_C, B_9, 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.

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

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

A. Sodium bicarbonate
B. Trypsin
C. Festal
D. Gastrocepin
E. Ascorbic acid

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

A. Epomax
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

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

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.

Unit 35. CHECKING OF PRACTICAL SKILLS ON "DRUGS ACTING ON METABOLISM, BLOOD AND IMMUNITY"

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. B*e 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 36. 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 DESINFECTANTS 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*: nitrofuran (Furatsilin); thiosemicarbazone (Faringosept); containing hexetidine (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.);
- Nitrofuran derivatives (Furazolidone, Furadoninum, Furoplast, Furaginum etc.);
- Imidazole derivatives (Metronidazole, Tinidazole etc.);
- oxazolidinones (Linezolid);
- Quinoxaline derivatives (Dioxydinum, Chinoxydin, Dioxicol).

Anti – infectives used under special indications:

1. *Antituberculosis;*
2. *Antisyphilitic;*
3. *Antiprotozoal;*
4. *Antiviral;*
5. *Antifungal;*
6. *Anthelmintic;*
7. *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, Solcoseril, etc.).

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

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

№	Name of the drug	Drug form
1.	**Chlorhexidine digluconate** *(Chlorhexidinum bigluconas)*	Vials 0,5 % – 100 ml.
2.	**Iodine, spirit sol.** *(Solutio Iodi spirituosa)*	Sol. 2 – 10 %, 5 ml.
3.	**Potassium permanganate** *(Kalii permanganas)*	0,02 %, 0,5 %, 10 % sol.s
4.	**Hydrogen peroxide diluted** ***(S****olutio Hydrogenii peroxydi diluta)*, **concentrated** ***(****concentrata)*	Vials 3% 25, 30, 50 ml.; Solutio Hydrogenii peroxydi concentrata 30 – 33 %.
5.	**Methylene blue** *(Methylenum coeruleum)*	1 – 3 % spirit sol.s and water sol.s; *Chromosmon* **—** 1 % sol in 25 % sol of glucose in amp. 20 and 50 ml.
6.	**Brilliant green** *(Viride nitens)*	2 % spirit sol.s
7.	**Salicylic acid** *(Acidum salicilicum)*	Spirit sol. 1% and 2 %
8.	**Zinc sulphate** *(Zinci sulfas)*	0,25 %, 0,5 % sol.s
9.	**Protargol** *(Protargolum)*	1 – 5 % sol.s
10.	**Hexamethylenetetramine** *(Hexamethylentetraminum)* syn.: Urotropine	Tab. 0,25; 0,5 and amp. 40 % 5 ml. and 10 ml.
11.	**Ethyl alcohol** *(Spiritus aethylicus)*	40 %, 70 %, 95 % sol.s
12.	**Resorcin** *(Resorcinum)*	Water and spirit sol.s 2 – 5 %; ointments 5 – 10 – 20 %
13.	**Decametoxine** *(Decamethoxinum)*	Tab. 0,1 for sol. preparation (0,025%; 0,5%); vials 0,05% alcohol sol. 10 ml. (ear drops)
14.	**Furatsilin** *(Furacilinum)* syn.: Nitrofurazone	Tab. 0,02 for sol. preparation (1:5000); 0,2 % ointment

Tasks for self-control. Choose the correct answers.

1. Which drug belongs to organic antiseptics?

A. Salicylic acid
B. Potassium permanganate
C. Resorcin
D. Chlorhexidine
E. Protargol

2. Antiseptic, which bactericidal mechanism of action is based on the formation of atomic oxygen:

A. Potassium permanganate
B. Boric acid
C. Furacillin
D. Ethonium

E. Silver nitrate

3. Which antiseptic has additional anti – itching and regenerative properties:

A. Pantocid
B. Zinc sulphate
C. Hydrogen peroxide
D. Ethyl alcohol
E. Ethonium

4. Name the antiseptic that is used parenterally in the case of cyanide poisoning:

A. Silver nitrate
B. Ethacridine lactate
C. Ethyl alcohol
D. Methylene blue
E. Potassium permanganate

5. Specify the antiseptic that can be used for local intravaginal contraception:

A. Potassium permanganate
B. Resorcin
C. Benzalkonium chloride
D. Vagotil
E. Furacillin

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) Antiseptic from halogens group for hands processing;
2) 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 form 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 nitrofuran for rinsing the mouth and throat during tonsillitis, pharyngitis, stomatitis;
8) Agent for treatment urogenital tract inflammation;
9) Agent with keratolytic and keratoplastic activity.

Unit 37. CHEMOTHERAPEUTIC AGENTS. ANTIBIOTICS (I)

Actuality of the unit. Antibiotics are the most important chemotherapeutic agents. Thanks to them it became possible to cure the pulmonal form of plague, to decrease abruptly mortality in case of such infection diseases as typhus, meningitis, tuberculosis, etc. Excessive use of this highly – effective group of chemotherapeutic drugs and un – derestimation 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 endogenic, 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 (Erlich P., Domagh 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) sntibiotics for special indications — rifamycins (Rifampicin), lincosamins (Lincomycin, Clindamycin), glycopeptides (Ristomycin, Vancomycin), sodium fuzidin, etc.

