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"Pharmacology: practical manual" is prepared for the discipline "Pharmacology" in accordance with the Federal state educational standard of higher professional education for students enrolled in the basic educational program of the specialty General medicine (bilingual program).

Reviewer

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ABBREVIATIONS

INN — international nonproprietary name

FDA — food and drug administration

BP — blood pressure

ATP — adenosine triphosphate

ACE — angiotensin converting enzyme

AT — angiotensin

ET — endothelin

HIV — human immunodeficiency virus

GABA — γ-aminobutyric acid

5HT — 5-hydroxytryptamine

BBB — blood brain barrier

DNA — deoxyribonucleic acid

RNA — ribonucleic acid

IHD — ischemic heart disease

MAO — monoamine oxidase

COMT — catechol-O-methyltransferase

NSAIDs — nonsteroidal anti-inflammatory drugs

TD — therapeutic dose

DD — daily dose

TTS — transdermal therapeutic system

cAMP — cyclic adenosine monophosphate

ERP — effective refractory period

IV — intravenously

* — brand name drug

Lesson 1
Introduction to the general prescription. Solid dosage forms.

Learning objective is to study how to write prescriptions for solid dosage forms.

QUESTIONS FOR PREPARATION FOR THE LESSON

1. Organization of the pharmacy service in Russia.
2. Rules of dispensing drugs, forms of prescription.
3. Technologies to produce solid dosage forms. Classification of drug forms (solid, liquid, soft).
4. Differences between the concepts of "medicinal raw materials", "medicinal product (pharmaceutical substance, medicinal product)", "dosage form".
5. Differences between the expanded and short forms of prescription.
6. International non-proprietary name of drugs and brand names.
7. Rules for prescribing drugs.
8. The structure and components of the prescription.
9. Rules for writing a prescription.
10. Solid dosage forms (tablets, pills, capsules, powder, granules).

QUESTIONS AND TASKS IN CLASS

Task 1. Theoretical material to get ready for the class.

Powders are dosage forms consisting of solid, dry particles and have the property of flowability.

1. Classification of powders by composition:
   A. Simple powders (pulveres simplices) - consist of one medicinal substance;
   B. Complex powders (pulveres compositi), consist of two or more medicinal substances;
2. Classification by dose division:
   A. Separated (divided into separate doses);

B. Undivided (powder is produced in one package; the dosage is carried out by the patient independently);

3. Classification by the way of application:
   A. Powders for external and local use (for example, applied to the affected area of the skin);
   B. Powders for the preparation of solutions and suspensions (powders which must be dissolved in a solvent before use. The solvent can be water, 0.9% solution of sodium chloride);
   C. Powders for oral administration;
   D. Powders for inhalations;

Tablets are solid dosage forms which is obtained by pressing powders and granules containing one or more drugs with or without adjuvants.

1. Classification by composition:
   A. Simple (one-component);
   B. Complex (multicomponent).
2. Classification by the speed and nature of the release:
   A. The tablets are coated with enteric coating (resistant to route of administration, to gastric juice and releasing drug substance in the small intestine);
   B. Modified-release tablets (coated or uncoated tablets, containing excipients and/or obtained by a specific technology that allows the speed and/or time and/or release location of the active ingredient to be controlled). The drug release can occur by diffusion after swelling or biodegradation of the membrane (matrix and membrane systems). The osmotic system releases the drug substance as a result of an increase in the osmotic pressure in the reservoir that contains the drug substance.
   C. Sustained-release tablets (tablets containing special substances or obtained by special technology that provides sustained release of active ingredients);
3. Classification by the way of application:
   A. Chewing tablets (tablets that need to be chewed before swallowing);
   B. Soluble tablets (tablets which must be dissolved in a solvent before use. The solvent can be water);
   C. Sublingual and buccal tablets (tablets that are placed under the tongue or behind the cheek until completely dissolved);

Capsules are dosage forms containing one or more active substances, enclosed in a hard or soft shell (gelatin, starch).

1. Classification by the way of application:
   A. For oral administration;
   B. Capsules with powder for inhalation;
2. Classification by the speed and nature of the release:
   A. Modified-release capsules;
   B. The capsules are coated with enteric coating;

Granules are solid dosage form in the form of grains of round, cylindrical or irregular shape, containing one or more medicinal substances.

Dragee is a solid dosage form, which is obtained by multiple layering of medicinal and auxiliary substances onto sugar granules.

The units used in pharmacology

1,0 g (gram) = 1,000 mg (milligram) =1,000 000 mcg (microgram)
1 teaspoon = 5 ml (milliliter)
1 dessertspoon = 10 ml (milliliter)
1 tablespoon = 15 ml (milliliter)
1 ml of an aqueous solution = 20 drops

Permissible mass of powders and forming substances

Powders	Weight, g	Forming substances
Simple undivided	5,0 — 100,0 and more	-
Complex undivided	5,0 — 100,0 and more	Amylum, Talcum, Zinci oxydum
Simple separated	0,1— 1,0	-
Complex separated	0,1 — 1,0	Saccharum, Saccharum lactis, Glucosum

Principles of prescription order writing

A prescription is a written request from a doctor to a pharmacy to dispense a medicine to a patient in a certain dosage form and amount, indicating the method of its administration. There are certain rules how a prescription must be written.

The prescription order should be written legibly because prescription orders are medico-legal documents.

Traditionally, a prescription order follows a definite pattern that facilitates its interpretation. This pattern is essentially the same whether the prescription order is for a single drug or a mixture of two or more drugs. Only one prescription should be written on an order blank.

The prescription consists of several parts:

1. **Date.** The date when the prescription is released.
2. **Name. Address. Age of the patient.** These are necessary to facilitate the handling of the prescription and to avoid possible confusion with medications.
3. **The symbol R** (not "Rx") is an abbreviation for Recipe, the Latin for «take»
4. **Drug, Strength, and Inert Additives.** The body of prescription order contains the name and strength of the desired drug. Most drugs can be prescribed by their official names, by their nonproprietary names, or by the manufacturers' proprietary (brand) names. The nonproprietary name is often referred to as the generic name. When two or more preparations are required in the same prescription, the name and quantity of each drug are recorded consecutively under each other.
5. **Direction to the Pharmacist.** In prescription orders for a single drug this usually consist of 'Dispense tablets', 'Dispense 200 ml, 'Dispense the oral syringe' and so forth. In the case of prescription orders for one or more drugs it is usually either a short sentence such as 'Make a solution' or 'Mix and place into 10 capsules' or a word such as 'Mix'.
6. **Direction to the Patient.** The direction to the patient should be written in a language that the patient understands. The use of Latin abbreviations serves no useful purpose. The direction to the Patient contains instruction as to the amount of drug to take, the time and frequency of the dose, and other facts such as dilution and route of administration. If the drug is to be used externally only, or to be shaken

well before using, or if it is a poison, such facts are included. If the drug is to be taken at a specific time of day or if it is to be three or four times a day, the exact time or times must be specified on the label. Patients are often confused by direction such as every 8 hours. However, if it is therapeutically important to take the drug at an 8-hours interval, this should be emphasized and explained to the patient. The physician should be particularly sensitive to the needs of aged, ill and handicapped patients as well as those with language difficulties. The directions for these individuals also should be written in greater detail on a separate instruction sheet and left with the patient. To avoid possible error, the first word of the directions to the patient should serve as a reminder of the correct route of administration. Direction for the drug to oral use must start with the word 'take', for drug to the local and external use, the word 'apply'; for suppositories the word 'insert' and for drugs to be placed in the conjunctival sac, external auditory canal, or nostril the word 'place'. The directions to the patient must be employed as a reminder of the intended purpose of the prescription, by including such phrases as 'for relief of pain', 'for relief of headache', or 'for relief of itching'. However, directions that would be embarrassing to the patient if placed on the prescription order or label should be given in private.

7. **Signature.** The prescription order is completed by the practitioner signing the bottom of the blank, with the appropriate professional degree following the signature.

Example of prescription

1. Date	May 3, 2017
2. Patients name, age, address	Dee Fleming, Age 6 817 Woodhaven Dr Cincinnati, OH 45229
3. ℞ (Recipe)	℞ (Recipe): Suspension Ampicillin 25%—200 ml
4. Directions to the Pharmacist	Dispense 200 ml (with oral syringe)

5. Directions to the Patient	Label(Signa): Take 5 ml orally at 8 a.m., 12 noon, 4 p.m., and 8 p.m. daily for 10 days for infection
6. Refill Information	Do not refill
7. Signature	Jonas J. Selina, M.D. DEA No. AB1234321 21 Garfield Pl. Cincinnati, OH 45202

Task 2. Pay attention to the collection of powders, capsules, tablets, dragees, granules, spansules, caramels, pastilles.

Task 3. An example of the card for the class work.

Prescribe drugs:

1. 70,0 powders containing 5% Benzocainum and 95% Talcum.
2. 20 powders of Acetylcysteine 0,6. Prescribe a therapeutic dose (TD 0,3) two times a day, dissolving the powder in 1 glass of boiling water.
3. 10 powders of Theophyllinum 0,03. Prescribe 1 powder two times a day.
4. 20 capsules and tablets of Acidum valproicum 0,3. Prescribe 1 capsule (tablet) three times a day.
5. 20 tablets of Rutozidum 0,025 and Acidum ascorbinicum 0,05. Prescribe 1 tablet a day.
6. Granules of Cefalexin 5,0. Dissolve the contents of the vial in 100 ml of boiled water. Prescribe TD 0,25 two times a day.

HOMEWORK

Prescribe drugs:

1. Acidum boricum 20,0. Prescribe for mouth rinse, dissolving 1 teaspoon of powder in a glass of boiling water.
2. Powders 60,0 containing 15% Zinci oxydum and 85% Talcum.
3. Barii sulfas 50,0. Dissolve powder in 1/2 cup of water, take it inside.

4. 10 powders of Nimesulide 0,1. Prescribe 1 powder two times a day, dissolving in 1/2 cup water.
5. 20 powders of the following composition: Phenylephrinum 0,01; Pheniramine 0,02; Paracetamol 0,325. Prescribe 1 powder two times a day, dissolve in 1 glass of boiled water.
6. 3 bottles of Azithromycin powder 0,3. Dissolve the powder in 15 ml of boiled water. Prescribe inside the TD 10 mg / kg of body weight to a child weighing 20 kg one time per day for 3 days.
7. 60 capsules of Pyracetam 0,4. Prescribe 1 capsule two times a day.
8. 30 tablets and capsules of Isosorbide mononitrate 0,04. Prescribe 1 tablet (capsule) one time per day.
9. 30 capsules of Acidum cromoglicicum 0,1. Prescribe TD 0,1 four times a day before meal.
10. 6 tablets of “Citramonum”. Prescribe 1 tablet for headache.
11. 15 coated tablets containing Amoxicillin 0,5 and Acidum clavulanicum 0,125 ("Augmentin"). Prescribe 1 tablet three times a day. Write down in the expanded and short forms (using the commercial name of drug).
12. 40 dragee of Ergocalciferolum 500 IU. Prescribe DD 2500 IU a day.
13. Granules of Midecamycin 20,0. Dissolve the contents of the vial in 100 ml of boiled water, prescribe inside the TD 50 mg / kg of body weight to a child weighing 20 kg two times a day.

Lesson 2
Liquid dosage forms (solutions, drops)

Learning objective is to study how to write prescriptions for liquid dosage forms, to calculate concentration of solutions and therapeutic doses.

QUESTIONS FOR PREPARATION FOR THE LESSON

1. Compound of solutions, volume and compound of solvents.
2. Technologies for making solutions for external use and oral administration, eye drops and dosage forms for injections.
3. Routes of administration of solutions.
4. The therapeutic dose of solution for oral administration, drops or dosage forms for injection.
5. Classification of solutions by the method of administration: for external, internal uses and injection.
6. Characteristics of solvents: purified water (Aqua purificata), water for injections (Aqua pro injectionibus), ethanol 70%, 90%, 95% (Ethanolum), glycerin (Glycerin), olive oil (Oleum olivarum), peach oil (Oleum persicorum).
7. Rules for prescribing solutions for external and internal use.
8. Drops as a kind of solutions. Dosing solutions in drops. Rules for prescribing drops for external and internal use.
9. Requirements to solutions for injection. Methods of sterilization of solutions for injection.
10. Forms of release and rules for prescribing solutions for injections (vials, ampoules, syringe tubes).
11. Rules for prescribing dry substances in ampoules and vials, liquid biotechnological preparations.

QUESTIONS AND TASKS IN CLASS

Task 1. Theoretical material to get ready for the class

Solutions are a liquid dosage form obtained by dissolving liquid or solid substances in a solvent.

1. Solutions for external and local use are intended for application to the skin and mucous membranes; injection into the body cavity. Also they are used for the treatment of wounds and bedsores.
2. Solutions for internal use
    - Dosed by drops;
    - Dosed by spoons.
3. Solutions for parenteral administration.

A. Aqueous solutions:

For subcutaneous administration: a volume of 1-2 ml. It is forbidden to inject irritating agents (e.g. calcium chloride) and drugs with a strong vasoconstrictor effect (e.g. norepinephrine). When these solutions are administered under the skin, they lead to the necrosis.

For intramuscular injection: the maximum volume is 10 ml. It is forbidden to inject irritating agents (e.g. calcium chloride) and drugs with a strong vasoconstrictor effect (e.g. norepinephrine) because of the reason stated above.

For intravenous administration: it is acceptable to use hypertonic solutions and agents with mild irritant properties (irritants are diluted in a large volume of solvent). The volume of the injected solution can reach up to 1000 ml.

B. Oily solutions:

- For subcutaneous injection;
- For intramuscular injection.

Intravenous administration of oily solutions is prohibited (die to fat embolism development).

C. Ultraemulsions:

- For intravenous administration (e.g. Propofol).

The substance may be produced in the form of dry matter (powder) in vials or ampoules. The solution is prepared immediately before use (ex tempore) by a nurse. Water for injection, physiological saline (0,9% NaCl), 5% glucose solution and solution of Lidocain are usually used as solvents.

Suspensions are a liquid dosage form, which consists of one or several insoluble powders as active ingredients, evenly distributed in the liquid. The particles of the active substance are suspended in the form of fine droplets.

- For internal use;
- For subcutaneous injection;
- For intramuscular injection;
- For insertion into the body cavity.

Syrup is a thick, viscous liquid consisting primarily of a solution of sugar in water, containing medicinal substances.

Task 2. Pay attention to the collection of solutions.

Task 3. An example of the card for the class work.

Prescribe drugs:

1. Solution Methylthioninii chloridum for irrigating a bladder (1: 2,000), 300 ml (expanded and short forms, expressing the concentration in a percentage and in a ratio).
2. 5% solution for internal use Calcii chloridum, 200 ml. Prescribe TD 1,5 two times a day.
3. 4% solution of Periciazine, 125 ml. Prescribe inside the drops TD 0,004 three times a day.
4. 1% Morphinum solution in ampoules of 1 ml, 5 ampoules. Prescribe under the skin TD 0,005.
5. Thiopentalum natrium in vials of 0,5; 6 bottles. Administer into the vein in the form of 2% solution, calculating the amount of isotonic sodium chloride solution for dilution of the contents of 1 vial.

HOMEWORK

Prescribe drugs:

1. A solution for irrigating wounds Nitrofural (1: 5000), 600 ml (in expanded and short forms, expressing the concentration as a percentage and as a ratio).
2. 5% ethanol solution Iodum, 20 ml in a dark bottle. Apply to the operating field.

3. 2% solution Kalii bromidum 120 ml for internal use. Prescribe TD 0,2 two times a day.
4. 0,75% solution Sodium picosulfate, 15ml. Prescribe TD 0,0075 (in drops) one time a day.
5. 1% solution in eye drops of Pilocarpinum, 5 ml. Prescribe TD 0,0005 to each eye.
6. 0,25% solution of Lidocainum in 500 ml of isotonic solution of Natrii chloridum with the addition of 20 drops of 0,1% solution Epinephrinum (in the expanded form). Apply for infiltrative anesthesia.
7. 0,025% solution Digoxinum in ampoules of 1 ml, 6 ampoules. Dissolve the content of ampoule in 10 ml of a 5% solution of glucose. Enter into the vein TD 0,000125.
8. 5% Ketamine solution in ampoules of 10 ml, 5 ampoules. Administer 4 mg/kg of body weight into the muscle to a patient who weighs 80 kg.
9. "Microlax" 5 ml, 4 microclysters. Prescribe rectally the contents of 1 microclyster.
10. Oxytocinum in ampoules of 2 ml (1 ml — 5 units), 10 ampoules. Administer into the muscles (TD 2 Units).
11. Thiopentalum natrium in vials of 1,0; 10 vials. Administer into the vein in the form of 2% solution, calculating the amount of isotonic sodium chloride solution for dilution of the contents of 1 vial.
12. Gentamycinum in bottles of 0,08; 10 bottles. Administer into the muscles TD 0,4 mg/ kg to a patient, who weighs 60 kg, dissolving the contents of the vial in 2 ml of water for injection.
13. Choriogonadotropin alfa in ampoules of 1500 IU, 5 ampoules. Administer under the skin 3000 IU, dissolving the contents of ampoules in 1 ml of isotonic sodium chloride solution.
14. Interleukin beta in ampoules of 1 μg, 5 ampoules. Administer into the muscles TD 0,0000005, dissolving the contents of the ampoule in 2 ml isotonic sodium chloride solution.
15. Benzylpenicillinum-natrium in vials of 500000 units. Dissolve the contents of the vial in 2 ml of 0,5% solution of Lidocaine, administer into the muscles at a daily dose (DD) 50000 units / kg of body weight to a child weighing 30 kg every 4 hours.

Lesson 3
Liquid dosage forms (mixtures, suspensions, aerosols). Soft dosage forms (TTS, ointments, gels, pastes, creams, suppositories)

Learning objective is to study how to write prescriptions for liquid and soft dosage forms.

QUESTIONS FOR PREPARATION FOR THE LESSON

1. Mixtures: composition, rules for prescription.
2. Mucilage and syrups as components of mixtures.
3. Suspensions: composition, rules for prescription.
4. Emulsions: composition, rules for prescription.
5. Aerosols and sprays: composition, dosage, rules for prescription.
6. Phytopharmaceuticals:
   a) infusions and decoctions — preparation, dosage; mixtures containing infusions and decoctions;
   b) tinctures — methods of preparation, rules for prescription *per se* (in pure form) and the composition of other dosage forms.
7. Ointments, pastes, creams, gels: composition, rules for prescription, uses.
8. Eye ointments: rules for prescriptions, features.
9. Liniment: varieties, composition, rules for prescriptions.
10. Suppositories: varieties; substances used as a basis, rules for prescriptions.
11. Transdermal therapeutic systems (TTS): design, rules for prescriptions, uses.

QUESTIONS AND TASKS IN CLASS

Task 1. Theoretical material to get ready for the class

Suppositories are mild dosage forms, solid at room temperature, melting at body temperature, used to insert into the body cavity. Cocoa butter and gelatin-glycerol mixtures are used as a basis for suppositories.

Suppositories are divided into:

1. Vaginal (spherical or ovoid, with approximate weight –1,5-4 g);
2. Rectal (cone-like or cylindrical with a pointed end, with approximate weight – 1,1-3 g).

Ointment is a mild dosage form, which consists of oil and evenly distributed medicinal substances. They are used for application to the skin, wounds and mucous.

Basics that are used for the production of ointments are divided into:

A. Hydrophobic: fat (natural fats, vegetable oils), hydrocarbon (petrolatum ointment (vaseline), liquid petrolatum);
B. Hydrophilic: esters of starch, agar, gelatin, collagen, synthetic compounds.

Isolate simple and complex ointments:

a. Simple ointments consist of one active substance and one ointment base);
b. Complex ointments contain more than 2 ingredients).

Currently, most ointments are available in ready-made form.

Cream is a soft dosage form, which is an emulsion of the water/oil or oil/water type.

Pastes are ointments of dense consistency, the content of powdery substances must not exceed 65% and cannot be less than 25%.

Gels are ointments that use gelling agents of natural or synthetic origin. They have an elastic consistency and are able to maintain their shape.

Transdermal therapeutic systems (TTS) are soft dosage forms for external use as patches or membranes releasing the drug.

TTS are divided into:

1. Systems bound by a membrane (consisting of a reservoir with a drug substance and a polymer membrane that limits the release rate);

2. Adhesive systems (the drug substance is distributed in an adhesive polymer).

Emulsion is a liquid dosage form containing two or more mutually insoluble/immiscible liquids. In this case, the particles of the active substance are suspended in the form of fine droplets.

Oil emulsions are prepared from liquid oils, for example castor or almond oil. Emulsifiers are added to emulsify the oil during preparing the emulsion.

Infusions and decoctions are liquid dosage forms representing aqueous extracts from medicinal plant material. They are used for internal and external use and administered with spoons.