II. With primary activity against Gram – negative bacteria:
1) aminoglycosides — Streptomycin, Gentamicin, Amikacin, etc.;
2) polymixins — 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.

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

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 penitsillinaz resistant* (isoxazolilpenicillins) — Oxacillin, Dicloxacillin, Flucloxacillin;
- *antipseudomonal* — carboxypenicillins (Carbenicillin, Ticarcillin) and ureidopenicillins (Azlocillin, Piperacillin);
- *Combined* — Ampiox, Helicocid (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, Cephaloridine, etc .;
- *2nd generation* — Cefoxitin, Cefamandole, Cefprozil, Cefuroxim, Cefaclor, etc .;
- *3rd generation* — Cefotaxime (Klaforan), Ceftriaxone, Cefotaxime, Ceftazidime, Cefixim, Ceftibuten 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 ß-LAKTAM LIKE drugs – carbapenems (Imipenem, Meropenem) and monobactams (Aztreonam). The mechanism of action and spectrum of action. Side effects.

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

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

Tasks for self-control. Choose the correct answers.

1. Specify the antibiotic that is administered once every four weeks:

A. Bicillin-5
B. Extencillin
C. Penicillin
D. Phenoxymethylpenicillin
E. Benzylpenicillin potassium salt

2. What mechanism of bactericidal action of penicillin:

A. Increasing of permeability of the cytoplasmic membrane
B. Inhibition of intracellular protein synthesis
C. Inhibition of microbial cell wall synthesis
D. Inhibition of SH – groups of enzymes of microorganisms
E. Antagonism with para – aminobenzoic acid

3. Point out a cephalosporin agent for meningitis treatment:

A. Cefazolin
B. Cefalothin
C. Cefaclore
D. Ceftriaxone
E. Cefalexir

4. Which of these substances belongs to a group of ß-lactamase inhibitors?

A. Acid carbolic
B. Acid mefenamic

C. Salicylic acid
D. Clavulanic acid
E. Benzoic acid

5. Name the antibiotic that is used for eradication of H.pylori in gastric ulcer:
A. Benzylpenicillin sodium salt
B. Bicillin – 5
C. Amoxicillin
D. Cefazolin
E. Aztreonam

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 during streptococcal infection;
2) 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.

Unit 38. **ANTIBIOTICS (II)**

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** *(Erythromycinum)*	Tab. 0,1; 0,25 capsules 0,1
2.	**Azithromycin** *(Azithromycinum)* syn.: Sumamed	Tab. 0,125, 0,5; caps. 0,5.
3.	**Lincomycin hydrochloride** *(Lyncomycini hydrochloridum)*	Amp. 30 % 1 ml.; caps. 0,25; ointment 2 % 15,0
4.	**Tetracycline** *(Tetracyclinum)*	Tab. 0,05, 0,1, 0,25
5.	**Doxycycline hydrochloride** *(Doxycyclini hydrochloridum)*	Caps. 0,05 and 0,01
6.	**Laevomycetin** *(Laevomycetinum)* 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** *(Gentamycini sulfas)*	Vials 0,08; amp. 4 % 1 – 2 ml.; ointment 0,1 %.
8.	**Amikacin sulfate** *(Amykacini sulfas)*	Vials 0,1, 0,25 and 0,5; amp. 5, 12,5 and 25 % 2 ml.
9.	**Polymyxin B sulfate** *(Polymyxini B sulfas)*	Tab. 500000 IU; 0,025 vials (250000 IU), 0,05 (500000 IU).
10.	**Synthomycin** *(Synthomycinum)*	Emulsion, liniment in Bot. 25,0

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. Laevomycetin
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) 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.

Unit 39. SULFONAMIDES. ANTIMICROBIAL PREPARATION OF A DIFFERENT CHEMICAL STRUCTURE

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*).

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).

MISCELLANEOUS SYNTHETIC ANTI – INFECTIVES. Classification (see unit 34).

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.

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

№	Name of the drug	Drug form
1.	**Sulfalen** *(Sulfalenum)*	Tab. 0,2 and 0,5
2.	**Ftalazol** *(Phthalazolum)*	Tab. 0,5
3.	**Biseptol** *(Biseptol)* 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** *(Sulfacylum – natrium)* syn.: Albucidum	Eye drops 30 % 10 ml.
5.	**Chlorquinaldol** *(Chlorchinaldolum)*	Tab 0,1 (for adults) and 0,03 (for children)
6.	**Nitroxoline** *(Nitroxolinum)* syn.: 5 – NOK	Tab 0,05
7.	**Furazolidon** *(Furazolidonum)*	Tab 0,05
8.	**Furadonin** *(Furadoninum)* syn.: Nitrofurantoin	Tab 0,05 and 0,1
9.	**Ciprofloxacin** *(Ciprofloxacine)* syn.: Tsiprobay, Tsiprinol, Tsifran	Tab. 0,25; 0,5, 0,75; amp. 1 % 10 ml.; vials 0,2 % 50, 100 ml.
10.	**Moxifloxacin** *(Moxifloxacinum)* syn.: Aveloks	Tab,4; vials 400 mg sol of 250 ml. for infusions

11.	Dioxidin ***(Dioxydinum)***	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. Why sulfonamides can cause such side effects as anemia, leukopenia, agranulocytosis?

A. Disturbance of the synthesis of vitamins
B. Activation of lipolysis
C. The destruction of the cell membrane
D. Inhibition of glycolysis
E. Catabolic disorders

2. Why during therapy of sulfonamides doctor recommends the patient to monitor urine output and use daily 1.5 – 2 liters of alkaline mineral water?

A. In order to prolong the action
B. To reduce the irritant effect on the stomach
C. To neutralize gastric acid
D. For the shift of blood pH to the alkaline side
E. To prevent crystallization during excretion of acetyl derivatives via the renal tubules

3. What is the mechanism of antimicrobial activity of fluoroquinolones?

A. Inhibition of peptidoglycan synthesis
B. Inhibition of DNA – gyrase
C. Increase the bacteria wall permeability
D. Inhibition of RNA polymerase
E. Antagonism with PABA

4. Select a drug that reduces the formation of cartilage tissue:

A. Furadonin
B. Co – trimoxazole
C. Ciprofloxacin
D. Sulfadimezin
E. Nitroxoline

5. Which of antimicrobials have disulfira – like action?

A. Ampiox
B. Sulfalen
C. 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) 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) nitrofuran derivative in case of acute cystitis;
6) nitrofuran derivative in case of enterocolitis;
7) 8 – oxyquinolone derivative in case of acute pyelonephritis;
8) naphthyridine derivative in pyelonephritis;
9) fluoroquinolone for the treatment of sepsis;
10) fluoroquinolone with anti – anaerobic activity;
11) quinazoline derivative in case of purulent pleurisy;
12) antimicrobial with immunosuppressive action.

Unit 40. ANTITUBERCULOSAL, ANTISPIROCHETAL, ANTIPROTOZOAL PREPARATIONS

Actuality of the unit. There was no effective way for the chemotherapeutic treatment of tuberculosis up to 1940. The first step in development of tuberculosis cure was discovery of PASA in 1941. The main role in the converting of tuberculosis from untreatable to treatable disease played two other agents – Streptomycin and Isoniazid, which were introduced in 1944 and 1952. In the latest years the arsenal of antitubercular drugs have been enriched with the row of new highly effective drugs: Rifampicin (Rifampin), Ethambutol. The main cause of decreased efficacy of the treatment is increased mycobacteria resistance due to irregular and wrong use of antitubercular drugs. Treating tuberculosis presents therapeutic problems. Because strains of the organism resistant to a particular agent emerge during treatment, multiple drug therapy is employed to delay or prevent their emergence. For example, at the beginning of the treatment course it is recommended to use three agents simultaneously. Today tuberculosis is still the leading cause of death by infections throughout the word.

The list of spirochetal diseases includes syphilis, recurrent typhus, Sodoku disease, etc. Syphilis is a chronic disease. In case of absence of treatment, it may last for many years.

Protozoal infections are common among people in underdeveloped tropical and subtropical countries where sanitary conditions, hygienic practices, and control of vectors of transmission are inadequate. However, with increased world travel, protozoal diseases such as malaria, amebiasis, leishmaniasis, trypanosomiasis, trichomoniasis, and giardiasis are no longer confined to specific geographic locales. In Ukraine lambliasis (giardiasis), toxoplasmosis and trichomoniasis are more commonly spread.

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, Micobutin;
- 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. Haematoschisotropic (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. Histoschizotropic (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. Hamontotropic drugs (influencing on the sexual forms of plasmodia):
   - Hamontocides — Primaquine, Chinocide;
   - Sporicides — Chloridin (Pyrimethamine)
4. Combined preparations — Fansidar, Metakelfin.

Common principles of the malaria therapy. Mechanism of action of separate groups.

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.