Tincture is a liquid dosage form, which represents alcohol or water-alcohol extracts from medicinal plant material. Tinctures are dosed with drops.

Extracts are produced in different forms. They can be liquid (*fluidum*), dense (*spissum*) and dry (*siccum*). For extraction of active substances not only alcohol is used, but also chloroformate (cloroformic acid ester) at high temperature and pressure. Liquid extracts are administered as drops; dense extract can be put into the capsules or they can be coated with membrane. Dry extracts can be administered as tablets or powders.

Mixture is a liquid dosage form, which is obtained by mixing several solids and / or liquids. Mixture is prescribed for internal use and administered with spoons. Sugar syrup could be added to a mixture to change the taste (add 10-20% of sugar syrup from a total volume of a mixture). If the active substance has irritating action, mucilage or starch should be added to a mixture (10-30% from total volume)

Aerosol is a dosage form consisting of solutions, suspensions or emulsions of medicinal substances under pressure with a propellant gas in a sealed package equipped with a valve-spray system.

Spray is an aerosol free of propellant. The release of the contents occurs by means of a mechanical sprayer or when the package is compressed.

Task 2. Pay attention to the collection of liquid, soft dosage forms and phytopharmaceuticals.

Task 3. An example of the card for the class work.

Prescribe drugs:

1. Mixture of Diphenhydraminum (TD 0,02) and sugar syrup for 10 intakes with dessert spoons. Prescribe one dessert spoon at night.
2. A suspension "Maalox", 250 ml. Prescribe 1 tablespoon three times a day.
3. Aerosol Salbutamolum, 10 ml. Prescribe 1 inhalation dose.
4. Tincture Absinthium, 25 ml. Prescribe 15 drops three times a day.
5. Liquid extract of Eleutherococcus, 50 ml. Prescribe 20 drops three times a day.
6. 3% eye ointment Aciclovir, 2,0.
7. Rectal suppositories and vaginal with Hyaluronidase (TD 3000 IU) for 10 injections.
8. 7 TTS patches with Nicotinum 0,005 each. Apply on the skin 1 patch once a day in the morning, remove before bed.
9. 5 TTS with 0,0025 Fentanylum in each patch. Apply 1 patch one time in 3 days.

HOMEWORK

Prescribe drugs:

1. Mixture of Kalii bromidum (TD 0,1), Natrii bromidum (TD 0,2), starch mucilage and sugar syrup for 12 times with dessertspoon. Prescribe 1 dessert spoon three times a day.
2. Phenoxymethylpenicillin syrup, 60 ml (1 ml — 150 000 IU). Prescribe inside the TD 750 000 four times a day.
3. Oseltamivir in vials of 0,9. Prescribe inside TD 0,09 one time a day, dissolving the contents of the vial in 50 ml of boiled water.
4. 2,5% suspension of Hydrocortisonum in ampoules of 2 ml, 10 ampoules. Prescribe into the muscles TD 0,025.
5. 6% suspension of Mesalasine in microclyster of 30 ml, 7 microclysters. Prescribe TD 30 mg / kg of body weight to a patient weighing 60 kg one time a day before bedtime.

6. Aerosol Beclometasone 10 ml. Prescribe 2 inhalation doses.
7. Tincture of Crataegus 25 ml. Prescribe 20 drops three times a day.
8. Liquid extract of Rhodiola 25 ml. Prescribe 20 drops in the morning.
9. Hypericum thick extract in capsules 0,425 for 30 doses. Prescribe TD 0,85 one time per day.
10. 50,0 ointment containing 1% Acidum salicylicum and 5% Bismuthi subgallas.
11. 50,0 pasta containing 1% Diclofenac and 10% Bismuthi subgallas.
12. 1% ophthalmic ointment Erythromycinum, 10,0.
13. 1% gel of Indometacin, 50,0.
14. Rectal suppositories and vaginal with Benzocainum (TD 0,2) for 10 administrations.
15. Rectal suppositories "Relief" for 10 administrations.
16. 3 TTS "Evra" patch containing Norelgestromin 0,006 and Ethinylestradiol 0,0006. To stick one plaster once a week (write down using international non-proprietary and commercial name.

Lesson 4
Final lesson about general prescription

Learning objective is to check the students' skills in writing prescriptions of all medicinal forms which have been studied.

QUESTIONS FOR PREPARATION FOR THE LESSON

1. Revise the knowledge of the theoretical course about the general prescription.
2. Repeat the rules for prescribing solid, soft and liquid dosage forms and phytopharmaceuticals.

EXAMPLES OF INDIVIDUAL TASKS

Card № 1

Prescribe:

1. 10 tablets Acidum ascorbinicum, 0,05. Prescribe 1 tablet three times a day.
2. 20 coated tablets of Bromhexinum, 0,008. Prescribe 1 tablet three times a day.
3. 0,05% solution of Kalii permanganas for gastric lavage 250 ml in a dark bottle (in the expanded form and short form).
4. 2,5% solution of Phenylephrinum, 5 ml. Prescribe TD 0,0025 to each eye.
5. 0,1% solution of Metoprolol in ampoules of 5 ml, 10 ampoules. Enter into the vein TD 0,005 in 20 ml of 5% glucose solution.
6. 0,025 Cisplatin in a bottle; six bottles. The content of one bottle should be dissolved in 10 ml of water for injection. Inject into the vein TD 0,05.
7. Aerosol Fenoterolum. 15 ml. Prescribe 1 inhalation dose.
8. Ginseng tincture. 25 ml. Prescribe 20 drops 2 times a day.
9. 2% pasta Acidum fusidicum. 15,0 (in expanded form).
10. Rectal suppositories with Indometacin TD 0,05 for 10 administrations.

Card № 2

Prescribe:

1. 50,0 powders containing 20% Bismuthi subgallas and 80% Zinci oxydum.
2. 20 drops of Chlorpromazine at 0,025. Prescribe TD 0,05 three times daily after a meal.
3. 1% alcohol solution Viride nitens 10 ml to smooth the affected skin areas (in short form).
4. 0,5% solution of Tropicamide 5 ml. Prescribe TD 0,00025 to each eye.
5. 1% Trimeperidinum solution 1 ml in ampoules, 10 ampoules. To inject under a skin TD 0,005.
6. 25% solution of Amicacin in ampoules of 2 ml, 1 ampoule. Inject into the muscle 2 times a day TD 5 mg/kg to a patient, who weighs 50 kg.
7. Liquid extract of Leuzeae, 25 ml. Prescribe 20 drops three times a day.
8. 1% ophthalmic ointment Tetracyclinum, 5,0.
9. Rectal suppositories "Cefeconum" for 10 administrations.
10. 5 TTS patches with Lidocainum 0,7. Apply 1 patch once a day for 12 hours.

Lesson 5
General Pharmacology. Pharmacokinetics

Learning objective is to study the general patterns of absorption, distribution, biotransformation and elimination of drugs, individual features of pharmacokinetics.

QUESTIONS FOR PREPARATION FOR THE LESSON

1. Pharmacology: tasks, stages and methods of preclinical and clinical research, pharmacokinetics and pharmacodynamics.
2. The concept of drugs and poisons, pharmacoprophylaxis and pharmacotherapy; types of pharmacotherapy (etiotropic, pathogenetic, replacement, symptomatic).
3. Penetration of drugs through the biological membranes, types of transport (passive diffusion, active transport, pinocytosis).
4. Route of drug administration: effects on pharmacokinetics, pharmacological effect, disadvantages, rational dosage forms:
   - enteral — sublingual, buccal, oral, rectal;
   - parenteral — under the skin, in the muscles, in the vein, in the artery, sub-arachnoid, epidural, intraosseous, inhalation, cutaneous.
5. Bioavailability of drugs: methods of detection and factors affecting bioavailability (physicochemical properties of drugs, dosage forms, pH of digestive juices, elimination).
6. Biological barriers and their permeability for medicinal products — capillary wall, blood-brain barrier (BBB), placental barrier.
7. Distribution of drugs through organs and tissues, factors affecting distribution (physical and chemical properties of drugs, blood supply to organs, transport proteins and barriers). The importance of P-glycoprotein.
8. Biotransformation: the concept of endobiotics and xenobiotics, biological significance, localization, enzymes and types of reactions (metabolic transformation, conjugation).
9. Factors affecting biotransformation: age, sex, individual characteristics of the organism (polymorphism of genes of biotransformation enzyme).

10. Induction and inhibition of biotransformation, medical significance.
11. Pharmacogenetics, pharmacogenomics as the basis for personalized, predicative therapy.
12. Elimination of drugs from the body (with urine, bile, exhaled air, secret glands, breast milk during lactation). Factors affecting the excretion of drugs (physicochemical properties of drugs, functional state of excretory organs, urine pH). Enterohepatic circulation.
13. Modeling of pharmacokinetic processes: zero order and first order kinetics. Quantitative indicators of pharmacokinetics: volume of distribution, clearance, elimination half-life, constant of elimination. Bioequivalence of drugs.

QUESTIONS AND TASKS FOR SELF-CONTROL

Task 1. After studying the theoretical material, answer the following questions:

1. Give the definitions of "placebo", "nocebo", "double-blind method", "randomization", "compliance", "pleiotropic effect."
2. Indicate the ratio of neutral molecules and ions in a weak acid with pKa = 4,4 in gastric juice (pH 1,4) and blood (pH 7,4); similar ratio at a weak base with the same pKa. List medicines with properties of weak acids and weak bases.
3. What medicinal products — endobiotics or xenobiotics — penetrate membranes by filtration and active transport? Why?
4. Can the bioavailability of a drug, when administered orally, be 5%, if it is completely absorbed in the intestine?
5. The binding of the drug with plasma albumin is 98%. Will the pharmacological effect of this drug change if the proportion of its bound fraction decreases by 2% after being replaced by another drug?
6. What is directional drug delivery? How is it done?
7. What can be assumed about the pharmacokinetic properties of a synthetic chemotherapeutic agent, if it is known that its volume of distribution is 128 liters?
8. What toxic products are formed during the oxidation of drugs with cytochrome P-450 and how are they neutralized? What are the “suicide substrates” of cytochrome P-450?

9. What genes of cytochrome P-450 isoenzymes are most susceptible to polymorphism?
10. Why does warfarin at a dose of 5 mg/day cause more bleeding in patients who are carriers of CYP2C9*3 than in those with genotypes CYP2C9*1 and CYP2C9*2?
11. It is known that the antituberculosis drug isoniazid is inactivated in the acetylation reaction. Why do some patients experience mild side effects in the treatment of tuberculosis with isoniazid, while other patients complain of headache, dizziness, nausea, vomiting, pain behind the sternum, irritability, insomnia, tachycardia and polyneuritis?
12. How does the effect of warfarin, an anticoagulant of indirect action, change in case of combined administration with rifampicin (chloramphenicol)? Why?
13. What is the purpose of injecting sodium bicarbonate into the vein in case of poisoning with acetylsalicylic acid?
14. Which antibiotic — benzylpenicillin (weak acid) or erythromycin (weak base) — creates a high concentration in breast milk (pH 6,5—7,0) during lactation? Why?

Task 2

a. Match each parameter with the appropriate description.

A. T½ (elimination half-life)	1. The fraction of administered drug reaching systemic circulation unchanged
B. T C max	2. The volume of plasma cleared of drug per unit time
C. f (bioavailability)	3. Theoretical volume occupied by the total amount of drug in the body relative to its plasma concentration
D. Vd (volume of distribution)	4. The time required to change the amount of drug in the body by 50% during elimination
E.Cl (clearance)	5. The time which is required to reach maximum concentration of administered drug in blood

b. Match each route of administration with the appropriate description

A. Enteral	1. The route in which bioavailability is 100%
B. Sublingual	2. The route in which volume of injected drug cannot be more than 2 ml
C. Intravenous	3. The route which provides rapid delivery of a drug across the large surface area of the mucous membranes of the respiratory tract and pulmonary epithelium
D. Under the skin	4. The route which is available for lipophilic drugs and allows to avoid first-pass metabolism
E. Inhalation	5. The route in which drugs are absorbed into the portal circulation and initially distributed to the liver

Task 3. Topics for reports.

1. The contributions of Paul Ehrlich, Oswald Schmiedeberg and Rudolf Buchheim to pharmacology.
2. Controlled, double-blind, randomised methods in clinical trials.
3. Ethical issues in clinical research.

QUESTIONS AND TASKS IN CLASS

Task 1. Analyze the tasks that reflect the relations of pharmacokinetics with the physicochemical properties of drugs (the collection of graphic tasks).

Task 2. Analyze case tasks.

1. An 85-year-old man was recently admitted to a nursing facility. Diseases listed in his medical record on admission were depression with anxiety symptoms, atrial fibrillation, chronic obstructive pulmonary disease, and osteoarthritis. Medications taken orally by the patient included the following:

   a. Sertraline (base, pKa = 9,5)
   b. Diazepam (base, pKa = 3,0)
   c. Amiodarone (base, pKa = 7,4)
   d. Theophylline (acid, pKa = 8,8)
   e. Ibuprofen (acid, pKa = 4,8)

Shortly after administration, which drug was most likely concentrated inside the patient's gastric cells?

2. A patient was given a 200 mg dose of a drug IV, and 100 mg was eliminated during the first two hours. If the drug follows first-order elimination kinetics, how much of the drug will remain 6 hours after its administration?
3. At 6 h after IV administration of bolus dose, the plasma level of a drug is 5 mg/L. If the Vd = 10 L and the elimination half-life = 3 h, what was the dose administered?
4. Warfarin (an anticoagulant with indirect action) was prescribed to a patient with a burn of 50% of the body surface for the prevention of thrombosis in a dose usually used to prevent thrombophlebitis. After 2 days, the patient had gastric bleeding. What is the possible reason of a relative overdose of warfarin? It is known that up to 97% of warfarin circulates in the blood in the form associated with albumins.
5. A 10-mg dose of a new drug that follows first-order, one compartment model kinetics was given intravenously to healthy subjects in a phase 1 clinical trial. The volume of distribution (Vd) of the drug turned out to be 80 L. Which would have been the volume of distribution of the drug (in liters) if the administered dose were 20 mg?
6. A 49-year-old obese man recently diagnosed with vasospastic angina started a treatment with nifedipine. The drug has a volume of distribution (Vd) of about 55 L in a 70-kg person, but in this obese patient, the Vd turned out to be 110 L. The standard loading dose of nifedipine for a patient weighing 70 kg is 30 mg. Which of the following should be the therapeutic loading dose administered to this patient (in mg) in order to achieve the same target concentration?

Task 3. Answer the test questions (in the computer lab).

Lesson 6
General Pharmacology. Pharmacodynamics

Learning objective is to study the general patterns of drug action, the effects after repeated and combined uses of drugs, dependence of pharmacodynamics on individual characteristics of a body.

QUESTIONS FOR PREPARATION FOR THE LESSON

1. The concept of the pharmacological effect, the primary pharmacological reaction and receptors.
2. Classification, active and allosteric centers, molecular structure of receptors.
3. Mechanisms of interaction of agonists (mimetics) and antagonists (blockers) with receptors.
4. Types of drugs action: local, resorptive, direct (primary), indirect (secondary), reflex, selective, reversible, irreversible, adverse.
5. Functional changes caused by drugs: stimulation, sedation, oppression, paralysis.
6. Principles of the drug classification.
7. Dependence of the drug effect on the chemical structure and physical properties.
8. Dependence of the drug effect on sex, age, individual characteristics of the organism.
9. Dependence of drug action on a dose or a concentration. Classification of doses.
10. Repeated administration of drugs: mechanisms of development, medical significance
    - cumulation (material, functional);
    - tolerance, tachyphylaxis;
    - abuse, addiction, drug dependence;
    - sensitization;
    - rebound and withdrawal syndromes.
11. Combined administration of drugs: the mechanisms and the medical significance of the drug interaction

- synergism (summarized, potentiated);
- antagonism (physical, chemical, physiological indirect, direct competitive and noncompetitive);

12. Side effects, undesirable phenomenon, undesirable reaction, complication of pharmacotherapy.

QUESTIONS AND TASKS FOR SELF-CONTROL

Task 1. After studying the theoretical material, answer the following questions:

1. It is known that β_1-adrenoreceptors activate adenylate cyclase and increase the synthesis of cyclic adenosine monophosphate (cAMP); m2-cholinergic receptors reduce the activity of this enzyme and the synthesis of cAMP. How will the heart rate change when these receptors are activated?
2. Histamine receptors function with the participation of various effector systems: smooth muscle H_1 receptors, activating phospholipase C, increase the production of inositol triphosphate and diacylglycerol, H_2 receptors of the gastric glands activate cAMP and synthesis. What are the effects of these cyoreceptors activation?
3. Caffeine is used to increase blood pressure in case of arterial hypotension, as well as to improve mental performance in healthy people. What functional changes does caffeine cause in the first and second cases?
4. What deficiency of liver enzymes in newborns can unconjugated hyperbilirubinemia cause? What drugs activate bilirubin conjugation?
5. What medications are forbidden for people with a deficiency of glucose-6-phosphate dehydrogenase erythrocytes? Why?
6. What quantitative indicators characterize the degree of drug safety?
7. Determine the type of antagonism in the following situations:
    a. sodium thiosulfate was administered in case of poisoning with iodine;
    b. gastric lavage was performed with a suspension of activated carbon in case of poisoning with morphine;
    c. caffeine was administered in case of acute ethanol poisoning;

d. naloxone (the opioid receptor antagonist) was administered in case of acute morphine poisoning.

8. Calculate the maintenance dose of the drug if the loading (initial) dose is 0,002 and the elimination coefficient is 20%.
9. Are there any differences between the biochemical processes that underlie tolerance and dependence?

Task 2.

a. Match each type of receptor with the appropriate description

A. Ligand-gated ion channels	1. Receptors for thyroid hormones
B. G protein-coupled receptors	2. Nicotinic receptor
C. Enzyme-linked receptors	3. Adrenergic receptors
D. Intracellular receptors	4. Insulin receptors
E. Cytokines receptors	5. Receptors for erythropoietin

b. Match each type of drug interaction with the appropriate description

A. Potentiation	1. The competition of an antagonist with an agonist for the same binding site of the receptor
B. Competitive antagonism	2. An antagonist may act at a completely separate receptor, initiating effects that are functionally opposite those of the agonist
C. Non-competitive antagonism	3. The formation of a complex between effector drug and another compound
D. Chemical antagonism	4. The effect of substance A and B together is equal to the sum of their individual effects
E. Additive (summarized) type of interaction	5. Effect of substance A and B together is greater than the sum of their individual effects

Task 3. Topics for reports.

1. The concept of the pharmacological "target" — a receptor, ion channel, transport protein, cytokine, enzyme. Principles and methods of the action of targeted therapies.
2. The definition of teratogenic drugs. FDA pregnancy categories of drugs.
3. The regulation of intracellular calcium: calcium entry mechanism, calcium release mechanism.
4. Channel functioning: sodium and potassium channels.
5. Biotransformation and effects of drugs in cases of enzymopathy.

QUESTIONS AND TASKS IN CLASS

Task 1. Analyze the tasks about pharmacodynamics (the collection of graphic tasks).

Task 2. Analyze case tasks.

1. A 45-year-old woman recently diagnosed with a urinary tract infection started therapy with a trimethoprim − sulfamethoxazole combination. Both trimethoprim and sulfamethoxazole are bacteriostatic drugs when given alone. However, a bactericidal effect is obtained when the two drugs are given in combination. Identify these drugs interaction.
2. A 2-year-old girl was rushed to the emergency department after ingesting several tablets of a medication containing iron. An emergency treatment was started that included the intravenous administration of deferoxamine. This drug is able to combine with iron in plasma to form an inactive complex and therefore to antagonize iron effects. Which term best defines this antagonism?
3. A 46-year-old woman complained to her physician that the sedative effect of the drug she was taking had increased substantially. The woman, who was suffering from generalized anxiety disorder, had been taking diazepam, one tablet daily. A few days earlier, she had started taking cimetidine to treat her heartburn. Cimetidine is an inhibitor of the cytochrome P-450 system in the liver. Which term best defines this cimetidine−diazepam interaction.
4. A 57-year-old man who was in the hospital after a surgical procedure complained of a severe abdominal pain. The physician decided to start analgesic treatment with an opioid. The drugs he was considering were morphine (10 mg IM) and buprenorphine (0,3 mg IM). Morphine is a

full agonist at mu (μ) opioid receptors, whereas buprenorphine is a partial agonist at the same receptors. The above-mentioned doses of the two drugs are equieffective. Which of the following pairs of statements correctly defines the potency and efficacy of morphine and buprenorphine?

a. Morphine is more potent. Buprenorphine is more effective.
b. Morphine is more potent. Buprenorphine is less effective.
c. Morphine is less potent. Buprenorphine is more effective.
d. Morphine is less potent. Buprenorphine is less effective.