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

№	Name of the drug	Drug form
1.	**Isoniazid** *(Isoniazidum)*	Tab 0,3; amp 10 % sol 5 ml.
2.	**Rifampicin** *(Rifampicinum)*	Caps 0,15, 0,3, 0,45; amp 0,15
3.	**Sodium para – aminosalicylate** *(Natrii para – aminosalicylas)* syn.: PASA	Tab 0,25 and 0,5
4.	**Ekstentsillin** ***(****Extencilline)* syn.: Bicillin 1, Benzyl penicillin benzathine	Vials 1 200 000 and 2 400 000 IU
5.	**Biyohinol** *(Biiochinolum)*	Vials 100 ml.
6.	**Chloroquine** *(Chloroquinum)* syn.: Quingamin, Delagil	Tab 0,25; amp 5 % sol 5 ml.
7.	**Hloridin** *Chloridinum* syn.: Pyrimethamine	Tab 0,005 and 0,01
8.	**Quinine sulfate** *(Chinini sulfas)*	Tab. 0,25 and 0,5
9.	**Metronidazole** *(Metronidazolum)*	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 B_6;
3) antituberculosis antibiotic that causes red discoloration of urine;
4) metal – containing drug for the treatment of syphilis;
5) drug for removal of acute malaria fit;
6) for prophylaxis of malaria;
7) drug for treatment of intestinal amebiasis;
8) drug with anti – amebial, anti – lamblial and anti – toxoplasma activity;
9) antibiotic for toxoplasmosis treatment;
10) drug for the treatment of chlamydiosis.

Unit 41. ANTIHELMINTHAL, ANTIFUNGAL AND ANTIVIRAL 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 numersous 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** (*ascaridiasis, 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 helmintoses**:

- **trematodosis** *(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 rer day, course – 2 – 6 weeks): Clotrimazole, Miconazole, Isoconazole, Amikazole, Bifonazole;
      – 2nd generation (locally, course – 2 – 3 days): Econazole, Tioconazole;
      – 3d 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.

ANTIVIRAL DRUGS

1. General characteristics.
2. Classification *according to origin*:

– **Interferons** (Interferon, Interlock, Reaferon, Alferon, Betaferon) and **interferon inductors** (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. 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);

* Imidazol derivatives also have antibacterial, antiprotozoal and antihelmintic agents (metronidazol, tinidazol, mebendazol etc.).

- **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, antiflu, antiherpetic drugs. Undesirable effects.

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

№	Name of the drug	Drug form
1.	**Mebendazole** *(Mebendazolum)* syn.: Vermoxum	Tab. 0,1
2.	**Pyrantel** *(Pyrantelum)*	Tab. 0,25; susp. in Bot. 15 ml. (50 mg/1ml.)
3.	**Fenasal** *(Phenasalum)*	Tab. 0,25
4.	**Praziquantel** *(Praziquantel)*	Tab. 0,6
5.	**Amphotericin B** *(Amphotericinum B)*	Vials 50.000 units
6.	**Nystatin** *(Nystatinum)*	Tab. 250000 and 500000 units; vaginal supp. 250000 units; ointment in tubes 15,0 (1 g – 100.000 units)
7.	**Griseofulvin** (*Griseofulvinum)*	Tab. 0,125; susp. in Bot. 100 ml.
8.	**Clotrimazole** *(Clotrimazole)*	Intravaginal tab. 0,1; cream 1% 20,0; sol. 1% 15 ml.
9.	**Fluconazole** *(Fluconazole)* syn.: Diflucan	Sol. in vial 0,2 %; caps. 0,05; 0,1; 0,15 and 0,2
10.	**Rimantadine** *(Remantadinum)*	Tab. 0,05
11.	**Laferon** *(Laferonum)* syn.: interferon alfa – 2b recombinant	Vial by 1000000 IU
12.	**Pegasys** *(Pegasys)* syn.: peginterferon alfa – 2a	Vial by 0,5 and 1 ml. (0,18 and 0,135)
13.	**Acyclovir** *(Aciclovir)*	Tab. 0,2; ophthalmic ointment 3 %, creme in tubes 5 % 5,0
14.	**Azidothymidine** *(Azidotimidin)* syn.: Zidovudine	Caps. 0,1 and 0,25; sol. for infusion in vial 2% 20 ml.

Tasks for self-control. Choose the correct answers.

1. Name the antihelminthic agent that has immunomodulatory properties:

A. Piperazine
B. Mebendazole
C. Pyrantel
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 preparation is necessary to appoint for the prevention of influenza A?

A. Acyclovir
B. Azidothymidine
C. Remantadin
D. Bonafton
E. Gancyclovir

5. At what disease appointed zidovudine?

A. Influenza
B. Varicella
C. Viral hepatitis
D. HIV
E. Herpes Zoster

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 teniarinhosis;
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) a recombinant a drug with antiviral and antitumor activity;
8) an antiretroviral drug, which is a nucleotide analogue.

Unit 42. CHECKING OF PRACTICAL SKILLS ON “ANTIMICROBIAL AGENTS”

DRUGS ACTING ON SPECIAL SYSTEMS AND ORGANS

Unit 43. AGENTS ACTING ON GASTROINTESTINAL TRACT

Actuality of the unit. The most common disorders involving gastrointestinal tract are peptic ulcer, vomiting, diarrhea and constipation, liver and pancreas pathology. Many drugs encountered in this unit have been already discussed in previous topics. Other drugs (for example, H_2 – receptor antagonists) are used almost exclusively to treat gastrointestinal tract disorders.

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

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* To anorexigenic also belong agents that decrease lipids absorption (orlistat) and carbohydrates (biguanides) in GI tract

** SSRI antidepressants also possess anorexigenic action (unit №19)

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 H_2 – histaminoreceptors: 1 generation — Cimetidine ***; 2 generation — Ranitidine, 3 generation — Famotidine, Nizatidine, Roxatidine etc.;
3) M_1 – cholinoblockers — Gastrocepin;
4) drugs diminishing excitement of vagal endings – antacids, adsorbents, coating demulcents, astringents, local anaesthetics (see unit 12);
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, H_2 – 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, Potassium orotate) vitamin U (Methylmethionine), DOXA, Gastropharm, Sodium oxyferrouscarbon, Dalargin. Mechanisms of action. Indications to application.

9. Emetic drugs (see unit 11).

10. ANTI – EMETIC drugs:

- Central – acting — neuroleptics (Aminazinum, Etaperazine), antiserotonin (Granisetron, Ondansetron, Tropisetrone); 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.

*** Exluded from medical practice because of significant toxicity

- Anti – regurgitants — Cisapride.

Indications to application.

11. Drugs STRENGTHENING PERISTALSIS of gastrointestinal tract tract:

- enhancing efferent innervation — M – cholinomimetics, anticholinesterase agents, serotonin and dophamine – blokers (Metoclopramide, Dromperidon, 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, Attapulgite, 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, cholelitolytic (Henofalk, Ursofalk), choleretic).

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, Panzitrat, Panzynorm, 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.

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

№	Name of the drug	Drug form
1.	**Ranitidine** *(Ranitidine)*	Tab. 0,15, 0,3

2.	**Famotidine** *(Famotidine)*	Tab. 0,02, 0,04
3.	**Omeprazole** *(Omeprazole)*	Tab. 0,02
4.	**Rabeprazole** *(Rabeprazole)* syn.: Pariet, Controlok	Tab. 0,02
5.	**Peritol** *(Peritol)* syn.: Cyproheptadine	Tab. 0,004
6.	**Fenfluramine hydrochloride** (*Fenfluramine hydrochloridum)*	Caps. 0,06
7.	**Riboxinum** *(Riboxinum)* syn.: Inosine	Tab. 0,2, amp. 2 % sol. 10 ml.
8.	**Metoclopramide** (Metoclopramide) syn.: Cerucalum	Tab. 0,01, amp. 2 ml.
9.	**Essentiale** *(Essentiale)*	Amp. 10 ml.; caps. patented.
10.	**Silibor** *(Silibor)*	Tab. 0,04
11.	**Geptral** *(Heptral)*	Tab. and vial 0,4
12.	**Loperamide** *(Loperamide)* syn.: Imodium	Caps. 0,002; vials 0,002 % 100 ml.
13.	**Linex** *(Linex)*	Caps. patented

Tasks for self-control. Choose the correct answers.

1. Point out drug that reduce gastric secretion and causes anti-androgenic effect:

A. Ranitidine
B. Rabeprazole
C. Gastrocepin
D. Almagel
E. Helicocin

2. Patients with diarrhea appointed drug regulating intestinal biocenosis. Identify drug.

A. Loperamide
B. Intetrix
C. Phtalazol
D. Smecta
E. Linex

3. A patient with chronic constipation was appointed synthetic laxative with predominant effect on the colon. Find out it.

A. Castor oil
B. Bisacodyl
C. Magnesium sulfate
D. Decoction of Frangula bark
E. Forlax

4. To the obese patient doctor prescribed an anorexigenic agent with antiparkinsonian action. Specify the drug.

A. Bromocriptine
B. Fenfluramine
C. Phepranon
D. Metformin
E. Mazindol

5. For the symptomatic treatment of diarrhea was appointed antidiarrheal drug – opioid receptor agonist. Specify the drug.

A. Intetrix
B. Metoclopramide
C. Ftalazol
D. Loperamide
E. Linex

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 alimentary obesity;
2) H_1 – 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 ademetionine by toxic hepatitis;
12) in acute pancreatitis.

Unit 44. AGENTS ACTING ON RESPIRATORY TRACT

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 respose. 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 21.
2. EXPECTORANTS – see unit 11.
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 H_1 – 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** *(Codeini phosphas)*	Tab. 0,015
2.	**Glaucine** *(Glaucine)*	Dragee 0,01 and 0,04
3.	**Bronholytin** *(Broncholytin)*	Syrup bot. by 125 ml.
4.	**Acetylcysteine** *(Acetylcysteinum)*	Powder 0,1, 0,2; amp. 20 % sol. 5 and 10 ml. for inhalation
5.	**Salbutamol** *(Salbutamolum)*	Aerosol 0,1 mg/dose, 10 ml. bot.; Tab. 0.002, 0.004
6.	**Tiotropium bromide** *(Tiotropium bromide)* syn.: Spiriva	Powder. for/ing. in caps. 18 mcg
7.	**Theophylline** *(Theophyllinum)* syn.: Neofillin	Tab. 0,1 and 0,3
8.	**Ethymizol** (*Aethimizolum)*	Tab. 0,1; amp. 1 % or 1,5 % sol. 3 and 5 ml.