5. A 64-year-old man with terminal cancer had been suffering from continuous pain and started treatment with morphine. After a few days of treatment, the initial dose was no longer effective, and the physician gradually increased the dose, knowing that pharmacodynamic tolerance most likely had occurred. Which of the following best explains the mechanism of tolerance in this patient?

a. Accelerated morphine metabolism
b. Increased affinity of receptors to morphine
c. Decreased binding of morphine to plasma proteins
d. Decreased morphine receptor density
e. Decreased concentration of morphine in the brain

6. Characterize effects of the drugs:

a. Prednisone is a synthetic glucocorticoid drug that is mostly used to suppress the immune system. After abrupt discontinuation patients complain of weakness, fatigue, decreased appetite, weight loss, nausea, vomiting, diarrhea.
b. Benzodiazepines are widely used anxiolytic drugs for anxiety or insomnia. Abrupt discontinuation of the benzodiazepines results in confusion, anxiety, agitation, restlessness, tension, and (rarely) seizures.
c. Sodium bicarbonate is a weak base that reacts with gastric acid to form water and a salt to diminish gastric acidity. Discontinuation of sodium bicarbonates after long treatment makes the stomach produce even more acid after the consumption of foods and drinks.

Task 3. Answer the test questions (in the computer lab).

Lesson 7
Vitamins and drugs for bone disorders

Learning objectives are to study the classification, the mechanisms of action, pharmacokinetics and indications for the use of vitamins, side effects of vitamin therapy, measures for their prevention and correction; to study the mechanisms of action and the use of drugs for bone disorders; to study and practice prescription writing.

QUESTIONS FOR PREPARATION FOR THE LESSON

1. Vitamins: the history of discovery, sources of production, significance for the organism, participation in metabolic reactions, classification by physicochemical, biochemical and pharmacological properties.
2. Causes, symptoms and preventive measures for hypovitaminosis.
3. Natural sources, daily requirements, mechanisms and features of action, pharmacokinetics, use, side effects, contraindications to the use of fat-soluble vitamins and their synthetic analogues:
   - vitamin A — retinol, beta-carotene;
   - retinoids — acitretin, isotretinoin, tretinoin;
   - vitamin D2 — ergocalciferol;
   - vitamin D3 and its analogues — cholecalciferol, calcitriol, alfacalcidol;
   - vitamin E — alpha-tocopherol acetate;
   - vitamin K — menadione sodium bisulfite.
4. Natural sources, daily requirements, mechanisms and features of action, pharmacokinetics, use, side effects, contraindications to the use of water-soluble vitamins and their synthetic analogues:
   - vitamin B1 — thiamine;
   - vitamin B2 — riboflavin;
   - vitamin B3 — sodium dimercaptopropanesulfonate + calcium pantothenate, dexpanthenol;
   - vitamin B6 — pyridoxine, pyridoxal phosphate;
   - vitamin B12 — cyanocobalamin;
   - vitamin B — folic acid;
   - vitamin PP — nicotinic acid, nicotinamide;
   - vitamin C — ascorbic acid;

- vitamin P — rutoside (rutine), dihydroquercetin.

5. Hypervitaminosis A and D: causes, pathogenesis, symptoms, prevention, treatment.
6. Mechanisms, features of action, use, side effects, contraindications to the use of drugs for the treatment of osteoporosis:
   - agents inhibiting the resorption of bone tissue,
     hormonal agents — estradiol, calcitonin;
     bisphosphonates — alendronate, zoledronate, ibandronate, pamidronate, etidronate;
     human monoclonal antibody to receptor activator of NF-κB ligand (RANKL) — denosumab;
   - agents that increase bone formation, — sodium fluoride, teriparatide, strontium ranelate, anabolic steroids (methandienone, nandrolone);
   - drugs that have a multifaceted effect on bone tissue —vitamin D preparations.

PRESCRIPTIONS

1. Ergocalciferol (Ergocalciferolum) — dragees of 500 IU; 0,625% oil solution in bottles of 10 and 15 ml (1 drop contains 700 IU). TD: orally — a prophylactic dose of 500 IU once a day, therapeutic doses — 2100-14000 IU once a day with meals; for the prevention and the treatment of osteoporosis — 2800-3500 IU once a day.
2. Thiaminum (Thiaminum) — 3% and 6% solutions in ampoules of 1 ml. TD: into the muscle 0,03—0,06 one time per day.
3. Pyridoxine (Pyridoxinum) — tablets 0,01; 1% and 5% solutions in 1 ml ampoules. TD: orally0,02 two times daily after meals; into the muscle 0,02—0,1.
4. Nicotinic acid (Acidum nicotinicum) — tablets 0,05; coated tablets 0,5; 1% solution in 1 ml ampoules. TD: orally 0,05—0,1 three times a day; for the treatment of atherosclerosis 0,5 one times a day in the morning after meal; into the vein 0,01 in 10 ml of 5% solution of glucose.
5. Ascorbic acid (Acidum ascorbinicum) — tablets 0,05 and 0,1; 5% solution in ampoules of 1 and 2 ml. TD: orally 0,05—0,1 three times a day after meal; into the muscle 0,1 one time a day; in a vein 0,1 in 10 ml of 5% solution of glucose.

QUESTIONS AND TASKS FOR SELF-CONTROL

Task 1. Pharmacotherapeutic questions. Write prescriptions, justifying the choice of a drug.

1. Drug for the prevention of rickets.
2. Drug for the treatment of rickets.
3. Drug for the treatment of osteoporosis.
4. Drug for neuropathic pain.
5. Drug for the treatment of metabolic acidosis.
6. Drug for the correction of anti-tuberculosis medication side effects.
7. Drug for the treatment of dermatitis.
8. Drug for the treatment of atherosclerosis.
9. Drug g for cerebral circulation disorders.
10. Drug for the treatment of hemorrhagic diathesis.
11. Drug for the immunodeficiency treatment.
12. Drug for bleeding gums.
13. Drug for influenza.
14. Drug for anemia.
15. Drug for liver diseases.
16. Drug for allergic diseases.
17. Drug for hypotrophy in children.

Task 2. After studying the theoretical material, answer the following questions:

1. What fat-soluble vitamin has the hormone function in the body? What type of metabolism does it regulate and how?
2. What vitamins are used in ophthalmology? Consider the mechanisms of their action in diseases of the eye.
3. What vitamins are involved in the carbohydrate and energy metabolism in the nervous tissue? In what diseases of the nervous system are these drugs used?
4. What vitamins have an anabolic effect? In what diseases of adults and children is this effect used?
5. What drugs have a therapeutic effect in case of anemia? What are the mechanisms of their action?
6. What vitamins can stimulate the immune system? In what diseases is this effect used?

7. What groups of drugs are used for the treatment of osteoporosis? Explain the mechanisms of the action of drugs which are used in bone disorders.

Task 3.

a. Match each drug for bone disorders with the appropriate description

A. Alendronate	1. This drug can induce osteoclast apoptosis
B. Calcitonin	2. This drug is a recombinant human parathyroid hormone
C. Calcitriol	3. This drug binds and neutralizes RANKL (receptor activator of nuclear factor κB)
D. Denosumab	4. This drug can inhibit the gene expression of parathyroid hormone
E. Teriparatide	5. This hormone is secreted by the parafollicular cells of the thyroid gland

b. Match each vitamin with the appropriate description

A. Thiamine	1. A vitamin which is essential for normal vision
B. Vitamin K	2. The major biologic function of this vitamin is to maintain normal blood levels of calcium and phosphorus
C. Vitamin D	3. A vitamin which is a necessary participant in synthesis of several proteins that mediate both coagulation and anticoagulation
D. Vitamin A	4. The co-enzyme of this vitamin plays a role in activating transketolase, an enzyme involved in direct oxidative pathway for glucose
E.Riboflavin	5. A vitamin which is required by the body to use oxygen and the metabolism of amino acids, fatty acids, and carbohydrates
F. Vitamin C	6. A vitamin which is required in the synthesis of collagen in connective tissues

Task 4. Topics for reports.

1. Multi-vitamins: the pros and cons.
2. Functions of RANKL/RANK and Wnt signals in bone modeling and remodeling. Drugs affecting RANKL/RANK and Wnt signals in bone tissue.
3. The skeletal-related events of denosumab versus zoledronic acid in patients with bone metastases.
4. Potential new therapies: cathepsin K inhibitors (odanacatib).

QUESTIONS AND TASKS IN CLASS

Task 1. Analyze the tasks, reflecting the mechanisms and features of the action of drugs, indications for their clinical use, side effects (the collection of graphic tasks).

Task 2. Analyze case tasks.

1. A patient, 55 years old, complains of the difficulties with driving at night, sudden visual impairment in poor light. At the same time, daytime vision remains normal. Food irregular, in history — pancreatitis. What is the cause of the symptoms described by the patient?
2. On consultation with a dermatologist, a woman, 22 years old, complains of dry skin, poorly healing wounds (ulcers) on the skin and mucous membranes, dry mouth, blurred vision. A history of anorexia (was observed by a psychiatrist). On examination, hyperkeratosis, papular rash, atrophy of sweat glands, and xerophthalmia were revealed. Explain the mechanism of the symptoms.
3. A 7-year-old boy was brought to the emergency department after he fell while playing in the yard. Physical examination revealed only minor skin scratches, but an X-ray showed two rib fractures, clearly demineralized bone, and widening and cupping of metaphyses with exaggerated normal concavity and irregular calcification. Pertinent serum values on admission were calcium 8,3 mg/dL (normal 8,5−10,5 mg/dL), phosphate 2,2 mg/dL (normal 3,0−4,5 mg/dL), and a two-fold increase in alkaline phosphatase. What drug would be most appropriate for this boy?
4. A 52-year-old woman complained to her physician of a persistent gastric pain every time she took a prescribed drug. The woman, recently

diagnosed with severe osteoporosis, had started a therapy with oral alendronate 1 week earlier. The physician suspended alendronate and prescribed intravenous administration of zoledronate, explaining to the patient that a single injection would be effective for at least 5 to 6 months. Zoledronate has a half-life of about 7 days. Explain the reason for the exceptionally long efficacy of the drug?

Task 3. Answer the test questions (in the computer lab).

Lesson 8
Hormones and antihormonal agents

Learning objectives are to study the classifications, mechanisms of action, pharmacokinetics, indications for the use and side effects of hormones and antihormonal agents; to study and practice prescription writing.

QUESTIONS FOR PREPARATION FOR THE LESSON

1. Characteristics of hormones: classification, biosynthesis, secretion, principles of action, receptors. Hormonal regulation of body functions. The history of hormonal drugs discovery and study.
2. Mechanisms of action, receptors, pharmacokinetics, use, side effects and contraindications to the use of hormonal and antihormonal agents.
3. Drugs affecting the production of hormones of the pituitary gland
   - drugs of somatostatin — octreotide, lanreotide, pasireotide;
   - inhibitors of the secretion of gonadotropic hormones — goserelin, danazol;
   - inhibitors of prolactin and growth hormone secretion — D-receptor agonists (bromocriptine), selective agonists of D_2- receptors (cabergoline).
4. Anterior pituitary hormones:
   - somatotropin;
   - drugs of gonadotropins with luteinizing activity — lutropin alfa, choriogonadotropin alfa;
   - drugs of gonadotropins with follicle-stimulating activity — urofollitropin, follitropin alfa, menotropin.
5. Posterior pituitary hormones:
   - vasopressin and its analogues— desmopressin;
   - oxytocin.
6. Drugs of thyroid hormones and antithyroid drugs:
   - agents for the replacement therapy for hypothyroidism — potassium iodide, levothyroxine sodium, lyotyronine;
   - antithyroid drugs — thiamazole;
   - agents that reduce the level of calcium in the blood — calcitonin.
7. Parathyroid hormone drugs — teriparatide.

8. Drugs of human genetically engineered insulin and its analogs:
   - ultra-short-acting insulin — insulin aspart, insulin glulisin, insulin lispro;
   - short-acting insulin — soluble insulin
   - intermediate-acting insulin —isophane insulin
   - long-acting insulin — insulin glargine, insulin detemir.
9. Synthetic hypoglycemic agents:
   a) drugs that increase the secretion of endogenous insulin
      - derivatives of sulfonylurea — glibenclamide, glyclazide, glimepiride;
      - meglitinides (prandial regulators) — nateglinide, repaglinide;
      - incretin mimetics (glucagon-like peptide-1 receptor agonists) — exenatide, liraglutide;
      - inhibitors of dipeptidylpeptidase-4 (gliptins) — vildagliptin, saxagliptin, sitagliptin;
   b) drugs that increase glucose uptake by peripheral tissues
      - biguanides — metformin;
      - thiazolidinediones — rosiglitazone, pioglitazone;
   c) drugs that reduce glucose uptake in the intestine
      - inhibitors of alfa-glucosidase — acarbose;
   d) inhibitors of glucose reabsorption in the renal tubules — dapagliflozin, empagliflozin.
10. Diabetic and hypoglycemic coma: causes, mechanisms of development, symptoms, treatment.
11. Drugs of hormones of the adrenal cortex:
   a) synthetic drugs of mineralocorticoids — fludrocortisone;
   b) drugs of natural glucocorticoids — hydrocortisone;
   c) synthetic drugs of glucocorticoids:
      - with resorptive action — prednisolone, methylprednisonelone, dexamethasone, triamcinolone, betamethasone, budesonide;
      - inhaled forms — beclomethasone, budesonide, fluticasone;
      - local forms — flumethasone, fluocinolone acetonide.
12. Drugs of sexual hormones:
   - drugs of estrogens — estradiol, ethinyl estradiol, estriol;
   - progestogen drugs — progesterone, gestoden, medroxyprogesterone, levonorgestrel;
   - androgen drugs — testosterone.

13. Antagonists of sex hormones:
    - antiestrogenic drugs — fulvestrant, clomiphene, tamoxifene;
    - antigestagenic agents — mifepristone;
    - antiandrogenic drugs — cyproterone, flutamide.

PRESCRIPTIONS

1. Potassium iodide (Kalii iodidum) — tablets 0,0001 and 0,0002. TD: oral prophylactic doses of 0,0001—0,0002 once time per day; therapeutic doses 0,0002—0,0006 once a day.
2. Levothyroxine sodium (Levothyroxin natrium) — tablets 0,00005 and 0,0001. TD: orally 0.00005—0,0002 once a day in the morning before meal.
3. Thiamazole (Thiamazole) — tablets 0,005. TD: orally 0,005—0,01 three times a day after meal.
4. Insulin soluble human genetically engineered (Insulin human) — bottles of 10 ml (1 ml — 100 IU). TD: under the skin 0,3 IU / kg body weight three times a day 30 minutes before meal; for a diabetic coma — in a vein in the form of a bolus 10 IU in 100 ml of isotonic sodium chloride solution every hour under the control of plasma glucose level.
5. Dextrose — 40% solution in 20 ml ampoules. TD: in a vein in the form of a bolus 8,0—10,0.
6. Glibenclamide (Glibenclamide) — tablets 0,00175 and 0,0035. TD: orally 0,00175—0,0035 two times a day 10 minutes before meals.
7. Metformin (Metformin) — tablets 0,5 and 1,0. TD: orally 0,5—1,0 one—two times a day with meals.
8. Prednisolonum (Prednisolonum) — tablets 0,005; 2,5% solution in ampoules of 1 ml; 0,5% ointment in tubes of 10,0 and 20,0; 0,5% solution in 5 ml vials (eye drops). TD: orally 0,005—0,02 once a day in the morning during a meal; in a vein dropwise 0,05—0,15 in 500 ml of 5% glucose solution.

QUESTIONS AND TASKS FOR SELF-CONTROL

Task 1. Pharmacotherapeutic questions. Write the prescriptions, justifying the choice of drug.

1. Drug for the prevention of endemic goiter.
2. Drug for the treatment of endemic goiter.
3. Drug for hypothyroidism.
4. Drug for replacement therapy after removal of the thyroid gland.
5. Drug for the treatment of thyrotoxicosis.
6. Drug for type 1 diabetes mellitus.
7. Drug for the treatment of type 2 diabetes mellitus.
8. Drug for diabetic coma.
9. Drug for hypoglycemic coma.
10. Drug stimulates the secretion of insulin, for the treatment of diabetes mellitus.
11. Drug for overcoming resistance to insulin in diabetes mellitus.
12. Drug for the treatment of metabolic syndrome.
13. Drug for the treatment of obesity.
14. Drug for the treatment of rheumatoid arthritis.
15. Drug for the treatment of glomerulonephritis.
16. Drug for emergency aid in case of shock.
17. Drug for the treatment of allergic conjunctivitis.
18. Drug for the treatment of allergic dermatitis.

Task 2. After studying the theoretical material, answer the following questions:

1. What medicines are used to treat hypothyroid and euthyroid goiter? What is the difference between the mechanisms of action of iodine-containing drugs and hormone replacement therapy agents? Why is a rational combination of thyroid hormone drugs with potassium iodide considered?
2. In which cases is it preferable to prescribe levothyroxine sodium, and in which cases — liothyronine? What enzyme dysfunction makes the administration of levothyroxine sodium in case of hypothyroidism ineffective?
3. How do insulin receptors function? How does their function change with different types of diabetes?

4. Which human genetically engineered insulin preparations are recommended for patients for a long-term therapy of diabetes mellitus, and which for the treatment of diabetic coma? Why is the knowledge of pharmacokinetics of insulin preparations important for a doctor?
5. What medications for the treatment of type 2 diabetes mellitus have lipid-lowering, anorexigenic and angioprotective effects? What is the significance of these effects in diabetes? Why?
6. It is known that mineralocorticoids and glucocorticoids interact with the same corticosteroid receptor. Concentration of glucocorticoid in blood is 400 — 1 600 times higher than mineralocorticoid concentration. Specify the mechanisms of implementation of mineralocorticoids pharmacological effects in sensitive tissues.
7. What is the difference between the effects of glucocorticoids in physiological and pharmacological concentrations?
8. Describe the permissive effect of glucocorticoids.
9. Why are drugs of glucocorticoids administered for the treatment of shock? Consider the mechanisms of glucocorticoids anti-shock action.
10. What hormonal agents have anti-inflammatory action? Explain the mechanisms of this effect. In which diseases is the anti-inflammatory effect of hormonal drugs used?
11. How to correctly prescribe glucocorticoids, taking into account the daily biorhythms of the adrenal cortex and sensitivity of receptors functioning? Indicate the benefits of such administration.

Task 3.

a. Match each drug with the appropriate description

A. Levothyroxine	1. This drug is targeted to thyroid deiodinase
B. Potassium iodide	2. This drug causes thyroid cell necrosis
C. Radioactive iodine	3. This drug acts mainly by inhibiting hormone release from the thyroid gland

b. Match each drug with the appropriate description

A. Dexamethasone	1. A glucocorticoid devoid of salt-retailing activity
B. Fludrocortisone	2. A mineralocorticoid antagonist

C. Mifepristone	3. A mineralocorticoid used to treat adrenal insufficiency
D. Spironolactone	4. This drug blocks the cytoplasmic glucocorticoid receptors

Task 4. Topics for reports.

1. The history of insulin and glucocorticoids discovery.
2. Combination therapy of oral hypoglycemic agents in patients with type 2 diabetes mellitus.
3. Insulin: an anabolic hormone.
4. Localization, structure and function of estrogen receptors.
5. Modern methods of emergency contraception.
6. Contraceptives and menopausal hormone therapy (MHT).
7. Anabolic agents:
   - with steroid structure — nandrolone;
   - with non-steroidal structure — inosine, levocarnitine, orotic acid.

QUESTIONS AND TASKS IN CLASS

Task 1. Analyze the tasks that reflect the relations of pharmacokinetics with the physicochemical properties of drugs (the collection of graphic tasks).

Task 2. Analyze case tasks.

1. A 52-year-old alcoholic man was brought unconscious to the emergency department. On admission, the patient was sweating, his body temperature was 34,7°C (94,5°F), and his cardiac pulse was 135 bpm. Shortly after admission, the patient developed a tonic-clonic seizure. His wife reported the man was a diabetic on insulin therapy. What disorder most likely caused the patients syndrome? Prescribe treatment for this patient.
2. A 17-year-old girl was admitted to the emergency department following a motor vehicle accident. She was obtunded and responded only to pain. Medical history obtained from her mother was unremarkable. Physical examination showed a patient with contusions on her face and arms but no signs of cranial trauma. Vital signs were temperature 36,1°C (97°F), blood pressure 105/70 mm Hg, pulse 112 bpm, respirations 22/min. Pertinent serum values were bicarbonate 6 mEq/L (normal 22−28

mEq/L), glucose 847 mg/dL (normal 70−110 mg/dL), creatinine 1,1 mg/dL (normal 0,6−1,2 mg/dL). Urinalysis showed the following: specific gravity 1,036, glucose 4+, ketones 4+. Make the diagnose and prescribe appropriate emergency treatment.