9.	**Ketotifen** *(Ketotifenum)* syn.: Zaditen	Tab. 0,001
10.	**Beclomethasone dipropionate** *(Beclometasonum dipropionas)*	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. Isadrin
C. Adrenaline
D. Formoterol
E. Ortsiprenalina 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 β2-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.

Unit 45. AGENTS ACTING 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:

А. 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 B_1, 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.

Б. 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, H_1 – 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*:
  - monophase — 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** *(Oxytocinum)*	Amp. 1 and 2 ml. (5 and 10 IU)
2.	**Dinoprostone** *(Dinoproston)*	Tab. 0,0005
3.	**Ergometrine maleate** *(Ergometrini maleas)*	Amp. 0,05 % 1 ml., tab. 0,001
4.	**Partusisten** *(Partusisten)* syn.: Fenoterol	Tab. 0,005; amp. 0,005 % 10 ml.
5.	**Triziston** *(Trisiston)*	Dragee No. 21. From 1st till 6th day of menstrual cycle – 1 dragee of violet colour; from 7th till 12th day – on 1 dragee of pink colour; from 13th till 21st 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 appointt?

A. Estrone
B. Progesterone
C. Retabolil
D. Menopausal gonadotropin
E. Estradiol

3. Select uterotonic from ganglionic blockers group:

A. Propranolol
B. Neostigmine
C. Terlipressin
D. Ergometrine
E. Pachycarpin

4. What are the undesirable effects of contraceptives require a change of drug or dose reduction?

A. Breast tenderness
B. Vaginal infection, urethral extension
C. Hyperpigmentation
D. Profuse bleeding
E. Amenorrhea

5. What component of oral contraceptives can cause development of venous thromboembolism?

A. Gestagen
B.Oxytocin
C. Estrogen
D. Vasopressin
E. Androgen

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) plant-origin drug to reduce postpartum uterine bleeding;
2) uterotonic from prostaglandin drugs;
3) hormonal drug for induce labor;
4) adrenergic tocolytic drug;
5) three-phasic oral contraceptive

Unit 46. PHARMACOGENETICS AND PERSONALIZED THERAPY

Actuality of the unit. Pharmacogenetics (modern term – pharmacogenomics) is the study of genetic factors that underlie variation in drug response.

As a scientific field, pharmacogenomics has advanced rapidly since the sequencing of the human genome. It's development included following stages: I stage – discription of pharmacogenetic phenomenon (1930-1960-yy); II stage – development of pharmacogenetics as a discipline (1960-1990-yy); III stage – develompent of the clinical approach of the pharmacogenetics (pharmacogenomics) (since 2000 and to present)

I. Individual work

Control questions

BASICS OF INDIVIDUAL HUMAN SENSITIVITY TO THE EFFECTS OF DRUGS.

The emergence and development of pharmacogenetics. Basics of individual sensitivity of a person to the action of drugs. Characteristics of pharmacogenetic tests – their informativeness, interpretation of results, practical application. Peculiarities of drug action associated with polymorphism of pharmacokinetic processes.

PHARMACOGENETICS OF DRUGS AFFECTING THE CARDIOVASCULAR SYSTEM AND HEMOSTASIS.

Pharmacogenetics of the drugs that act on cardiovascular system (beta-blockers, statins etc). Pharmacogenetics that act on hemostasis (anticoagulants, antiaggregants).

Tasks for self-control. Choose the correct answers.

1. The subject of pharmacogenetics is about:

A. Mechanism of action of drugs
B. Genetic factors that determine body's response to the medicines
C. Mechanisms of the drugs absorption, distribution and excretion
D. Adverse effects of the drugs
E. Dependance of drugs action from time of administration

2. Metabolism of which antituberculosis agent needs participation of NAT-2 enzyme?

A. Streptomycini sulfate
B. Levofloxacin
C. Rifampicine
D. Isoniazid
E. Lomefloxacin

3. How does change warfarin blood concentration in "rapid metabolizers"?

A. Increases
B. Does not change
C. Decreases in 2 times
D. Decreases in 3 times
E. --

4. An anti-atherosclerotic agent is prescribed to the patient. Find out this agent.

A. Cyclomethiazide
B. Piracetam
C. Dexamethasone
D. Butadion
E. Fenofibrate

5. What is the name of phenomenon, when two medicines increase action of each other?

A. Potentiation
B. Antagonism
C. Sensibilization
D. Abstinentia
E. Tachyphylaxia

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 agent – potent inducer of CYP-450;
2) anticoagulant, prescription of which needs detection of *CYP2C9* and *VKORC1* genotype;
3) an antiaggregant that is a precursor and undergo activation by CYP2C19;
4) agent that could inhibit CYP-450