3. A 40-year-old woman was admitted to the hospital complaining of nausea and vomiting, weight loss, fatigue, and weakness. She also reported a persistent feeling of faintness on standing and decreased tolerance to cold. Physical examination showed a patient in moderate distress with increased pigmentation around the nipples, absence of axillary and pubic hair, and diffuse tanning of exposed portions of the body. Significant serum levels on admission were Na^+ 125 mEq/L (normal 136−145 mEq/L), K^+ 6,2 mEq/L (normal 3,5−5,0 mEq/L), fasting blood glucose 42 mg/dL (normal 70−110 mg/dL). The patient's signs and symptoms indicate that she was suffering from Addison disease. Explain the mechanism of symptoms and prescribe appropriate treatment for this patient.
4. A 55-year-old woman was admitted to the hospital because of increasing muscle weakness, anxiety, and loss of emotional control. The patient was diagnosed with polymyositis 5 months ago and have been receiving an appropriate therapy since then. The physical examination showed a patient with face and trunk obesity and thin and easily bruised skin. Vital signs were blood pressure 168/98 mm Hg, pulse 84 bpm, respirations 18/min. A bone X-ray revealed diffuse osteoporosis. What drug most likely caused the patients signs and symptoms?
5. A 29-year-old woman complained to her physician of fatigue, constipation, and menstrual irregularities for the past 2 months. Physical examination showed delayed deep tendon reflexes, mild bradycardia, and a nontender, nodular thyroid goiter. A blood analysis showed thyroid peroxidase antibodies of 120 IU/L (normal < 0,8 IU/L). Make a diagnosis, explain the mechanism of symptoms and prescribe treatment.

Task 3. Answer the test questions (in the computer lab).

Lesson 9
Drugs affecting functions of adrenergic synapses

Learning objectives are to study the classifications, mechanisms of action, pharmacokinetics, indications for the use, contraindications and side effects of drugs affecting functions of adrenergic synapses; to study and practice prescription writing.

QUESTIONS FOR PREPARATION FOR THE LESSON

1. Mechanisms of synaptic transmission: the structure of synapses, chemical structure, synthesis, storage, isolation and inactivation of neurotransmitters, interaction of neurotransmitters with receptors, regulation of synapse functions.
2. The structure of the peripheral nervous system: structure of sympathetic and parasympathetic nerves. Adrenergic and cholinergic fibers.
3. Adrenergic synapses: localization, structure, functions.
4. Chemical structure, synthesis, secretion and ways of noradrenaline inactivation. Metabolism and functions of adrenaline.
5. Adrenergic receptors: types (α,β, presynaptic, postsynaptic, extrasynaptic), localization, significance.
6. Adrenomimetics: mechanism of action, classification
   a. direct adrenomimetics
      - α, β-adrenomimetics — epinephrine;
      - α-adrenomimetics — norepinephrine, phenylephrine, xylometazolin, naphazoline;
      - β—adrenomimetics — dobutamine;
      - selective β_2-adrenomimetics:
        short-acting — salbutamol (albuterol), fenoterol;
        long-acting — salmeterol, formoterol, vilanterol, indacaterol, olodaterol;

   b. adrenomimetic with indirect action — ephedrine.
7. Local action of epinephrine, phenylephrine, xylometazoline, naphazoline, ephedrine on the eye, skin vessels and mucous membranes.

8. Resorptive effect of adrenomimetics on the central nervous system (CNS), cardiovascular system, organs with smooth muscles and metabolic processes. Pharmacokinetics.
9. Adverse effects of adrenomimetics, contraindications to use.
10. Dopamine: dependence of pharmacological effects on dose, use, side effects and contraindications to use.
11. α-Adrenoblockers: mechanisms of action, classification
    - α_1, α_2-adrenoblockers — nicergoline, propoxane;
    - selective α_1-adrenoblockers — prazosin, alfuzosin, doxazosin, tamsulosin, terazosin.
12. Effect of α-adrenoblockers on the cardiovascular system and organs with smooth muscles. Pharmacokinetics. Indications, side effects, contraindications to use.
13. β-Adrenoblockers: mechanisms of action, classification.
    - nonselective β-adrenoblockers — propranolol, timolol;
    - cardioselective β_1-adrenoblockers — atenolol, bisoprolol, metoprolol, esmolol;
    - β_1-adrenoblockers with vasodilator action — nebivolol.
14. α, β-adrenoblockers — carvedilol.
15. Effect of β-adrenoblockers and α, β-adrenoblockers on the central nervous system, cardiovascular system and metabolic processes.
16. Features of cardioselective β_1-adrenoblockers, β-adrenoblockers with vasodilator action, α,β-adrenoblockers.
17. Pharmacokinetics, use, side effects, contraindications of β-adrenoblockers.

PRESCRIPTIONS

1. Epinephrinum — 0,1% solution in ampoules of 1 ml and vials of 10 ml. TD: into the vein 0,0003—0,001 in 20 ml of isotonic sodium chloride solution; moisten the tampon and apply to the bleeding site.
2. Norepinephrinum — 0,2% solution in ampoules of 1 ml. TD: into the vein 0,004—0,008 in 1000 ml of 5% glucose solution dropwise.

3. Phenylephrinum — 1% solution in ampoules of 1 ml; 2,5% solution in vials of 1 ml (eye drops); 0,125% solution in vials of 10 ml (nasal drops). TD: into the vein 0,001—0,003 in 500 ml of 5% glucose solution dropwise; subcutaneously and into the muscles 0,003—0,005; 1-2 drops to each eye one – two times a day; 1 drop in each nasal meatus two times a day.
4. Fenoterol — tablets by 0,005; aerosol of 10 ml (200 inhalations of 0,0001). TD: orally 0,005 every 3-4 hours (as tocolythic); inhalation 1-2 doses three—four times a day.
5. Metoprolol — tablets by 0,05 — 0,1; 0,1% solution in ampoules of 5 ml. TD: orally 0,05 — 0,1 one or two times a day; into the vein 0,002 — 0,005 in 10 — 20 ml of 5% glucose solution slowly.

QUESTIONS AND TASKS FOR SELF-CONTROL

Task 1. Pharmacotherapeutic questions. Write the prescriptions, justifying the choice of drug.

1. Drug for cardiac arrest treatment.
2. Drug for nasal bleeding treatment.
3. Drug for hypotension treatment.
4. Drug for treatment of hypotension on the background of poisoning.
5. Drug for treatment of hypotension on the background of total anaesthesia.
6. Drug which is added to local anaesthetic.
7. Drug for anaphylaxis treatment.
8. Drug for conjunctivitis treatment.
9. Drug for rhinitis treatment.
10. Drug for asthma treatment.
11. Drug for premature labor prevention.
12. Drug for angina treatment.
13. Drug for hypertension treatment.
14. Drug for dysrhythmias treatment.
15. Drug for myocardial infarction treatment.
16. Adrenoceptor antagonist for thyrotoxicosis treatment.
17. Drug decreasing renin release.
18. Drug for supraventricular dysrhythmias treatment.

Task 2. After studying the theoretical material, answer the following questions:

1. Why are adrenomimetics used in ophthalmology? Explain their mechanisms.
2. What undesirable effect does norepinephrine cause when administered under the skin? What medications should be used urgently to prevent this side effect?
3. Why is adrenomimetic used to stop cardiovascular collapse during anesthesia?
4. Why is dobutamine not used for the course treatment of heart failure, despite its pronounced cardiac stimulating effect?
5. What is the difference between salbutamol and salmeterol?
6. What β-adrenergic blocker should be chosen for the treatment of arrhythmia in a patient suffering from liver cirrhosis — lipophilic propranolol or hydrophilic atenolol?
7. Why did a patient with angina, who had been taking propranolol for a long time, after the rapid discontinuation of propranolol, have a chest pain again?
8. Which pharmacological effects of nebivolol are due to the blockade of β-adrenoreceptors, and which of them are pleiotropic?

Task 3.

a. Match each drug with the appropriate description

A. Bisoprolol	1. The drug which is used to treat anaphylactic shock
B. Epinephrine	2. The drug of choice for cardiogenic shock
C. Dopamine	3. β-adrenergic drug which is used to treat asthma attack
D. Salbutamol	4. β-adrenergic drug which is used to prevent asthma attack
E. Salmeterol	5. The drug of choice for myocardial infarction

b. Match each drug with the appropriate description

A. Atenolol	1. This drug is a partial agonist at β_1 and β_2 receptors
B. Esmolol	2. This drug is a selective β1 antagonist frequently used for the chronic treatment of atrial fibrillation
C. Pindolol	3. This drug is a β-blocker that can also block potassium channels
D. Sotalol	4. This drug is frequently used in the treatment of prostatic hyperplasia
E. Tamsulosin	5. This drug is sometimes given in cardiovascular emergencies by intravenous infusion because of its extremely short half-life

Task 4. Topics for reports.

1. The mechanisms of antihypertensive action of beta-adrenergic blocking drugs.
2. The role of beta-blockers in treating cardiovascular disease: benefits, risks.
3. Beta-blockers in diabetes mellitus.
4. Performance-enhancing drugs (doping) — ephedrine, beta-agonists, beta-blockers.

QUESTIONS AND TASKS IN CLASS

Task 1. Analyze the tasks that reflect the mechanisms and features of adrenergic drugs action (the collection of graphic tasks).

Task 2. Analyze case tasks.

1. A 33-year-old man was brought to the emergency room after a car accident. Upon admission, the patient was lucid but completely paralyzed, with loss of all sensation and reflex activity below the thorax. Vital signs were blood pressure 80/40 mm Hg, heart rate 42 bpm, respirations 36/min. A preliminary diagnosis of spinal shock, due to spinal cord injury, was made, and an intravenous infusion of an appropriate drug was started. Which drug was most likely administered?
2. A 43-year-old woman was in the emergency department for the treatment of shock due to spinal trauma. Despite Fluid therapy, she

was still hypotensive (80/50 mm Hg) and tachycardic (125 bpm). An intravenous infusion of norepinephrine was started, and a few minutes later the blood pressure was 120/85 mm Hg, and the heart rate decreased to 85 bpm. Which of the actions best explains the drug-induced decrease of heart rate in this patient?

3. A 47-year-old man who had been suffering from diabetes for 10 years was admitted to the hospital following a myocardial infarction. He was discharged 10 days later with a postdischarge therapy that included atenolol. The patient was instructed to monitor his blood glucose level carefully for both hyper- and hypoglycemia after the drug was initiated. What is the reason for glucose monitoring during atenolol treatment?
4. A β-blocker propranolol was prescribed for hypertension in a female asthma patient. After about a week of treatment, the asthma attacks got worse, and the patient was asked to stop taking the β-blocker. Which of the β-blockers would you suggest as an alternative in this patient that is less likely to worsen her asthma and why?

Task 3. Answer the test questions (in the computer lab).

Lesson 10
Drugs affecting functions of cholinergic synapses

Learning objectives are to study classification, mechanism of action, pharmacokinetic, indications for the use, contraindications and side effects of drugs affecting functions of cholinergic synapses; to study and practice prescription writing.

QUESTIONS FOR PREPARATION FOR THE LESSON

1. Cholinergic synapses: localization, structure.
2. Chemical structure, synthesis, secretion and inactivation of acetylcholine.
3. Cholinergic receptors: types (muscarinic, nicotinic), localization, functional significance.
4. Cholinomimetics: origin, mechanisms of action, classification
   - M, N-cholinomimetics — acetylcholine, carbachol;
   - M-cholinomimetics — pilocarpine.
5. Inhibitors of cholinesterase: origin, mechanisms of action, classification
   - reversible:
     tertiary amines — physostigmine,
     quaternary amine — neostigmine, pyridostigmine;
   - selective reversible inhibitor of acetylcholinesterase of the brain — rivastigmine;
   - irreversible (organophosphate toxic agents) — ecothiophate.
6. Nature and mechanisms of action of cholinomimetics and cholinesterase inhibitors on the eye; its importance for ophthalmology.
7. Resorptive effect of cholinesterase inhibitors with reversible action: effect on the central nervous system, cardiovascular system, smooth muscle organs, glands, skeletal muscles. Pharmacokinetics. Use, side effects and contraindications.
8. Anticholinergic agents (M-cholinoblockers): origin, mechanisms of action, classification
   - M-cholinoblockers of plant origin — atropine, scopolamine (hyoscine), platyphyllin;

- synthetic M-cholinoblockers — tropicamide, ipratropium bromide, tiotropium bromide, oxybutynin.

9. Mechanisms of action of anticholinergic agents on the eye. Features of the action of atropine, platyphyllin and tropicamide. Indications and contraindications to the use of anticholinergic agents in ophthalmology.
10. Resorptive effect of anticholinergic agents: action on the central nervous system, cardiovascular system, organs with smooth muscles, glands. Pharmacokinetics. Application, side effects, contraindications to use.
11. Organophosphates and atropine poisonings: causes of intoxication, stages, pathogenesis, symptoms and treatment.
12. Cholinesterase reactivators: mechanisms and features of the action of trimedoxime bromide, pralidoxime.

PRESCRIPTIONS

1. Pilocarpinum — 1% solution in vials of 5 ml. TD: 1-2 drops to each eye two—four times a day; in acute glaucoma attack — 1-2 drops in the first hour every 15 minutes, in the second hour — 2 times.
2. Neostigmini methylsulfas — tablets by 0,015; 0,05% solution in ampoules of 1 ml. TD: orally 0,015; subcutaneously 0,0005 one—two times a day.
3. Atropinum — 0,1% solution in ampoules of 1 ml; 1% solution in vials of 5 ml. TD: subcutaneously, into the muscles 0,00025—0,0005 one—two times a day; 1-2 drops in the eye one—two times a day; in poisoning of organophosphate into the vein 0,002—0,003, then repeat injection into the vein or muscle fractionally to DD 0,03—0,05.
4. Tropicamide — 1% solution in vials of 10 ml. TD: 1-2 drops to each eye.
5. Platyphyllinum — tablets by 0,005; 0,2% solution in ampoules of 1 ml. TD: orally 0,005; subcutaneously 0,002—0,004 one—two times a day.
6. Tiotropii bromidum — powder for inhalation in capsules by 0,000018. TD: inhalation 0,000018 once a day.
7. Trimedoxime bromide — 15% solution in ampoules of 1 ml. TD: into the vein and muscles 0,15 every 1—2 hours to DD 0,45 — 0,6.

QUESTIONS AND TASKS FOR SELF-CONTROL

Task 1. Pharmacotherapeutic questions. Write the prescriptions, justifying the choice of drugs.

1. Drug for the course treatment of glaucoma.
2. Drug for arresting an attack of acute glaucoma.
3. Drug for reducing the consequences of poliomyelitis.
4. Drug for myasthenia gravis.
5. Drug for intestinal atony.
6. Drug for the stimulation of labor.
7. Drug which paralyzes accommodation, for choosing eyeglasses.
8. Drug for the treatment of iritis.
9. Drug for examining the fundus oculi.
10. Drug that prevents reflex heart failure during anesthesia.
11. Drug that reduces salivation during anesthesia.
12. Drug for the treatment acute renal colic.
13. Drug for the treatment of chronic obstructive bronchitis.
14. Antagonist in Amanita poisoning.
15. Physiological antagonist in organophosphates poisoning.
16. Reactivator of cholinesterase during organophosphates poisoning.
17. Drug that eliminates bronchospasm in case of organophosphates poisoning.
18. Antagonist in atropine poisoning.

Task 2. After studying the theoretical material, answer the following questions:

1. It is known that M_3-cholinoceptors are localized in the smooth muscles of arteries and organs. Why do cholinomimetics, activating M3-cholinergic receptors, cause dilation of arteries, but increase the tone of organs with smooth muscles?
2. Name the toxic substances of the mushrooms. What is the difference between their toxicokinetics and effects on the body?
3. Name non-anticholinesterase mechanisms of action of cholinesterase inhibitors.
4. What agents are used to treat myasthenia gravis? Which forms of myasthenia are they effective in? Why atropine is administered simultaneously with these drugs?

5. Which M-cholinoblockers are used in ophthalmology for diagnostic purposes, and which — for medical?
6. Which M-cholinoblockers with selective action are used in peptic ulcer disease, chronic obstructive pulmonary disease, urinary incontinence? What mechanisms underpin the selective action of these drugs?

Task 3.

a. Match each drug with the appropriate description

A. Muscarine	1. Inhibition of cholinesterases by this drug is very short (2−10 minutes)
B. Carbachol	2. This drug can inhibit cholinesterases equally well in the periphery as in the central nervous system
C. Neostigmine	3. This compound can be absorbed effectively through the intact skin
D. Bethanechol	4. This drug is able to regenerate cholinesterases blocked by organophosphates
E. Edrophonium	5. This drug can inhibit cholinesterases and directly activate Nm cholinergic receptors

b. Match each drug with the appropriate description

A. Ipratropium	1. The drug which is used as an antispasmodic agent to relax the GI tract
B. Atropine	2. One of the most effective anti-motion sickness drugs available.
C. Pilocarpine	3. The drug which is used in the acute management of bronchospasm in asthma
D. Scopolamine	4. The drug of choice for emergency lowering of intraocular pressure of both open-angle and angle-closure glaucoma

Task 4. Topics for reports.

1. History of research on nicotinic and muscarinic cholinergic receptors.
2. Edrophonium: the drug which is used as a test for myasthenia gravis.
3. Bethanechol: mechanism of action, use.

4. Organophosphates as an insecticide and pesticides.
5. Glaucoma: types, causes, and symptoms.
6. Myasthenia gravis: causes, symptoms and diagnosis.
7. Calabar beans: Pre-history's lie detectors.

QUESTIONS AND TASKS IN CLASS

Task 1. Analyze the tasks that reflect the mechanisms and features of the action of cholinergic agents (the collection of graphic tasks).

Task 2. Analyze case tasks.

1. A 71-year-old man suffering from myasthenia gravis was admitted to the hospital for evaluation. His therapy included neostigmine, three tablets daily. It was found that the patient had a slow heart rate (46 bpm), which the physician thought was related to neostigmine therapy. Which molecular mechanism most likely mediated this adverse effect of the drug? What is a preventive measure for this case?
2. A 49-year-old farmer came to the emergency department complaining of blurred vision, nausea, and painful muscle contractions in his legs. He said the symptoms started soon after coming in from his soybean field. An agent from which drug class most likely caused the patients symptoms? What drug should be administered to this patient to relief the symptoms of overdose?
3. A 41-year-old man was brought to the emergency department because of severe vomiting and diarrhea that started about 1 hour after a meal. The patient showed profuse salivation, lacrimation, and wheezing. His skin was moist, and his pupils were miotic. Skeletal muscle movements were normal. Blood pressure was 80/50 mm Hg, pulse 46 bpm. Which of the agents was the most likely cause of this patient’s poisoning?
4. A 3-year-old boy was rushed to the emergency department with mental confusion, restlessness, incoherence, and hallucinatory behavior. His mother stated that the child had eaten several black berries of a wild plant while playing with friends in the woods. Physical examination revealed mydriasis; dry, hot, and scarlet skin; and a distended abdomen with no bowel sounds. Vital signs were temperature 104.5°F (40.3°C), heart rate 145 bpm, blood pressure 105/60 mm Hg. Which of the agents was the most likely cause of this patient’s poisoning? Prescribe treatment in this case.

5. A 55-year-old woman was admitted to the hospital with shallow breathing, wheezing, profuse rhinorrhea, lacrimation, ocular pain, and diminished vision. She reported that the symptoms started when she was in her garden spraying flowers with an insecticide. Which of the agents was the most likely cause of this patient's poisoning? Which drug would be appropriate to treat this disorder?
6. Atropine was given intramuscularly to several dogs during a lab experiment. One hour later each dog received an intramuscular injection of an autonomic drug, and the effects of that drug were recorded. Which of the following expected drug-induced effects was most likely best antagonized by atropine pretreatment?

   a. Physostigmine-induced sweating
   b. Epinephrine-induced hypertension
   c. Nicotine-induced skin vasoconstriction
   d. Prazosin-induced reflex tachycardia

Task 3. Answer the test questions (in the computer lab).

Lesson 11
Drugs affecting function of cholinergic synapses (n-cholinomimetics, ganglionic blockers, neuromuscular blockers).
Drugs affecting afferent innervation (local anesthetics, astringents, adsorbents and irritating agents)

Learning objectives are to study the classifications, mechanisms of action, pharmacokinetic, indications for the use and contraindications, side effects of n-cholinomimetics, ganglionic blockers, neuromuscular blockers and drugs affecting afferent innervation; acute and chronic cocaine poisoning; harmful effects of smoking; to study and practice prescription writing.

QUESTIONS FOR PREPARATION FOR THE LESSON

1. Cholinergic synapses: localization, structure. Localization and functions of N-cholinergic receptors.
2. N-cholinomimetics (ganglionic stimulants): the origin, effects, medical significance and use.
3. Toxic effect of nicotine. Harmful effects of smoking.
4. Ganglion-blocking agents: mechanisms and localization of action, effects of blockade of sympathetic and parasympathetic ganglia.
5. Features of the action, use, side effects and contraindications to the use of hexamethonium.
6. Neuromuscular-blocking agents: mechanisms and localization of the action, classification (non-depolarizing, depolarizing).
7. Non-depolarizing neuromuscular blockers (curare-like drugs, pahicurare): mechanisms and features of the action, synergists and antagonists, classification
   - long-acting — tubocurarine, pancuronium, pipecuronium;
   - medium duration of action — atracurium, cisatracurium, vecuronium;
   - short-acting — mivacurium.
8. Depolarizing neuromuscular blockers (leptokurare): mechanisms and features of the action, synergists — suxamethonium iodide or chloride.
9. Pharmacokinetics of neuromuscular blockers. Uses.

10. Side effects of neuromuscular blockers, contraindications to the use. Drugs for non-depolarizing neuromuscular blockers overdose — neostigmine methylsulfate, galantamine.
11. Botulinum neurotoxin type A: mechanisms and features of action.
12. Local anesthetics: history of use, requirements for local anesthetics, classification
    - esters — procaine, benzocaine, tetracaine;
    - substituted amides — lidocaine, articaine, bupivacaine, mepivacaine, ropivacaine, trimecaine;
    - drug combinations — articaine + epinephrine, bupivacaine + epinephrine.
13. Mechanism of action of local anesthetics. Pharmacokinetics.
14. Types of local anesthesia. Drugs of choice for different types of local anesthesia.
15. Resorptive action of local anesthetics on the central nervous system and cardiovascular system. Side effects of local anesthetics.
16. Acute cocaine poisoning: pathogenesis, stages, symptoms, treatment.
17. Chronic cocaine poisoning (cocainism): mechanism of addiction, prevention measures against drug addiction.
18. Astringents: mechanisms and features of action, indications for use
    - metal salts — bismuth chelate, sucralfate, calcium chloride and gluconate, copper sulfate, zinc sulfate;
19. Absorbents: mechanism of action; use of activated charcoal, talcum powder.
20. Irritating drugs: mechanisms of action, indications for use. Vanilloid receptors (TRPV).
21. Features of the action and use of irritating agents:
    a) drugs of plant origin;
        - drugs of levomenthol — levomenthol + benzocaine + procaine;
        - drugs of racementhol — eucalyptus oil + racementhol;
        - mustard plaster;
        - chili pepper extract (pepper plaster);
    b) synthetic products — ammonia (hartshorn — aqueous ammonia solution).

PRESCRIPTIONS

1. Atracurium besilate — 1% solution in ampoules of 5 ml. TD: into the vein 0,3—0,6 mg/kg.
2. Lidocainum — 2 and 4% solution in vials of 5 ml (eye drops); 1 and 2% solution in ampoules of 10 ml; TTS (patches) 0.7.

   For surface anesthesia — 2 drops into the eye; apply 1 patch once a day for 12 hours;

   For conduction and epidural anesthesia — 10—30 ml of 1—2% solution;

   For infiltration anesthesia — 200—600 ml of 0,5% solution (solvent is isotonic sodium chloride solution) with addition of 1 drop (no more than 1 ml) of 0,1% solution of epinephrine to 20 ml of prepared solution.
3. Bismuthi trikalii dicitras — tablets by 0,12. TD: orally 0,12—0,24 three times a day 30 minutes before a meal and bedtime.
4. Calcii chloridum — 5—10% solution for oral use; 10% solution in ampoules of 5 and 10 ml. TD: orally 0,5 — 1,0 three times a day 30 minutes before a meal, drink a glass of water; into the vein 0,5—1,0 slowly.
5. Carbo activatus — undivided powder; tablets by 0,25 and 0,5. TD: on the lavage of the stomach 20,0 — 30,0 dissolve in 1 liter of water; orally 0,5 three times a day after a meal drink a ½ glass of water.
6. Solutio Ammonii caustici — vials, ampoules of 1 ml. TD: for inhalation 2—3 drops; lotion.
7. Repeat: Neostigmini methylsulfas.

QUESTIONS AND TASKS FOR SELF-CONTROL

Task 1. Pharmacotherapeutic questions. Write the prescriptions, justifying the choice of drugs.

1. Drug for potentiated anesthesia.
2. Drug to facilitate tracheal intubation during anaesthesia.
3. Drug for the relief of severe seizures.
4. Drug for recurarization.
5. Physiological antagonist for the treatment of non-depolarizing neuromuscular blocking agents overdose.

6. Drug for anesthesia of the cornea.
7. Local anesthetic for the treatment of low back pain.
8. Drug for regional anesthesia.
9. Drug for infiltration anesthesia.
10. Drug for epidural anesthesia.
11. Drug for the treatment of peptic ulcer disease.
12. Drug for the treatment hyperacidity gastritis.
13. Drug for the treatment of allergic diseases.
14. Drug to stop bleeding.
15. Physical antagonist in poisoning.
16. Drug for food poisoning.
17. Drug for fainting (syncope).
18. Drug for insect bites.

Task 2. After studying the theoretical material, answer the following questions:

1. Name the chemical ingredients of tobacco and explain the mechanisms of its toxic action.
2. What is orthostatic hypotension (or postural hypotension)? What synaptotropic drugs cause orthostatic hypotension? What rules should be followed when synaptotropic drugs, which cause orthostatic hypotension, are administered?
3. Under what conditions does the action of local anesthetics increase and prolong? In what surgical procedures are adrenomimetics not added to local anesthetics?
4. Why are local anesthetics of substituted amides preferred in modern anesthesiology?
5. How do cocaine, procaine, tetracaine and lidocaine affect the CNS?
6. Why is bupivacaine contraindicated in patients with cardiovascular disease?
7. What are the features of astrigents action? In what diseases are astringents used?
8. Consider the mechanisms of desensitizing and hemostatic effects of calcium chloride. Why is this drug unacceptable to enter under the skin and into the muscles?

Task 3.

a. Match each drug with the appropriate description.

A. Tubocurarine	1. An antagonist at Nn-acetylcholine receptors in autonomic ganglia
B. Succinylcholine	2. An agonist at Nm-acetylcholine receptors
C. Vecuronium	3. A drug which depolarizes autonomic ganglia, resulting first in stimulation and then in paralysis of all ganglia
D. Botulinum toxin	4. The amino steroid drug
E. Nicotine	5. A protein produced by the anaerobic bacillus *Clostridium botulinum*

b. Match each local anaesthetic with the appropriate description.

A. Lidocaine	1. A local anaesthetic of very low solubility, which is used as a dry powder to dress painful skin ulcers, or as throat lozenges
B. Cocaine	2. A local anaesthetic which produces euphoria
C. Benzocaine	3. A local anaesthetic which has a particularly long duration of action
D. Bupivacaine	4. A local anaesthetic suitable for surface application

Task 4. Topics for reports.

1. The history of discovery and use of neuromuscular blocking agents.
2. The positive and negative effects of nicotine.
3. Botulinum neurotoxin type A: uses in cosmetic and neurology.
4. The history of cocaine in medicine and its importance to the discovery of the different forms of anaesthesia.
5. Other drugs that affect sodium channels: tetrodotoxin and saxitoxin.

QUESTIONS AND TASKS IN CLASS

Task 1. Analyze the tasks that reflect the mechanisms and features of the action of cholinergic agents (the collection of graphic tasks).

Task 2. Analyze case tasks.

1. A 43-year-old man underwent an emergency minor arm repair procedure after a car accident. A standard dose of lidocaine was administered near the brachial plexus for peripheral nerve block. Fifteen minutes later, the anesthesia was still incomplete, and another dose of lidocaine was administered. Which adverse effect would most likely occur after the administration?
2. A 55-year-old diabetic man was admitted to the emergency department with fever 38,6°C (101,5°F,) and abdominal pain. Physical examination disclosed a superficial abscess on the right side of the abdomen. A local anesthetic was injected around the abscess in preparation for surgery. Which of the following tissue properties most likely account for the slower onset of local anesthetic action in infected tissues?
   a. High levels of drug-metabolizing enzymes
   b. Low vessel density
   c. Higher extracellular K^+
   d. High levels of para-aminobenzoic acid
   e. Lower extracelluar pH.
3. A 74-year-old man underwent abdominal surgery to remove a colon carcinoma. The patient had severely impaired hepatic and renal function, and the anesthesiologist decided to supplement general anesthesia with a muscle relaxant that is inactivated primarily by a form of spontaneous breakdown. Which drug was most likely given?
4. A 48-year-old woman underwent heart surgery for placement of an artificial valve. Anesthesia was induced by thiopental, and a muscle relaxant was then given intravenously to facilitate intubations. Soon after the administration of the drug, the patient exhibited transient muscle fasciculation that progressed to generalized paralysis within 1 minute. Which muscle relaxant was most likely given?
5. A 64-year-old woman complained to her physician of involuntary blinking and closing of the eyes. She noticed that the eyelid spasm was made worse by fatigue and anxiety. Further exams led to the diagnosis of benign essential blepharospasm, and a treatment with local injections of botulinum toxin was prescribed. Which adverse effect was most likely to occur in this patient?

6. A 28-year-old man was brought to the psychiatric clinic by the police after he attempted to assault a woman in the street. The man presented with elevated mood, rapid speech, muscle twitching, and dilated pupils. He kept on scratching himself repeatedly because he stated that “bugs are crawling under my skin.” Vital signs were blood pressure 170/105, heart rate 120 bpm, respirations 20/min. After a short time, stereotyped behavior developed accompanied by paranoid delusions, but the man remained oriented and alert. Which drug most likely caused the patients syndrome?

Task 3. Answer the test questions (in the computer lab).

Lesson 12
Final class about drugs affecting autonomic nervous system

Learning objectives are to check skills in prescription writing; to check and fix knowledge about the mechanisms of action, classifications, pharmacokinetics, use, side effects of agents, drug poisoning in the frame of the topics which have been studied.

QUESTIONS FOR PREPARATION FOR THE FINAL LESSON

1. Types of peripheral nerves. Types of neurotransmitters of the peripheral nervous system.
2. Localization, structure and function of adrenergic synapses. Classification of drugs affecting function of adrenergic synapses.
3. Adrenoreceptors: types, localization, functions.
4. Adrenomimetics: mechanisms of action, classification.
5. Epinephrine: mechanisms and features of action, use, side effects, contraindications to use.
6. α-Adrenomimetics: mechanism of action, use, side effects, contraindications to use.
7. β-Adrenomimetics: classification, mechanism of action, use, side effects, contraindications to use.
8. Ephedrine: mechanism of action, use, side effects, contraindications to use.
9. α-Adrenergic blockers: classification, mechanism of action, use, side effects, contraindications to use.
10. β-Adrenergic blockers: classification; mechanism of action and use of antianginal and antiarrhythmic effects.
11. β-Adrenergic blockers: mechanism of action and use of hypotensive action; side effects, contraindications.
12. Mechanisms of the action and use of cardioselective β_1-blockers, β-blockers with vasodilator action, α,β-blockers.

13. Localization, structure and function of cholinergic synapses. Classification of drugs affecting function of cholinergic synapses.
14. Cholinergic receptors: types, localization, functions.
15. Cholinomimetics: classification, mechanisms and features of action, application, side effects, contraindications to use.
16. Cholinesterase inhibitors: classification, mechanisms of action.
17. Indications, side effects and contraindications to the use of cholinesterase inhibitors.
18. Muscarinic antagonists: classification; mechanism of action on the eye, use in ophthalmology.
19. Muscarinic antagonists: resorptive effect, use, side effects, contraindications to use.
20. Non-depolarizing muscle relaxants: classification, mechanisms and features of action, synergists and antagonists, indications, side effects.
21. Depolarizing muscle relaxants: mechanisms of action, synergists, indications, side effects.
22. Local anesthetics: classification, mechanisms of action.
23. Types of local anesthesia: characteristic, medical value, choice of local anesthetics, resorptive action, side effects and contraindications.
24. Astringents and adsorbents: mechanism of action, drugs, use.
25. Acute cocaine poisoning: stages, pathogenesis, symptoms, treatment.
26. Acute amanita poisoning: stages, pathogenesis, symptoms, treatment.
27. Acute atropine poisoning: stages, pathogenesis, symptoms, treatment.
28. Acute organophosphate poisoning: stages, pathogenesis, symptoms, treatment.

PRESCRIPTIONS

Prescribe: epinephrine, norepinephrine, phenylephrine, fenoterol, metoprolol, pilocarpine, neostigmine methylsulfate, atropine, platyphyllin, tiotropium bromide, trimedoxime bromide, atracurium besilate, lidocaine, bismuthi trikalii dicitras, calcium chloride, activated charcoal.

PHARMACOTHERAPEUTIC QUESTIONS

1. Drug for stopping vascular collapse.
2. Drug for conjunctivitis.
3. Drug for the treatment of bronchial asthma.
4. Drug for the treatment of chronic obstructive bronchitis.
5. Drug for sinus tachycardia.
6. Drug for the treatment of angina.
7. Drug for the treatment of hypertension.
8. Drug for the treatment of glaucoma.
9. Drug for intestinal atony.
10. Drug for myasthenia.
11. Drug for the treatment of iritis.
12. Drug for the treatment of acute renal colic.
13. Drug for intestinal spasm.
14. Drug for potentiated anesthesia.
15. Drug for corneal anesthesia.
16. Drug for infiltration anesthesia.
17. Drug for the treatment of peptic ulcer disease.
18. Drug to stop bleeding.

CONTROL TASK

Answer the questions, reflecting the mechanisms and features of the action of drugs affecting autonomic nervous system (a computer-based test).

Lesson 13
Drugs affecting functions of the respiratory system and myometrium

Learning objectives are to study the classification, mechanisms of action, pharmacokinetics, use, side effects and contraindications to the use of drugs affecting the respiratory center; antitussive, expectorants; drugs for the treatment of bronchial obstruction syndromes and pulmonary edema; drugs affecting myometrium; to study and practice prescription writing.

QUESTIONS FOR PREPARATION FOR THE LESSON

1. Analeptics (central respiratory stimulants): classification, mechanism of action, use, side effects, contraindications to the use
   - analeptics with direct tonic action — caffeine;
   - analeptic with reflex action (n-cholinomimetics) — cytisine;
   - analeptic with direct and reflex action — camphor.
2. Antitussive agents: classification, origin, mechanism of action, pharmacokinetics, use, routes of administration, side effects, contraindications for use
   a) central-acting
      - opioid — codeine;
      - non-opioid — dextromethorphan;
   b) peripheral-acting — benzonatate.
3. Expectorants: classification, origin, mechanism of action, use, routes of administration, side effects, contraindications to use
   - with reflex action — roots of althea, thermopsis, terpin hydrate;
   - with resorptive action —creeping thyme herb;
   - mucolytics — ambroxol, bromhexine, acetylcysteine, sodium hydrogen carbonate.
4. Rational combinations of antitussive and expectorants: codeine + terpin hydrate, codeine + sodium bicarbonate + licorice roots + thermopsis*, creeping thyme herb extract + potassium bromide.
5. Bronchodilators: classification, mechanism of action, pharmacokinetics, drug of choice for bronchial asthma and other bronchial obstructive syndromes, side effects, contraindications to the use

- β_2-adrenomimetics
  short-acting — salbutamol (albuterol), fenoterol;
  long-acting — salmeterol, formoterol, vilanterol, indacaterol, olodaterol;
- adrenomimetics with indirect action — ephedrine;
- M-cholinoblockers — ipratropium bromide, tiotropium bromide, aclidinium bromide;
- myotropic antispasmodics — theophylline, aminophylline.

6. Drugs with anti-inflammatory and anti-allergic action for basic therapy of bronchial asthma: mechanism of action, pharmacokinetics, use, side effects, contraindications to the use
   a) glucocorticoids
      - for inhalation — beclomethasone, budesonid, fluticasone;
      - with resorptive action — prednisolone, dexamethasone;
   b) leukotriene receptors antagonists — montelukast;
   c) monoclonal anti-IgE antibody— omalizumab.
7. Combined drugs for the treatment of bronchial asthma — fenoterol + ipratropium bromide, formoterol + budesonide, salmeterol + fluticasone, vilanterol + umeclidinium bromide, vilanterol + fluticasone.
8. Drugs used for pulmonary edema: mechanism of action, drug of choice for pulmonary edema with different etiologies, routes of administration
   - glucocorticoids — prednisolone, hydrocortisone;
   - opioid analgesics — morphine;
   - vasodilators with myotropic action — nitroglycerin in the vein, sodium nitroprusside;
   - diuretics — furosemide;
   - cardiotonic drugs — dobutamine, levosimendan.
9. Neural and humoral controlling mechanisms of the tone and contractile function of the uterus.
10. Drugs affecting the myometrium: classification, origin, mechanisms of action, indications, contraindications for use
    - drugs that increase the contractile function of the myometrium — oxytocin, dinoprost (prostaglandin $F_{2\alpha}$), dinoprostone (prostaglandin E_2);
    - drugs that increase myometrium tone (uterotonic drugs) — ergometrine, ergotamine;

- drugs that decrease the contractile function of the myometrium (tocolytics) — fenoterol, sodium oxybutyrate, magnesium sulfate;
- drugs that reduce the tone of the cervix — atropine, dinoprost, dinoprostone.

PRESCRIPTIONS

1. Codeinum at 0,008 + Terpinum hydratum at 0,25. TD: orally 1 tablet two—three times a day.
2. Prenoxdiazine — tablets at 0,1. TD: orally 0,1 three—four times a day, without chewing.
3. Butamirate — coated tablets at 0,2; 0,08% syrup in bottle of 200 ml. TD: orally 0,04 three times a day, children under 12 years 0,004—0,012 three times a day.
4. Bromhexinum — tablets at 0,008. TD: orally 0,008—0,016 three—four times a day.
5. Aminophyllinum — tablets at 0,15; 2,4% solution in ampoules at 10 ml. TD: orally 0,15 one—three times a day; into the vein 0,12—0,24 in 20 ml of isotonic sodium chloride solution.
6. Oxytocinum — ampoules at 1 ml (5 Units). TD: into the vein 5 Units in 500 ml of 5% glucose solution dropwise; into the muscles, into the cervix 1—2 Units.

   Repeat:
7. Prednisolonum — tablets by 0,005; 2.5% solution in ampoules of 1 ml; 0,5% ointment in tubes of 10,0 and 20,0; 0,5% solution in vials of 5 ml (eye drops). TD: orally 0,005—0,02 once a day in the morning with a meal; into the vein 0,05—0,15 in 500 ml of 5% glucose solution dropwise.
8. Fenoterol — tablets by 0,005; aerosol in cylinder of 10 ml (200 inhalations of 0,0001). TD: orally 0,005 every 3—4 hours (as tocolytic); inhalation 1—2 doses three—four times a day.
9. Tiotropii bromidum — powder for inhalation in capsules by 0,000018. TD: inhalation 0,000018 once a day.

QUESTIONS AND TASKS FOR SELF-CONTROL

Task 1. Pharmacotherapeutic questions. Write the prescriptions, justifying the choice of drugs.

1. Combinations of drugs which is used to treat bronchitis.
2. Drug with local anesthetic effect which is used to treat cough.
3. Drug which reduces bronchial irritation in bronchitis.
4. Drug that depresses the cough center.
5. Drug that reduces viscosity of bronchial mucus, which is used to treat bronchitis.
6. Drug that increases the synthesis of surfactant.
7. α, β-adrenergic agonist which is used to treat bronchospasm.
8. Indirect adrenergic agonist which is used to treat asthma
9. Anticholinergic drug which is used to treat the chronic obstructive pulmonary disease.
10. Drug, relaxing the smooth muscles of the bronchi, which are used to treat asthma.
11. Basic anti-inflammatory drug which is used to treat asthma.
12. Drug which stabilizes mast cells and is used to treat asthma.
13. Drug that reduces the release of histamine, which is used to treat asthma.
14. Drug that reduces the risk of preterm labour.
15. Hormonal drug for stimulation of labour.
16. Drug which stimulates labor and does not increase blood pressure.
17. Drug for stopping postpartum uterine bleeding.
18. Drug for accelerating the involution of the uterus in the postpartum.

Task 2. After studying the theoretical material, answer the following questions:

1. Which expectorants are prescribed for respiratory diseases with scanty sputum, and which — for diseases with difficult to separate viscous sputum?
2. Consider the advantages and disadvantages of inhaled bronchodilators and anti-inflammatory drugs for the treatment of asthma.
3. Name bronchodilators that increase and decrease mucociliary clearance.
4. What is remodeling of bronchi? What drugs inhibit the development of bronchial remodeling and adhesion of microorganisms to the bronchial epithelium?
5. What medications are prescribed to prevent nighttime asthma attacks? Why?