Unit 47. PRINCIPLES OF TREATMENT OF ACUTE DRUG POISONING. PHARMACOTHERAPY OF EMERGENCY CONDITIONS

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:**

- *unabsorpted*— laxatives, cleansing enemas, etc.;

- *absorpted* — forced diuresis, alteration in the acid – base balance of urine, hemosorbtion, hemodialysis, gastrointestinal, peritoneal dialysis, blood transfusions and others.

3) **Antidote therapy**. Classification of antidotes mechanism of action:

а) 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 B_{12}.

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, H_1 – histamine blockers, hypothermia: poisoning of antipsychotics, opioids, alcohol);
- metabolic disorders (acidosis, alkalosis, electrolyte imbalance);
- dehydration;
- sharp pain;
- aggitation;
- hypoxia of various ethiologies (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 spasmolitics, 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** *(Corglyconum)*	Amp. 0,06 % 1 ml.
2.	**Epinephrine hydrochloride** *(Adrenalini hydrochloridum)*	Amp. 0,1 % 1 ml.
3.	**Dopamine** *(Dopaminum)*	Amp. 4 % sol. 5 ml.
4.	**Mezaton** *(Mesatonum)* syn.: Phenylephrine	Amp. 1 % 1 ml.
5.	**Diazepam** *(Diazepame)* syn.: Sibazon,	Amp 0,5 % sol. 2 ml.

	Relanium	
6.	**Furosemide** *(Furosemidum)* syn.: Lasix	Amp. 1 % 2 ml.
7.	**Proserin** *(Proserinum)* syn.: Neostigmine	Amp. 0,05 % 1 ml.
8.	**Naloxone** *(Naloxonum)*	Amp. 1 ml. (1 ml. — 0,0004 g)
9.	**Unitiol** *(Unithiolum)*	Amp. 5 % 5 ml.
10.	**Flumazenil** *(Flumazenilum)* syn.: Anexat	Amp. 0,01 % sol. 5 ml.
11.	**Deferoxamine** *(Deferoxaminum)* syn.: Desferal	Vials 0,5
12.	**Enterosgel** *(Enterosgelum)*	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 oraly

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.

Unit 48. **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. Inhibiotion of β1-adrenoceptors
C. Stimulation of α1-adrenoceptors
D. Inhibiotion of α1-adrenoceptors
E. Stimulation β1-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. Work with the tests (Krok-1).

ETHALONS
answers to the tasks for self-control

Тема	1	2	3	4	5
5.	D	A, E	E	A	B
6.	B	A	D	E	E
7.	B, E	D	A, C, E	A, B, D	B
8.	A, C	A, C, D	B, C, D	A, C, E	B, C, E
9.	A, B, D	B, D, E	C	A, C, E	B, C, E
10.	B, E	A, C, E	A	B, C	A, C, E
11.	B, D	A, E	B, D, E	C	C, D
12.	D	A, C	A, C	D, E	B, C, E
13.	C	B	B, C	A, D, E	C
14.	B, C	B, D, E	A, C, E	A, C, E	A, D, E
15.	B	A, C, E	B, E	A, B	B, C, D
16.	C	B, C, D	C	A, C	B
17.	A, B, E	A-D	B, D, E	B, C, D	A, B, D, E
18.	E	A, D, E	A, B, E	B, D, E	A, C, E
19.	A, D, E	A, B, D	C	B	D
20.	-	-	-	-	-
21.	C	A, C, E	B	D	B
22.	A	B	A	B	B
23.	A, E	B, D, E	B, C	D	B, D, E
24.	A, C, D, E	A, C	D	C	A
25.	E	A, D, E	B	A, C, E	B
26.	B	C	E	C	C, D
27.	-	-	-	-	-
28.	A	C	E	A	B
29.	C	D	D	E	A
30.	E	A	B	C	C
31.	C	C	B, D	B	A
32.	D	C	B	E	D
33.	C	B	B	C	D
34.	E	C	D	C, E	B
35.	-	-	-	-	-
36.	C	A	E	D	C
37.	A	C	D	D	C
38.	E	D	E	B	B
39.	A	E	B	C	D
40.	B	B	C	D	C
41.	D	A	E	C	D
42.	-	-	-	-	-
43.	A	E	B	A	D
44.	E	D	C	D	E
45.	B	B	E	A	C

46.	B	D	A	E	A
47.	E	A	B	B	A, D, E
48.	A	A	E	C	A

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6. Resource with essential point-of-care drug (www.medscape.org)