6. Why is it rational to combine β_2-adrenomimetics and M-cholinoblockers for the treatment of bronchoobstructive syndrome? What is a route of administration of these combinations?
7. What receptors are localized in the myometrium and how do they affect tone and contractile activity of the myometrium.

Task 3. Match each drug with the appropriate description

a**.** Match each drug with the appropriate description

A. Ipratropium	1. A long-acting β_2 adrenoceptor agonist
B. Omalizumab	2. A bronchodilator drug that can block neuronal n-acetylcholine receptors
C. Salmeterol	3. A drug that blocks high-affinity immunoglobulin E (IgE) receptors of sensitized mast cells
D. Cromolyn	4. A selective inhibitor of 5-lipoxygenase, preventing the formation of both LTB4 and the cysteinyl leukotrienes
E. Zileuton	5. An anti-inflammatory agent that inhibits mast cell degranulation and release of histamine

b**.** Match each drug with the appropriate description

A. Codeine	1. A drug which anesthetizes the stretch receptors located in the respiratory passages, lungs, and pleura
B. Benzonatate	2. A synthetic derivative of morphine that has no analgesic effects in antitussive doses, which in low doses has a low addictive profile
C. Acetylcysteine	3. An opioid which decreases the sensitivity of cough centers in the central nervous system
D. Dextrometrophane	4. A drug which breaks down disulfide bonds of sputum

E. Bromhexine	5. A drug which decreases mucus viscosity by increasing lysosomal activity

Task 4. Topics for reports.

1. Glucocorticoids in bronchial asthma: inhaled or systemically?
2. The inhalation of drugs: advantages and disadvantages.
3. Modern inhalation drug delivery.

QUESTIONS AND TASKS IN CLASS

Task 1. Analyze the tasks that reflect the mechanisms and features of action of drugs affecting functions of the respiratory system and myometrium (the collection of graphic tasks).

Task 2. Analyze case tasks.

1. A 34-year-old asthmatic man was brought to the emergency department with a severe asthma exacerbation. The patient's forced expiratory volume in 1 second (FEV1) did not improve upon administration of inhaled salbutamol, and the attending physician decided to administer parenteral triamcinolone. What is the benefit provided by parenteral glucocorticoids in this setting?
2. A 45-year-old man had been suffering from chronic obstructive pulmonary disease that was not adequately controlled by inhaled salmeterol and ipratropium. His physician decided to add a third drug that is thought to act by multiple mechanisms, including inhibition of phosphodiesterase 4 in inflammatory cells and enhancement of histone deacetylation. What drug was most likely added to the patient's therapeutic regimen?
3. A 43-year-old man complained to his physician that the therapy he was taking improved his breathing, but that he still had an annoying cough from time to time. He asked the physician for a cough suppressant. Two weeks earlier, the man was diagnosed with moderate persistent asthma and started a therapy with inhaled salbutamol and fluticasone. What drug would be appropriate to treat the patients cough?
4. A 21-year-old man with severe persistent asthma had been on daily inhaled salmeterol, inhaled beclomethasone, and oral zafirlukast for 2 months, with inhaled salbutamol as needed. However, his asthma was poorly controlled, and his physician decided to add another drug to the

current treatment. What drug would be most appropriate for the patient at this time?

5. A 32-year-old male with a history of opioid addiction presents with symptoms of an upper respiratory system infection for the past 5 days. It is determined to be viral in nature, and no treatment of the underlying infection is appropriate. Which of the following is appropriate symptomatic treatment for this patients cough?

Task 3. Answer the test questions (in the computer lab).

Lesson 14
Drugs affecting functions of the digestive system

Learning objectives are to study the classification, mechanisms of action, pharmacokinetics, use, side effects and contraindications to the use of drugs affecting secretory and motor functions of the gastrointestinal tract and liver, drug replacement therapy and antienzyme agents; to study and practice prescription writing.

QUESTIONS FOR PREPARATION FOR THE LESSON

I. Origin, mechanisms, features of action, pharmacokinetics, use, side effects and contraindications to the use of drugs affecting the appetite and function of the gastrointestinal tract.

1. Drugs affecting the appetite:
   - drugs that increase appetite — genetically engineered insulin;
   - anorectic drugs (diet pills) — orlistat, sibutramine.
2. Drug replacement therapy of hypofunction of the stomach glands — betaine + pepsin.
3. Drugs that reduce the secretion of gastric juice:
   - M-cholinoblockers — metocinia iodide, pyrensepin;
   - H_2-receptor blockers — ranitidine, famotidine;
   - proton pump inhibitors (PPIs) — omeprazole, lansoprazole, pantoprazole, rabeprazole, esomeprazole.
4. Antacid agents — sodium hydrogen carbonate, magnesium oxide, hydroxide and carbonate, aluminum hydroxide, oxide and phosphate, calcium carbonate.
5. Drugs that have a protective effect on the mucous membrane of the stomach and intestine — bismuth tripotassium dicitrate, sucralfate.
6. Antiemetic drugs:
   - non-selective antagonists of D-receptors — chlorpromazine, sulpiride;
   - antagonists of D_2-receptors — domperidone;
   - 5-HT_3-receptor antagonists — troposetron, ondansetron, granisetron;
   - antagonists of D_2-receptors and 5-HT_3-receptors — metoclopramide;
   - H_1-receptor antagonists — dimenhydrinate;
   - NK-receptor antagonists — aprepitant.

7. Laxatives:
   - agents that irritate the chemoreceptors of the intestine — castor oil, senna, bisacodyl, sodium picosulphate;
   - agents that irritate mechanoreceptors of the intestine (drugs with osmotic action) — lactulose, sodium and magnesium sulfates, macrogol.
8. Drugs that increase the tone and motility of the stomach and intestines:
   a) M-cholinomimetics — aceclidine;
   b) cholinesterase inhibitors — neostigmine methylsulfate;
   c) prokinetics
      - stimulants of the acetylcholine release, cholinesterase inhibitors and D_2-receptor antagonists — itopride;
      - antagonists of D_2-receptors and 5-HT_3-receptors — metoclopramide;
      - antagonists of D_2-receptors — domperidone.
9. Drugs that reduce the tone and motility of the stomach and intestines:
   a) M-cholinoblockers — atropine, platyphyillin, metocinia iodide;
   b) myotropic antispasmodics
      - inhibitors of phosphodiesterase — bencyclane, drotaverine;
      - blockers of sodium channels — mebeverine;
   c) antidiarrheal agents
      - agonists of opioid receptors — loperamide;
      - adsorbents — activated charcoal;

II. Origin, mechanisms, features of action, use, side effects and contraindications to the use of drugs that affect liver function.

1. Drugs that stimulate the formation of bile (choleretics):
   - true choleretics —garlic, tansy flowers, ursodeoxycholic acid;
   - hydrocholeretics — mineral waters.
2. Drugs that stimulate the secretion of bile:
   - cholecystokinetics — magnesium sulfate.
3. Hepatoprotective agents:
   - drugs that improve the detoxifying function of the liver and antioxidants — ademetionine, ornithine;
4. Drugs that promote the dissolution of cholesterol gallstones — ursodeoxycholic acid.

PRESCRIPTIONS

1. Omeprazole — capsules at 0,02. TD: orally 0,02—0,04 once a day.
2. «Maalox» — official tablets and suspension in a bottle of 250 ml. TD: orally 1 tablet or 1 tablespoon 1—1,5 hours after a meal or with pain in the stomach.
3. Metoclopramide — tablets at 0,01; 0,5% solution in ampoules of 2 ml. TD: orally 0,01 three times a day before a meal; into the muscles 0,01 one—two times a day; into the vein 0,01 in 10 ml of isotonic sodium chloride solution.
4. Bisacodyl — tablets and dragee at 0,005; suppositories rectal at 0,01. TD: orally 0,005—0,01to night; rectally 0,01.
5. Drotaverine — tablets at 0,04; 2% solution in ampoules of 2 ml. TD: orally 0,04—0,08 two—three times a day; into the muscles 0,04—0,08; into the vein 0,04—0,08 in 10—20 ml isotonic sodium chloride solution slowly.
6. Pancreatinum — dragee at 10 000 Units. TD: orally 10 000—20 000 three times a day with a meal.
7. Acidum ursodeoxycholicum — coated tablets at 0,5. TD: orally 0,5 three times a day.

   Repeat:

8. Neostigmini methylsulfas — tablets by 0,015; 0,05% solution in ampoules of 1 ml. TD: orally 0,015; subcutaneously 0,0005 once to two times a day.
9. Platyphyllinum — tablets by 0,005; 0,2% solution in ampoules of 1 ml. TD: orally 0,005; subcutaneously 0,002—0,004 one to two times a day.
10. Bismuthi trikalii dicitras — tablets by 0,12. TD: orally 0,12—0,24 three times a day half an hour before a meal and at bedtime.

QUESTIONS AND TASKS FOR SELF-CONTROL

Task 1. Pharmacotherapeutic questions. Write the prescriptions, justifying the choice of drugs.

1. Proton pump inhibitor for the treatment of ulcer disease.
2. M-anticholinegric drug for the treatment of ulcer disease.
3. Drug for the treatment of ulcer disease that neutralizes gastric HCl.
4. Drug for hyperpeptic gastritis treatment.

5. Drug for biliary reflux treatment.
6. Drug which is used to prevent vomiting.
7. Drug which is used to arrest vomiting.
8. Laxative for enterocolitis treatment.
9. Drug for chronic constipation treatment.
10. Drug for intestinal atony treatment.
11. Myotropic spasmolytic for cramping abdominal pain treatment.
12. M-anticholinegric drug for cramping abdominal pain treatment.
13. Drug for chronic pancreatitis treatment.
14. Drug which is used for dyspepsia caused by intestinal enzymes deficiency.
15. Drug for cholecystitis treatment.
16. Drug for biliary colic treatment.
17. Drug for hepatotoxicity treatment.
18. Drug for chronic hepatitis treatment.

Task 2. After studying the theoretical material, answer the following questions:

1. How do antacids affect the intestinal tone and motility? What are the rational combinations of antacids?
2. Explain the mechanisms of gastroprotective effect. Name the drugs with gastroprotective effect.
3. Choose antiemetics for the treatment of gastroduodenal reflux; motion sickness; endogenous and exogenous intoxication.
4. Name the pleiotropic effects of aprotinin.

Task 3.

a**.** Match each drug with the appropriate description

A. Ranitidine	1. The histamine H_2-receptor antagonists act selectively on H_2 receptors in the stomach
B. Misoprostol	2. A drug which binds to the H^+/K^+-ATPase enzyme system (proton pump) and suppresses the secretion of hydrogenions
C. Omeprazole	3. A weak base that reacts with gastric acid to form water and a salt
D. Sucralfate	4. A drug which forms complex gels with epithelial

	cells
E. Aluminum hydroxide	5. A drug which is approved for the prevention of NSAID-induced gastric ulcers

b. Match each drug with the appropriate description

A. Ondansetron	1. A drug targets the neurokinin receptor in the brain
B. Loperamide	2. An antiemetic drug which is 5-HT3 receptor antagonist
C. Senna	3. A drug which activates presynaptic opioid receptors in the enteric nervous system to inhibit acetylcholine release and decrease peristalsis
D. Castor oil	4. A group of sennosides, a natural complex of anthraquinone glycosides
E. Aprepitant	5. This agent is broken down in the small intestine to ricinoleic acid, which is very irritating and promptly increases peristalsis

Task 4. Topics for reports.

1. Antiemetic treatment of chemotherapy-induced nausea and vomiting.
2. Medication used in nausea and vomiting during pregnancy.
3. Pancreatic enzyme replacement therapy during pancreatic insufficiency.
4. Anti-fermental and hormonal agents for acute pancreatitis — aprotinin, octreotide.
5. Natural products with hepatoprotective activity.
6. Hepatoprotective agents: the pros and cons.

QUESTIONS AND TASKS IN CLASS

Task 1. Analyze the tasks that reflect the mechanisms and features of action of drugs affecting functions of the digestive system (the collection of graphic tasks).

Task 2. Analyze case tasks.

1. A 45-year-old woman had been self-medicating for heartburn. The preparation which physician decided to prescribe was a combination of magnesium hydroxide and aluminum hydroxide. Why do many antacid

preparations on the market contain a combination of these two antacids instead of a single product?

2. A 50-year-old woman complained to her physician of regurgitation of foul-tasting fluid into her mouth and occasional nausea and vomiting. The physician prescribed a drug that can both prevent nausea and vomiting and promote upper gastrointestinal motility. Blockade of which of the following receptors most likely contributed to the therapeutic effect of the drug in the patient's disease? What drug was prescribed?

   a. M3-cholinergic
   b. N-cholinergic
   c. β_2 adrenergic
   d. H_2 histaminergic
   e. D_2 dopaminergic

3. A 60-year-old man suffering from recurrent heartburn routinely took large quantities of different antacid preparations. Which antacid had the highest risk of metabolic alkalosis in this patient?

4. A 74-year-old patient suffering from chronic constipation complained of very loose stools after a treatment with bisacodyl, one tablet daily for 1 week. Which of the following would be the best advice to give to this patient?

   a. There is no cause for alarm; the situation is selflimiting.
   b. Continue bisacodyl, but take the medication with a small snack.
   c. Continue bisacodyl, and add lactulose.
   d. Discontinue bisacodyl, and increase fiber and fluid intake.
   e. Discontinue bisacodyl, and switch to castor oil.

5. A 45-year-old woman complains of persistent heartburn and an unpleasant, acid-like taste in her mouth. The clinician suspects that she has gastroesophageal reflux disease and advises her to raise the head of her bed 6 to 8 inches, not to eat for several hours before retiring, and to eat smaller meals. Two weeks later, she returns and says the symptoms have subsided slightly but still are a concern. Which drug will the clinician likely prescribe?

Task 3. Answer the test questions (in the computer lab).

Lesson 15
Antiseptic, disinfectant, antifungal, antiparasitic drugs

Learning objectives are to study the classification, mechanisms of action, pharmacokinetics, use, side effects of antiseptic, disinfectant, antifungal, antiparasitic drugs; poisoning with strong acids, alkalis, iodine; to study and practice prescription writing.

QUESTIONS FOR PREPARATION FOR THE LESSON

1. Mechanism of action and classification of antimicrobial agents (antiseptics, disinfectants, chemotherapeutic drugs). Differences between antiseptic and chemotherapeutic agents. Requirements for antiseptics and disinfectants.
2. Antiseptic and disinfectants: mechanisms of action, use, side effects.
   - acids — boric acid, salicylic acid, azelaic acid;
   - alkali — ammonia;
   - preparations of halogens — a solution of iodine;
   - oxidizers — hydrogen peroxide, potassium permanganate;
   - ethanol as an antimicrobial agent;
   - aldehydes — formaldehyde;
   - guanidines — chlorhexidine;
   - agents of metals — silver nitrate, zinc hyaluronate;
   - detergents — benzalkonium chloride;
   - nitrofuran derivatives — nitrofural, nitrofurantoin, nifuratel, nifuroxazide, furazolidone;
3. Acute poisoning with strong acids, alkalis, iodine: pathogenesis, symptoms, treatment.
4. Antifungal drugs: classifications, the spectrum of antifungal action, mechanism of the action, side effects, contraindications to the use

   a) amphotericin B, nystatin, natamycin;
   b) imidazole derivatives (azoles and triazoles)
      - for systemic use — fluconazole, itraconazole, voriconazole, posaconazole;
      - for topical application — isoconazole, clotrimazole;
      - for systemic and local application — ketoconazole;
   c) allylamines

- for topical use — naftifine;
- for systemic and topical application — terbinafine;

d) drugs of different groups
- for systemic use — caspofungin, flucytosine;
- for systemic and topical application — griseofulvin.

5. Classification of antifungal agents by the nature and spectrum of action:

a) classification by the nature of the antifungal action
- fungicidal — allylamines, voriconazole, posaconazole, caspofungin, flucytosine;
- fungicidal or fungistatic depending on the concentration — polyene antimycotics, azoles and triazoles;
- fungistatic — griseofulvin;

b) by the spectrum of antifungal action
- drugs of broad antifungal spectrum — amphotericin B, azoles and triazoles, caspofungin;
- drugs effective against candidiasis, — nystatin, natamycin;
- drugs effective against dermatomycosis, — allylamines, griseofulvin.

6. Choice and methods of application of antifungal agents for surface and invasive fungal infections.
7. Drugs for the treatment of giardiasis, amebiasis and trihomoniasis — furazolidone, metronidazole, tinidazole, diloxanide.
8. Drugs for the treatment of trypanosomiasis — suramin, pentamidine.
9. Drugs for the treatment leishmaniasis — miltefosine, sodium stibogluconate.
10. Anthelmintic drugs: classification, spectrum of antihelminthic action, mechanism of action, routes of administration, side effects, contraindications to use:
- broad anthelmintic spectrum — albendazole, mebendazole, praziquantel, ivermectin;
- drugs for the treatment of nematodes — levamisole, piperazine, niclosamide.

PRESCRIPTIONS

1. Kalii permanganas — 0,05% solution, 500 ml for the gastric lavage during poisoning; 0,1—0,5% solution, 100—250 ml for irrigation of the wounds; 2—5% solution, 5—10 ml for application to the ulcer and burn surfaces.
2. Nitrofural — 0,02% solution, 500 ml; tablets at 0,02 for the preparation of aqua solution.
3. Ethanolum — 40, 70, 90 and 95%, 50—100 ml.
4. Fluconazole — capsules at 0,15; 0,2% solution in a bottle of 1000 ml. TD: orally for candidiasis 0,15 once, for dermatomycosis 0,15 once in a week for 4—6 weeks; into the vein 0,4 dropwise on the first day, 0,2 — on the following days.
5. Metronidazolum — tablets at 0,25 and 0,5; suppositories vaginal at 0,5; 0,5% solution in a bottle of 100 ml. TD: orally 0,25 two times a day after a meal; intravaginal 0,5 at bedtime; into the vein 0,5.
6. Mebendazole — tablets at 0,1. TD: orally in enterobiosis 0,1 once, in other nematodes 0,2 in the morning and in the evening for 3 days.
7. Praziquantel — tablets at 0,3 and 0,6. TD: orally in opisthorchiasis 25 mg/kg three times with a break of 4 hours; for cestodiasis — 25 mg/kg once.

QUESTIONS AND TASKS FOR SELF-CONTROL

Task 1. Pharmacotherapeutic questions. Write the prescriptions, justifying the choice of drugs.

1. Antiseptic which is used to treat burns.
2. Drug with dehydrating effect which is used to treat burns
3. Drug with deodorizing effect for injury treatment.
4. Nitrofuran antiseptic for the treatment of pyogenic injury.
5. Drug which is used to disinfect an operating field.
6. Drug for sterilizing surgical instruments.
7. Chemical antagonist for alkaloid poisoning.
8. Drug to treat Gastrointestinal Candidiasis
9. Drug which is used for Mucosal Candidiasis Treatment.
10. Drug for dermatomycosis treatment.
11. Drug for treatment of invasive fungal infections.
12. Drug for treatment of severe infection caused by anaerobic microorganisms.

13. Drug for lambliosis treatment.
14. Drug for trichomoniasis treatment.
15. Drug for enterobiasis treatment.
16. Drug for ascariasis treatment.
17. Drug for opisthorchiasis treatment.
18. Drug for cestodiasis treatment.

Task 2. After studying the theoretical material, answer the following questions:

1. What effects (antiseptic, astringent, deodorizing) are important when using potassium permanganate for different indications?
2. In what concentrations does ethanol have the maximum bactericidal effect in aqueous and protein environments? Name indications of ethanol in different concentrations.
3. Write the chemical reactions between iodine and proteins, sodium thiosulfate.
4. Why do polyene antibiotics have an effect on fungi and do not have activity against bacteria?
5. It is known that voriconazole is able to reduce the activity of the enzyme chitin synthase of fungi and also inhibit 14-α-demethylase. Make assumptions about the mechanism of action of voriconazole. How does its activity change, compared with other triazoles?
6. Terbinafine, azoles, and amphotericin B damage the cytoplasmic membrane of fungi. What drug has a fungicidal effect as a result of inhibition of the fungal cell wall?
7. It is known that metronidazole is a prodrug and it is transformed by ferredoxin oxidoreductase of protozoa into a cytotoxic compound; levamisole selectively inhibits succinate dehydrogenase and nematode fumarate dehydrogenase; piperazine as an agonist of GABA receptors disrupts the neuromuscular transmission of nematodes. Make assumptions about the mechanism of selective toxicity of antiparasitic agents.
8. What microorganisms are sensitive to the action of metronidazole? What common property do they have?
9. Which antihelminthic drugs cause muscle paralysis of helminths, and which cause spasm of muscle?

10. Piperazine was prescribed to enhance the effect of pyrantel in the treatment of ascariasis. However, the treatment was unsuccessful. What is the cause of the treatment failure?