CONTENTS

Preface……..…….…… 3
List of abbreviations ……..…... 3
Section I. **MEDICAL PRESCRIPTION** ……...…… 4
Unit 1. Medical prescription. Structure of prescription. Solid medicinal forms..... 4
Unit 2. Liquid dosed medicinal forms……..… 6
Unit 3. Liquid dosed medicinal forms (II).…….. 8
Unit 4. Soft medicinal forms. Non-dosed medicinal forms. Checking of practical skills on “Medical prescription”…… 10
Section II. **GENERAL PHARMACOLOGY** …..……..... 12
Unit 5. General pharmacology. Pharmacokinetics ..……..…..….. 12
Unit 6. General pharmacology. Pharmacodynamics.……..…. 14
Section III. **SPECIAL PHARMACOLOGY** …….. 17
Drugs influencing the peripheral innervation …… 17
Drugs influencing the efferent innervation ……..……. 17
Unit 7. Cholinergic agents. Cholinomimetics...……. 17
Unit 8. Cholinergic blockers…….…….……... 20
Unit 9. Preparations influencing on transmission of neural impulse in adrenergic synapse. Adrenomimetics…….……. 23
Unit 10. Adrenonegative preparations……..…….…….. 26
Drugs influencing the afferent innervation ……..…..... 28
Unit 11. Preparations irritating receptors……. 29
Unit 12. Preparations protecting receptors. Checking of practical skills on “Agents influencing on afferent and efferent innervations»…….. 32
Drugs acting on the central nervous system ……..... 36
Unit 13. General anesthetics. Alcohols…… 36
Unit 14. Hypnotic and anticonvulsants……..... 39
Unit 15. Pharmacology of non-narcotical analgesics. NSAIDs.…….. 42
Unit 16. Pharmacology of narcotic analgesics……..…… 46
Unit 17. Neuroleptic drugs. Tranquilizers. Psychosedatives …….. 49
Unit 18. Antidepressants. Psychostimulators. Normothymics ……...…. 53
Unit 19. Nootrops. Adaptogens. Analeptics…….. 56
Unit 20. Preparations causing abuse. Checking of practical skills on “Drugs acting on the CNS”……..…… 59
Drugs acting onthe cardiovascular system ……. 59
Unit 21. Cardiotonics. Cardiac glycosides. Non-glycosides cardiotonics…… 59
Unit 22. Antiarrhythmic drugs…….…… 62
Unit 23. Antianginal drugs. Complex therapy of myocardial infarction…..…. 66
Unit 24. Diuretic drugs. Complex therapy of chronic heart failure. Anti-gout drugs ……..…… 70
Unit 25. Agents that regulate blood pressure. Antihypertensive and hypertensive preparations ……...…. 74
Unit 26. Agents acting on microcirculation and bloodflow……... 78

Unit 27. Checking of practical skills on “Drugs acting on cardiovascular system”…….. 82
Drugs acting on metabolism ……..…… 82
Unit 28. Hormonal preparations of polypeptide and aminoacid structure. Anti-hormonal drugs……..…… 83
Unit 29. Hormonal preparations of steroid structure……...… 87
Unit 30. Water-soluble vitamins…….. 90
Unit 31. Lipid-soluble vitamins. Enzyme preparations. Drugs acting of calcium-phosphorus balance…….. 93
Drugs influencing on the immune system …… 97
Unit 32. Antiallergic and immunotropic preparations..... 97
Drugs affecting the blood system…… 102
Unit 33. Drugs affecting the leucopoiesis, blood coagulation…… 102
Unit 34. Preparations affecting erythropoiesis. Blood substitutes……... 106
Unit 35. Checking of practical skills on “Drugs acting on metabolism, blood and immunity”……..…….. 109
Antimicrobial and antiparasitic drugs ……... ……. 109
Unit 36. Disinfectants and antiseptics……..... 110
Unit 37. Chemotherapeutic agents. Antibiotics (I)……... 113
Unit 38. Antibiotics (II) …….. 117
Unit 39. Sulfonamides. Antimicrobial preparation of a different chemical structure……..…….. 120
Unit 40. Antituberculosal, antispirochetal, antiprotozoal preparations. ……. 123
Unit 41. Antihelminthal, antifungal, and antiviral preparations.…… 126
Unit 42. Checking of practical skills on “Antimicrobial agents”. ……... 130
Drugs acting on special systems and organs…….. 131
Unit 43. Agents acting on gastrointestinal tract……... 131
Unit 44. Agents acting on respiratory tract…….. 135
Unit 45. Agents acting on myometrium. Contraceptives……. 138
Unit 46. Pharmacogenetics and personalized therapy……. 140
Unit 47. Principles of treatment of acute drug poisoning. Pharmacotherapy of emergency conditions…… 142
Unit 48. Pharmacotoxycodynamics……. 146
Ethalons answers to the tasks for self-control …….. 149
References……..…….. 150