Task 3.

a. Match each antifungal drug with the appropriate description

A. Amphotericin B	1. This drug has the broadest antifungal spectrum but is used only in case of severe mycoses because of its toxicity
B. Caspofungin	2. The mechanism of action of this drug involves the inhibition of the synthesis of β-glucan, an essential constituent of a fungal cell wall
C. Flucytosine	3. The drug is based on the imidazole nucleus
D. Ketoconazole	4. The drug is converted to the antimetabolite 5-fluorouracil in fungal

b. Match each anthelmintic drug with the appropriate description

A. Albendazole	1. The agent of choice for echinococcosis
B. Ivermectin	2. The drug is active against most trematodes and cestodes
C. Mebendazole	3. A benzimidazole derivative with less than 10% oral bioavailability
D. Praziquantel	4. The drug of choice for onchocerciasis

c. Match each antiseptic with the appropriate description

A. Formaldehyde	1. An agent which induces progressive leakage of intracellular constituents, including K^+
B. Ethanol	2. An agent that causes membrane damage and rapid denaturation of proteins
C. Chlorhexidine	3. An antiseptic which acts as a mutagenic agent, it forms protein-DNA cross-links, thereby inhibiting DNA synthesis
D. Phenol	4. A bactericidal agent with low irritation, which attacks the bacterial cytoplasmic or inner

	membrane or the yeast plasma membrane
E. Hydrogen peroxide	5. It is a strong oxidizing agent, which dissolves in water to give intensely pink or purple solutions
F. Potassium permanganat	6. It can rapidly degrade into the innocuous products water and oxygen. Its action is due to the formation of hydroxyl radicals (·OH), which oxidize thiol groups in enzymes and proteins

Task 4. Topics for reports.

1. A history of early antiseptics. First antiseptics which were used in medical practice.
2. Antiseptics in the treatment of the sore throat.
3. New targets for antifungal agents.
4. Drug resistance in human helminths: current situation.

QUESTIONS AND TASKS IN CLASS

Task 1. Analyze the tasks that reflect the mechanisms and features of the action of antiseptics, disinfectants, antifungal, antiparasitic drugs (the collection of graphic tasks).

Task 2. Analyze case tasks.

1. A 55-year-old female presents to the hospital with shortness of breath, fever, and malaise. She has a history of breast cancer, which was diagnosed 3 months ago, and has been treated with chemotherapy. Her chest X-ray shows possible pneumonia, and respiratory cultures are positive for *Aspergillus fumigatus*. What is the most appropriate choice for treatment?
2. A 48-year-old immigrant from Mexico presents with seizures and other neurologic symptoms. Eggs of *T. solium* are found upon examination of a stool specimen. A magnetic resonance image of the brain shows many cysts, some of which are calcified. What drug would be of benefit to this individual?
3. A 40-year-old woman with AIDS was admitted to the hospital because of fever 39,5°C (103,2°F,), cough, and chest pain over the past 12 hours. Physical examination revealed vesicular skin lesions on her arms

and face, and a chest X-ray showed scattered pulmonary lesions compatible with a granulomatous process. A blood culture displayed typical yeasts with chlamydospores. Which of the following correctly pairs the most likely offending pathogen with the appropriate treatment?

a. *Cryptococcus neoformans*: amphotericin B
b. *Trichophyton tonsurans*: griseofulvin
c. *Histoplasma capsulatum*: fluconazole
d. *Aspergillus fumigatus*: fluconazole
e. *Candida albicans*: amphotericin B

4. A 33-year-old woman presented to her gynecologist with a 4-day history of perineal pruritus and thick, cheesy vaginal discharge. The only medication the woman was taking was an oral contraceptive. A wet preparation of vaginal secretion showed budding yeast cells and pseudohyphae. A diagnosis was made, and a local therapy was prescribed. Which of the following correctly pairs the most likely offending pathogen with the appropriate treatment?

a. *Candida albicans*: griseofulvin
b. *Candida albicans*: terbinafine
c. *Candida albicans*: nystatin
d. *Blastomyces dermatitidis*: caspofungin
e. *Blastomyces dermatitidis*: terbinafine
f. *Blastomyces dermatitidis*: nystatin

5. A 34-year-old man complained to his physician that the drug he was taking caused nausea, abdominal pain, loose stools, and itching. Three days earlier, the man had been diagnosed with *Taenia solium* infection and had started an appropriate therapy. The physician told the patient that his symptoms were common adverse effects of the drug and should subside in 1 or 2 days. What drugs most likely caused the patients symptoms?

6. When the mother put on a video, a 5-year-old boy opened a cupboard, removed the cap from a container of dishwasher detergent and swallowed the powder. After a while the mother heard his cry and ran to the kitchen to find him vomiting blood. An ambulance rushed the boy to the hospital. The boy had excessive salivation, hoarseness, dysphagia. The child was restless, crying out loud. There were redness and ulceration of the oral mucosa, swelling of the mouth, epigastric

tenderness on palpation. Make a diagnosis, explain the pathogenesis and symptoms of poisoning, prescribe treatment.

7. A 10-year-old girl was admitted to the hospital within 2 hours of accidental ingestion of unknown liquid. She was irritable and had drooling of saliva. Lips, tongue were brown. Vital signs were body temperature 37,6 C, breathing was difficult due to swelling of the larynx, pulse — 90 beats per minute, blood pressure — 80/50. 1 hour after hospitalization vomiting appeared, emetic masses were blue, mixed with blood. Make a diagnosis, explain the pathogenesis and symptoms of poisoning, prescribe treatment.

Task 3. Answer the test questions (in the computer lab).

Lesson 16
Antibiotics and antitumor agents

Learning objectives are to study classifications, mechanisms of action, antimicrobial spectrum, pharmacokinetics, use, side effects and contraindications to the use of antibiotics, principles of antimicrobial therapy; to study the mechanism of action, indications for use and side effects of anticancer drugs; to study and practice prescription writing.

QUESTIONS FOR PREPARATION FOR THE LESSON

1. Antibiotics: requirements for antibiotics; history of antibiotics.
2. Classification of antibiotics:
   - by the mode of action — bactericidal, bacteriostatic;
   - by the mechanism of action — antibiotics that disrupt the synthesis of the cell wall, the permeability of the cytoplasmic membrane (detergents), the synthesis of nucleic acids and protein;
   - by the antimicrobial spectrum — narrow, broad, extended-spectrum;
   - by chemical structure — β-lactam antibiotics, glycopeptides, lipopeptides, aminoglycosides, tetracyclines, chloramphenicol, macrolides, lincosamides.
3. Antimicrobial spectrum, mechanism of action, pharmacokinetics, indications for use, routes of administration, side effects, contraindications to the use of antibiotics:
   a) antibiotics that disrupt the synthesis of the cell wall of microorganisms (bactericidal)
      - natural penicillins with narrow spectrum, unstable to β-lactamases, — benzylpenicillin (penicillin G), benzylpenicillin sodium salt, benzathine benzylpenicillin, phenoxymethylpenicillin (penicillin V);
      - semi-synthetic penicillins with narrow spectrum, resistant to β-lactamases, — oxacillin, nafcillin;
      - semi-synthetic penicillins with extended-spectrum, not resistant to β-lactamases, — ampicillin, amoxicillin, carbenicillin, piperacillin;
      - drug combination of broad-spectrum penicillins (that are unstable against β-lactamases) with β-lactamase inhibitors (inhibitor-protected penicillins) — ampicillinlin + oxacillin, ampicillin + sulbactam,

amoxicillin + clavulanic acid, amoxicillin + sulbactam, piperacillin + tazobactam;

- cephalosporins
  1st generation — cefazolin, cephalexin;
  2nd generation — cefuroxime, cefaclor;
  3rd generation — cefoperazone, cefoperazone + sulbactam, cephotaxime, ceftazidime, ceftriaxone, ceftibutene, cefditoren pivoxil;
  4th generation — cefepime;
  5th generation — ceftobiprole medocaril;
- carbapenems — imipenem + cilastatin, doripenem, meropenem, ertapenem;
- glycopeptides — vancomycin, teicoplanin;

b) Antibiotic-detergents that disrupt the permeability of the cytoplasmic membrane of microorganisms (bactericidal and fungicidal / fungistatic)

- polymyxins B and M;
- gramicidin C;
- lipopeptides — daptomycin;
- glycolipopeptides — telavancin;
- antifungal polyenes — amphotericin B, nystatin, natamycin;

c) antibiotics that disrupt the synthesis of nucleic acids and proteins of microorganisms

- rifampicin (bactericidal);
- aminoglycosides (bactericidal)
  1st generation — neomycin, streptomycin, kanamycin;
  2nd generation — gentamicin, tobramycin, amikacin;
  3rd generation — netilmicin;
- tetracyclines (bacteriostatic) — tetracycline, doxycycline;
- tigecycline (bacteriostatic);
- chloramphenicol (bacteriostatic);
- lincosamides (bacteriostatic) — lincomycin, clindamycin;
- macrolides (bacteriostatic / bactericidal) — erythromycin, clarithromycin, roxithromycin, azithromycin, josamycin, midecamycin, spiramycin.

4. Principles of rational antimicrobial therapy: choice, routes of administration, doses, regimens and duration of administration, combined use of antibiotics.

5. Mechanisms of resistance of microorganisms to antibiotics, methods of its prevention and overcoming.
6. Antitumor agents: classification, antitumor spectrum, mechanisms of action, application

   a) cytotoxic agents
      - alkylating agents — dacarbazine, ifosfamide, carboplatin, carmustine, lomustine, oxaliplatin, temozolomide, cyclofosfamide, cisplatin;
      - antitumor antibiotics — bleomycin, dactinomycin, daunorubicin, doxorubicin, idarubicin, mitoxantrone, mitomycin, epirubicin;
      - antimetabolites — gemcitabine, hydroxycarbamide, decitabine, capecitabine, mercaptopurine, methotrexate, pemetrexed, raltitreksid, fludarabine, fluorouracil, cytarabine;
      - alkaloids and other herbal products and their semi-synthetic analogues — vinblastine, vincristine, vinorelbine, docetaxel, irinotecan, paclitaxel, topotecan, etoposide;
      - inhibitors of protein kinases — dasatinib, imatinib, lapatinib, nilotinib, pazopanib, sorafenib, sunitinib, everolimus, erlotinib;
      - other cytotoxic agents — bortezomib, tretinoin;

   b) hormonal and antihormonal agents — cyproterone, goserelin, tamoxifen;

   c) monoclonal antibodies target antigens of tumor cells — alemtuzumab, bevacizumab, panitumumab, rituximab, cetuximab;

   d) enzyme— asparaginase.

7. Side effects of antitumour agents. Contraindications to use.

PRESCRIPTIONS

1. Benzathine Benzylpenicillin — powder in the vials of 1 200 000 Units and 2 400 000 Units. TD: into the muscles 1 200 000 — 2 400 000 Units in 5 ml 0,5% solution of lidocaine once in 4 weeks.
2. Amoxicillin + Acidum clavulanicum — coated tablets by 0,375 (Amoxicillin by 0,25 and Acidum clavulanicum by 0,125); powder in the vials of 1,2 (Amoxicillin by 1,0 and Acidum clavulanicum by 0,2). TD: orally 0,375—1,0 three times a day 1 hour before a meal; into the vein 1,2—2,4 in 500 ml of isotonic sodium chloride solution two—three times a day dropwise.

3. Meropenem — powder in the vials of 0,5 and 1,0. TD: into the vein 0,5—1,0 in 250 ml of 5% glucose solution every 8 hours dropwise.
4. Ceftazidime — powder in the vials of 0,5 and 1,0. TD: into the muscles 0,5—1,0 in 2—3 ml of water for injection; into the vein 0,5—1,0 in 10—20 ml of 5% glucose solution two—three times a day.
5. Rifampicin — capsules by 0,15 and 0,3. TD: orally 0,45—0,6 once a day 1 hour before a meal.
6. Doxycyclinum — capsules by 0,1. TD: orally 0,1 two times a day after a meal.
7. Azithromycin — tablets by 0,5. TD: orally 0,5 once a day 1 hour before a meal for 3 days.

QUESTIONS AND TASKS FOR SELF-CONTROL

Task 1. Pharmacotherapeutic questions. Write the prescriptions, justifying the choice of drugs.

1. Antibiotic for the treatment of pneumonia caused by pneumococcus.
2. Antibiotic for the treatment of pneumonia caused by Haemophilus influenzae.
3. Antibiotic for the treatment of sepsis caused by staphylococcus.
4. Antibiotic for the treatment of sepsis caused by Pseudomonas aeruginosa.
5. Antibiotic for the treatment of wound infection
6. Antibiotic for the treatment of gas gangrene.
7. Antibiotic for treatment of osteomyelitis.
8. Antibiotic for the treatment of diphtheria.
9. Antibiotic for treatment of syphilis.
10. Antibiotic for treatment of scarlet fever.
11. Antibiotic for the treatment of dysentery.
12. Antibiotic for the treatment of typhoid fever.
13. Antibiotic for the treatment of cholera.
14. Antibiotic for treatment of pyelonephritis.
15. Antibiotic for Lyme disease.
16. Antibiotic for treatment of rickettsial infections.
17. Antibiotic for the treatment of infections caused by chlamydia.
18. Antibiotic for the prevention of relapses in rheumatism.

Task 2. After studying the theoretical material, answer the following questions:

1. What is the minimum inhibitory concentration (MIC), post antibiotic effect (PAE), decontamination, biofilm?
2. Explain the mechanisms of selective toxicity of antibiotics, which violate the synthesis of the cell wall, against microorganisms. Why are these antibiotics more active against rapidly dividing bacteria?
3. What is the reason for the high toxicity of antibiotic-detergents (antibacterial cleaning products)? What route of these antibiotics administration is primarily used?
4. What stages of protein synthesis in microorganisms do antibiotics violate? Explain the mechanisms of antibiotics selective toxicity that violate protein synthesis.
5. Why do aminoglycosides, which violate the protein synthesis of microorganisms, have, nevertheless, a bactericidal effect?
6. Name the pleiotropic effects of macrolides.
7. Why are bacteriostatic antibiotics recommended to be combined with immunomodulating agents?
8. Why are over-the-counter selling of antibiotics and irresponsible self-medication with antibiotics dangerous?

Task 3.

a. Match each antibiotic with the appropriate description

A. Tigecycline	1. A penicillin active against *Klebsiella* species
B. Streptomycin	2. A third-generation cephalosporin active against *Pseudomonas aeruginosa*
C. Azithromycin	3. A glycylcycline antibiotic active against vancomycin—resistan*t Staphylococci*
D. Ceftazidime	4. An aminoglycoside antibiotic active against amebiasis and giardiasis
E. Piperacillin	5. A macrolide antibiotic with a very long half-life (about 40 hours)

b. Match each antibiotic with the appropriate side effect.

A. Tigecycline	1. Gray baby syndrome
B. Gentamicin	2. Acute pancreatitis
C. Tetracycline	3. Phototoxicity
D. Chloramphenicol	4. Red man syndrome
E. Vancomycin	5. Ototoxicity

Task 4. Topics for report.

1. The history of antibiotics and antibiotic therapy.
2. Current challenges in antibiotic resistance.
3. Antibiotics during pregnancy and breast feeding: what to choose?
4. Antitumor vaccination.

QUESTIONS AND TASKS IN CLASS

Task 1. Analyze the tasks that reflect the mechanisms and features of the action of antibiotics and antitumor agents (the collection of graphic tasks).

Task 2. Analyze case tasks.

1. A 54-year-old man was admitted to the hospital with fever 38,1°C (100,6°F), night sweats, arthralgias, and 6,8 kg (15lb) of unintentional weight loss. Past history was significant for rheumatic fever at the age of 9 and for dental surgery 1 month ago. The symptoms started about 2 weeks after the dental procedure. Physical examination was significant for mitral regurgitation, subungual splinter hemorrhages, and hemorrhagic plaques on the soles of both feet. Three blood cultures were ordered, and an empiric therapy was started. Which of the following should be an appropriate treatment for the patient at this time?
   a. Ampicillin and erythromycin
   b. Piperacillin and chloramphenicol
   c. Penicillin G and gentamicin
   d. Dicloxacillin and ciprofloxacin
2. A 6-year-old boy presented to his pediatrician with fever 38,5°C (101,3°F) and sharp pain in his left ear. On physical examination, the left tympanic membrane was red, opaque, and bulging. Amoxicillin was prescribed, but 3 days later, the symptoms were not reduced. The pediatrician decided to modify the therapy and prescribed

amoxicillin / potassium clavulanate. Explain the advantage of adding potassium clavulanate to amoxicillin.

3. A 53-year-old woman hospitalized for resection of breast carcinoma presented with fever 39,4°C (103,8°F), cough, dyspnea, and viscid, currant jelly-like sputum 3 days after surgery. A Gram stain showed numerous gram-negative bacilli with large capsules. A chest radiograph showed dense right upper field infiltrates. A diagnosis of nosocomial pneumonia was made. What groups of antibiotics would be most appropriate for the emergency therapy of this patient?
4. A 25-year-old man recently diagnosed with severe acne involving the face, back, and chest started a treatment that included tetracycline. The physician instructed the patient to avoid milk or dairy products within 2 hours of taking the medication. Explain the outcome of the interaction between tetracycline and dairy products.
5. A 7-year-old child presents with pharyngitis and fever of 2 days' duration, and microbiology reveals small, translucent, beta-hemolytic colonies sensitive *in vitro* to bacitracin. Past history includes a severe allergic reaction to amoxicillin when used for an ear infection. The physician needs to treat this infection, but prefers not to use a drug that needs parenteral administration. Which one of the following agents is most likely to be appropriate in terms of both effectiveness and safety? Explain the choice.
   a. Azithromycin
   b. Cefaclor
   c. Doxycycline
   d. Penicillin G
   e. Vancomycin

Task 3. Answer the test questions (in the computer lab).

Lesson 17
Sulfonamides, quinolones, antituberculosis, antiviral, antimalarial drugs

Learning objectives are to study classifications, mechanisms of action, antimicrobial spectrum, pharmacokinetics, use, side effects and contraindications to the use of sulfonamides, quinolones, antituberculosis, antiviral, antimalarial drugs; to study and practice prescription writing.

QUESTIONS FOR PREPARATION FOR THE LESSON

1. Sulfonamide drugs: the history of creation, connection of a chemical structure with an antimicrobial effect, classification:
   a) drugs with resorptive action
      - short-acting — sulfacaramide;
      - long-acting — sulfamethoxazole, sulfadoxine, sulfadimethoxine;
   b) drugs acting in the lumen of the intestine, — phthalylsulfathiazole, sulphaguanidine;
   c) locally-acting drugs — sulfadiazine;
   d) salicylic acid derivatives — sulfasalazine;
   e) combination drug — co-trimoxazole (sulfamethoxazole + trimethoprim).
2. Spectrum of antimicrobial action, mechanism of action, pharmacokinetics, use, side effects, contraindications to the use of sulfonamides.
3. Derivatives of 8-hydroxyquinoline: spectrum of antimicrobial action, mechanism of action, pharmacokinetics, use, side effects, contraindications to use — nitroxoline;
4. Quinolones: spectrum of antimicrobial action, mechanism of action, pharmacokinetics, use, side effects, contraindications for use
   a) non-fluorinated quinolones (NFQs) — nalidixic acid;
   b) fluoroquinolones
      - I generation— ofloxacin, norfloxacin, pefloxacin, ciprofloxacin, lomefloxacin;
      - II generation — levofloxacin, sparfloxacin;
      - III generation — gemifloxacin, moxifloxacin.

5. Spectrum of antimicrobial action, mechanism of action, pharmacokinetics, use, side effects, contraindications to the use of linezolid and tedizolid.
6. Antituberculosis drugs: mechanism of action, origin, classification
   - group I (the most effective drugs) — isoniazid, rifampicin, lomefloxacin;
   - group II (medium efficacy) — kanamycin, amikacin, ethambutol, pyrazinamide;
   - group III (drugs with moderate efficacy) — aminosalicylic acid.
7. Mechanism of action, pharmacokinetics, side effects, contraindications to the use of antituberculosis drugs.
8. Mechanisms of drug resistance in *Mycobacterium tuberculosis*, methods of its prevention and overcoming.
9. Principles of modern pharmacotherapy of tuberculosis. The first line (isoniazid, rifampicin, ethambutol, pyrazinamide) and the second line (lomefloxacin, kanamycin, amikacin, aminosalicylic acid) antituberculosis agents. Rational combinations of antituberculosis drugs.
10. Antiviral agents: requirements for antiviral agents; classification, spectrum of antiviral action, mechanism of action, pharmacokinetics, use, side effects, contraindications for use
    a) drugs for infections caused by herpes simplex virus and chickenpox — acyclovir, valaciclovir, penciclovir, famciclovir;
    b) drugs against cytomegalovirus infection — ganciclovir, valganciclovir;
    c) drugs for the prevention and treatment of influenza virus
       - blockers of membrane protein M_2 — rimantadine;
       - neuraminidase inhibitors — oseltamivir, zanamivir;
    d) antiretroviral agents
       - inhibitors of reverse transcriptase of human immunodeficiency virus (HIV)
         with nucleoside structure — zidovudine, didanosine, stavudine, abacavir;
         with non-nucleoside structure — nevirapine, efavirenz;
       - HIV protease inhibitors — fosamprenavir, saquinavir, lopinavir, ritonavir;
       - Inhibitors of HIV fusion with host cells — enfuvirtide;

- Integrase inhibitors — ratelgavir

e) antiviral drugs for the treatment of hepatitis B
   - nucleoside analogues:
     thymidine nucleoside analogue — telbivudine;
     guanosine nucleoside analogue — entecavir;
     cytidine nucleoside analogue — lamivudine;
   - analogues of nucleotides (adenosine monophosphate) — adefovir dipivoxil, tenofovir disoproxil fumarate.

f) antiviral drugs for the treatment of hepatitis C
   - NS3 / 4A protease inhibitors — telaprevir, boceprevir, simeprevir;
   - inhibitors of RNA-dependent RNA polymerase (NS5B protein) — sofosbuvir;

g) antiviral agents with broad-spectrum activity
   - ribavirin;
   - interferon drugs
   - recombinant — interferon alpha, interferon alfa-2a, interferon alfa-2b;
   - pegylated recombinant interferons — peginterferon alfa-2a (Pegasys), peginterferon alfa-2b (Intron A).

11. Antimalarial drugs: classification, mechanism of action, side effects, contraindications to the use
   - hematoschotropic drugs (drugs suppress erythrocyte forms) — quinine, chloroquine, mefloquine, pyrimethamine;
   - histosysotropic agents
     suppress pre-erythrocytic forms of plasmodium — pyrimethamine;
     suppress para-erythrocytic forms of plasmodum — primaquine;
   - gamontotropes
     gamontostatic — pyrimethamine;
     gamontocidal — chloroquine, primaquine.

12. Drugs for individual, public chemoprophylaxis, treatment of malaria.

PRESCRIPTIONS

1. Ciprofloxacine — coated tablets by 0,25 and 0,5; 0,3% solution in the vials of 5 ml (eye drops); 0,2% solution in the bottle of 100 ml. TD: orally 0,25—0,5 two times a day; 1—2 drops in each eye 2 times a day; into the vein 0,2—0,4 dropwise.

2. Isoniazidum — tablets by 0,2 and 0,3; 10% solution in ampules of 5 ml. TD: orally 0,2—0,3 three times a day after a meal; into the muscles, into the vein 5—10 mg/kg once a day.
3. Aciclovir — tablets by 0,2; powder in the vials of 0,25; 3% eye ointment and 5% cream in tubes of 2,0. TD: orally 0,2 four times a day; into the vein 0,25—0,5 in 10 ml of isotonic sodium chloride solution.
4. Oseltamivir — capsules by 0,075. TD: orally for the treatment of influenza — 0,075 every 12 hours; for the prevention of influenza — 0,075 once a day for 4—6 weeks
5. Rifampicin — capsules by 0,15 and 0,3. TD: orally 0,45—0,6 once a day 1 hour before a meal.

QUESTIONS AND TASKS FOR SELF-CONTROL

Task 1. Pharmacotherapeutic questions. Write the prescriptions, justifying the choice of drugs.

1. Drug for the treatment of conjunctivitis.
2. Drug for the treatment of sepsis.
3. Drug for the treatment of intra-abdominal infection.
4. Drug for skin and soft tissue pyogenic infections.
5. Drug for the treatment of cystitis.
6. Drug for the treatment of pyelonephritis.
7. Drug for the treatment of dysentery.
8. Drug for the treatment of typhoid fever.
9. Synthetic drug for the treatment of tuberculosis.
10. Antibiotic for the treatment of tuberculosis.
11. Drug for the treatment of cutaneous herpes simplex infection.
12. Drug for the treatment of herpes Zoster ophthalmicus.
13. Drug for herpes simplex encephalitis.
14. Drug for the treatment of chickenpox.
15. Drug for the prevention of influenza A virus.
16. Drug for the treatment of influenza A virus.
17. Drug for the prevention of influenza B virus.
18. Drug for the treatment of influenza B virus.

Task 2. After studying the theoretical material, answer the following questions:

1. Why do sulfonamide drugs not act on resting forms of microorganisms, as well as on microorganisms that synthesize para-aminobenzoic acid? Is it rational to combine sulfa drugs with local anesthetics? How to correctly prescribe sulfa drugs for the treatment of purulent wounds?
2. Why do sulfonamide drugs not violate metabolism of folic acid in humans?
3. What are the additional properties of sulfamethoxazole when it is combined with trimethoprim, the azo compounds of sulfanilamide with salicylic acid? In what diseases are such drugs used?
4. Why are sulfa drugs less commonly used for bacterial infections?
5. Modern fluoroquinolones have low toxicity, but there is a point of view that fluoroquinolones, especially generations II and III, should be used as reserve drugs. Why is it dangerous to widely use fluoroquinolones in clinical practice?
6. What is the effect of isoniazid on pyridoxine metabolism in mycobacterium tuberculosis and in humans?
7. Why does the choice of isoniazid dose depend on the genetic characteristics of the patient?
8. Why do acyclovir and other nucleoside analogues affect only cells infected by herpes virus and do not have effect on normal human cells?

Task 3.

a. Match each antiviral drug with the appropriate description.

A. Enfuvirtide	1. An integrase inhibitor
B. Efavirenz	2. An inhibitor of HIV fusion with host cells
C. Abacavir	3. Non-nucleoside reverse transcriptase inhibitors
D. Aciclovir	4. Nucleoside reverse transcriptase inhibitors
E. Ratelgravir	5. DNA polymerase inhibitors

b. Match each antibacterial drug with the appropriate clinical use

A. Sulfasalazine	1. Toxoplamsosis
B. Ethambutol	2. Inflammatory bowel disease

C. Ciprofloxacin	3. Mycobacterial infections
D. Co-trimoxazole	4. Acute cystitis

Task 4. Topics for report.

1. Drugs for the treatment of Hepatitis B and C.
2. Treatment and prevention of influenza virus caused by the H1N1 (swine flu) and H5N1 (avian flu).
3. Antiretroviral therapy (ART): what does it do?
4. HIV vaccine: truvada for PrEP (pre-exposure prophylaxis).
5. Artemether and its derivatives as the antimalarial drugs.

QUESTIONS AND TASKS IN CLASS

Task 1. Analyze the tasks that reflect the mechanisms and features of the action of sulfonamides, quinolones, antituberculosis, antiviral, antimalarial drugs (the collection of graphic tasks).

Task 2. Analyze case tasks.

1. A 75-year-old man with chronic obstructive pulmonary disease is diagnosed with suspected influenza based on his complaints of flu-like symptoms that began 24 hours ago. What agent is most appropriate to initiate for the treatment of influenza?
2. A 43-year-old woman with AIDS started a highly active antiretroviral therapy with zidovudine, lamivudine, and ratelgavir. Which of the following reasons best explains an important rationale for triple therapy in AIDS patients?
   a. To destroy both the replicating and nonreplicating viral genome
   b. To increase the half-life of any one of the agents
   c. To delay the appearance of drug resistance
   d. To inhibit each other's drug metabolism
   e. To expand the antimicrobial efficacy to opportunistic infections
3. A 44-year-old woman complained of blurred vision and inability to distinguish green objects from red objects. The woman, recently diagnosed with cavitary pulmonary tuberculosis, had been receiving a three-drug combination regimen for 2 months. An eye examination indicated a narrowing of her visual field. What drug most likely caused these adverse effects?

4. A 64-year-old alcoholic woman suffering from pulmonary tuberculosis complained of anorexia, nausea, and abdominal discomfort. She had been receiving isoniazid, ethambutol, and rifampin for 2 months. Lab results revealed an aspartate aminotransferase level of 330 U/L (normal 8−20 U/L). Explain the reason for the patient's signs and symptoms.
5. A 56-year-old woman complained to her physician of tiredness and fatigue. She also noticed that her urine had become dark. Medical history was significant for glucose-6-phosphate dehydrogenase deficiency and recurrent urinary tract infection. Five days earlier, the patient complained of burning sensation upon urination and started the prescribed antimicrobial therapy. Urinalysis revealed bilirubin and urobilinogen. What drug could have caused the patients signs and symptoms?
6. A 34-year-old black man living in the United States was planning to visit his seriously ill father who lives in Uganda. He was going to be accompanied by his wife and son. Knowing that chloroquine-resistant strains of malaria are present in Uganda, which drug used alone would be the most appropriate prophylaxis for the man, his wife, and their son before entering Uganda?

Task 3. Answer the test questions (in the computer lab).

Lesson 18
Final class about antimicrobial, antiviral and antiparasitic agents

Learning objectives are to check skills in prescription writing; to check and fix knowledge about the mechanisms of action, classification, pharmacokinetics, use, side effects of agents, drug poisoning in the frame of the topics which have been studied.

QUESTIONS FOR PREPARATION FOR THE FINAL LESSON

1. Antimicrobial agents: classification, differences between antiseptic and chemotherapeutic agents.
2. Halogen-containing antiseptics, oxidizing agents and detergents: mechanisms of action, use.
3. Nitrofuran antiseptics: mechanisms of action, use, side effects.
4. Acute poisoning with alkalis, strong acids and iodine: pathogenesis, symptoms, treatment.
5. Antibiotics: requirements for antibiotics; classification by nature of action on microorganisms and antimicrobial spectrum.
6. Classification of antibiotics by the mechanism of action. Mechanisms of selective toxicity of antibiotics against microorganisms.
7. The origin, classification, mechanisms of action, antimicrobial spectrum, use, side effects, contraindications to use:
   - penicillins;
   - cephalosporins and carbapenems;
   - aminoglycosides and rifampicin;
   - tetracyclines, chloramphenicol, lincosamides;
   - macrolides.
8. Antibiotic resistance mechanisms in bacteria, methods of its prevention and overcoming.
9. Principles of rational antibiotic therapy.
10. Sulfanilamide drugs: mechanism of action, antimicrobial spectrum, principles of administration, classification.

11. The choice of sulfa drugs for infectious diseases, side effects, contraindications for use.
12. Quinolones: antimicrobial spectrum, mechanisms of action, classification, use, side effects, contraindications to use.
13. Antituberculosis drugs: classification, mechanisms of action, application, side effects.
14. Antifungal agents: classification, spectrum of antifungal actions, mechanisms of action, use, side effects.
15. Antiviral drugs for the treatment of herpes virus: antiviral spectrum, mechanisms of action, use, side effects, contraindications to use.
16. Antiviral drugs for the prevention and treatment of influenza: mechanisms of action, use, side effects, contraindications to use.
17. Interferon drugs and its inductors: origin, mechanisms of action, use, side effects, contraindications to use.
18. Antimalarial drugs: classification, mechanisms of action, use, side effects, contraindications to use.
19. Anthelmintic drugs: classification, spectrum of anthelminthic action, mechanisms of action, use, side effects, contraindications to use.

PRESCRIPTIONS

Prescribe: potassium permanganate, ethanol, nitrofural, fluconazole, metronidazole, mebendazole, praziquantel, amoxicillin + clavulanic acid, meropenem, ceftazidime, rifampicin, doxycycline, azithromycin, ciprofloxacin, isoniazid, oseltamivir, acyclovir.

PHARMACOTHERAPEUTIC QUESTIONS

1. Drug which is used to disinfect an operating field.
2. Drug for the treatment of pyogenic injury.
3. Antibiotic for the treatment of pneumonia
4. Antibiotic for the treatment of syphilis.
5. A drug for the treatment of sepsis.
6. Antibiotic for the treatment of sepsis caused by *Pseudomonas aeruginosa*.
7. Antibiotic for the treatment of dysentery.
8. Antibiotic for the treatment of typhoid fever.
9. Drug for the treatment of tuberculosis.

10. Drug for the treatment of candidiasis.
11. Drug for the treatment of invasive fungal infections.
12. Drug for the treatment of influenza A virus.
13. Drug for the prevention of influenza A virus.
14. Drug for the treatment of herpes simplex infection
15. Drug for trichomoniasis treatment.
16. Drug for cestodiasis treatment.
17. Drug for nematodoses treatment.
18. Drug for opisthorchiasis treatment.

CONTROL TASK

Answer the questions, reflecting the mechanisms and features of the action of antimicrobial, antiviral and antiparasitic agents (a computer-based test).

Lesson 19
General anesthetics, sleeping pills, ethanol

Learning objectives are to study classifications, mechanisms of action, antimicrobial spectrum, pharmacokinetics, use, side effects and contraindications to the use of general anesthetics, sleeping pills; to study and practice prescription writing.

QUESTIONS FOR PREPARATION FOR THE LESSON

1. The concept of anesthesia. Inhalation and non-inhalation anesthetics (general anesthetics). Requirements for anesthetics.
2. History of anesthesia.
3. Mechanisms of inhalation anesthesia (anesthesia theory). Stages of anesthesia.
4. Liquid (gas-forming) agents for inhalation anesthesia: physical properties, features of anesthesia, pharmacokinetics — halothane, isoflurane, sevoflurane.
5. Gas anesthetic: features of anesthesia, pharmacokinetics — dinitrogen oxide, xenon.
6. Influence of inhalation anesthetics on respiratory system, cardiovascular system, kidneys, liver and metabolism.
7. Advantages and disadvantages of inhalation anesthetics.
8. Intravenous anesthetics: mechanism of action, pharmacokinetics, use, side effects, contraindications to the use of drugs
   - short-acting — propofol;
   - medium duration of action — ketamine, thiopental sodium;
   - long-acting — sodium oxybutyrate.
9. Ethanol: physical properties, chemical structure, mechanism of action, use.
10. Resorptive action of ethanol: toxicokinetics, effects on the central nervous system, cardiovascular system, blood, digestive system and metabolism.
11. Acute ethanol poisoning: pathogenesis, symptoms, treatment.

12. Chronic alcoholism: mechanism of addiction. Drugs for treatment — disulfiram, metronidazole.
13. Sleeping pills: requirements for sleeping pills; classification
    - benzodiazepine receptor agonists — nitrazepam, oxazepam;
    - modified benzodiazepine receptor agonists (Z-preparations) — zopiclone, zolpidem, zaleplon;
    - antagonists of central H_1-receptors — doxylamine;
    - synthetic analogues of the epiphyseal hormone — melatonin.
14. Mechanisms of action, pharmacokinetics, side effects and contraindications to the use of sleeping pills.
15. Principles of choosing and prescribing hypnotics for insomnia.
16. Acute poisoning with hypnotics (benzodiazepine derivatives, barbiturates): pathogenesis, symptoms, treatment.
17. Chronic poisoning with hypnotics: mechanism of addiction, prevention of drug addiction.

PRESCRIPTIONS

1. Propofol — 1% emulsion in ampoules of 20 ml. TD: into the vein 1,5—2,5 mg/kg.
2. Nitrazepam — tablets by 0,005. TD: orally 0,005—0,01 half hour before bedtime.
3. Zolpidem — tablets by 0,005 and 0,01. TD: orally 0,005—0,01 before bedtime.
4. Flumazenil — 0,01% solution in ampoules of 5 ml. TD: into the vein 0,0005, if necessary, the injections should be repeated to DD 0,002.
5. Atropinum — 0,1% solution in ampoules of 1 ml. TD: subcutaneously, into the muscles 0,00025—0,0005.
6. Atracurium besilate — 1% solution in ampoules of 5 ml. TD: into the vein 0,3—0,6 mg/kg.
7. Ethanolum — 40, 70, 90 and 95%, 50—100 ml.

QUESTIONS AND TASKS FOR SELF-CONTROL

Task 1. Pharmacotherapeutic questions. Write the prescriptions, justifying the choice of drugs.

1. Drug for induction of anesthesia.
2. Drug for potentiated anesthesia.
3. Drug for the prevention of acute pain associated with diagnostic procedures
4. Drug that prevents heart arrest in anesthesia.
5. Drug which reduces salivation and bronchorrhoea during anesthesia.
6. Drug for warming compresses.
7. Drug for the sterilization of the surgical field.
8. Drug for disinfection of surgical instruments.
9. Drug to prevent burn blisters.
10. Drug for the treatment of presomnia.
11. Drug for the treatment of postsomnia.
12. Drug for the treatment of insomnia that does not violate the physiological structure of sleep.
13. Drug with the anti-anxiety effect for the treatment of insomnia.
14. Drug with long duration of action for the treatment of insomnia.
15. Short-acting drug for insomnia treatment.
16. Drug with a rapid onset of action to treat insomnia.
17. Antidote for hypnotics poisoning.
18. Competitive antagonist for benzodiazepine receptor agonists poisoning.

Task 2. After studying the theoretical material, answer the following questions:

1. What receptors are affected by halothane? What clinical consequences do they have?
2. It is known that dinitrogen oxide does not inhibit the respiratory and vasomotor centers. Can it be considered as absolutely safe drug?
3. What is dissociative anesthesia? What anesthetic causes it?
4. What anesthetic agents have a neuroprotective effect? What mechanisms underlie this effect?
5. Consider the structure of glutamic acid receptors. How do they function? What is anti-excitotoxic effect?

6. Consider the structure and function of GABA receptors. What anesthetic and hypnotic drugs affect GABA-A receptors?
7. Formulate the requirements for an ideal hypnotic.

Task 3.

a. Match each drug with the appropriate description.

A. Sevoflurane	1. A halogenated anesthetic that causes fast induction and recovery
B. Nitrous oxide	A drug that can trigger an attack of acute porphyria in at-risk patients
C. Thiopental	2. A drug that creates the risk of "coronary steal syndrome"
D. Isoflurane	3. This inhaled anesthetic substantially reduces the required concentration of other inhaled anesthetics given concomitantly
E. Ketamine	4. A drug that can cause a cataleptic state called dissociative anesthesia

b. Match each drug with the appropriate description.

A. Melatonin	1. An analogue of the epiphyseal hormone
B. Flumazenil	2. A competitive antagonist at benzodiazepine receptors
C. Midazolam	3. A hypnotic drug with negligible effects on sleep architecture and stages
D. Thiopental	4. The barbiturate most frequently used to induce general anesthesia
E. Zolpidem	5. A benzodiazepine with a very short half-life (about 2 hours)

Task 4. Topics for report.

1. History of narcosis.
2. W. Morton and total analgesia.
3. Minimum alveolar concentration of volatile anesthetics.
4. Structure and localization of the benzodiazepine receptor.

5. A new clinical guideline for the pharmacologic treatment of chronic insomnia in adults.
6. Racial differences in alcohol sensitivity.

QUESTIONS AND TASKS IN CLASS

Task 1. Analyze the tasks that reflect the mechanisms and features of the action of general anesthetics and sleeping pills (the collection of graphic tasks).

Task 2. Analyze case tasks.

1. A 34-year-old woman was admitted to the day surgery center for strabismus surgery. This surgery is considered highly emetogenic due to a stimulation of the vomiting center during the operative manipulation of extraocular muscles. Which anesthetic would be most appropriate for this patient?
2. A 52-year-old woman underwent hysterectomy to remove an endometrial carcinoma. Anesthesia was induced with thiopental and maintained with nitrous oxide and halothane. Why was another anesthetic, in this case halothane, added to nitrous oxide?
3. A 60-year-old man was about to undergo surgery to remove a prostate cancer. The man had been suffering from ischemic heart disease for 2 years. The anesthesiologist decided to use nitrous oxide and another general anesthetic that causes a pronounced increase in coronary blood flow with concomitant decrease in myocardial oxygen consumption and negligible effects on cardiac output. What anesthetic was most likely given with nitrous oxide for anesthesia maintenance?
4. A 57-year-old man complained to his physician that he had difficulty in falling asleep. He was a schoolteacher and needed a good night's sleep to perform effectively during the day. Zolpidem was prescribed, one tablet at bedtime. Which of the following effects on ion conductance of central nervous system neurons did the prescribed drug most likely cause?

   a. Decreased Na^+ conductance
   b. Increased Cl^- conductance
   c. Decreased K^+ conductance
   d. Decreased Ca^{2+} conductance
   e. Increased K^+ conductance

5. A 30-year-old woman was admitted to the hospital. She had slurred speech, ataxia, and altered mental status, uncoordinated muscle movements. Her skin was pale, the lips were cyanotic, the pupils were constricted. Vital signs were body temperature 37,6 C, trouble breathing, pulse — 90 beats per minute, blood pressure — 80/50. Further investigation revealed that 1 month ago the patient has been prescribed diazepam to treat insomnia. Make a diagnosis, explain the pathogenesis and symptoms of poisoning, prescribe treatment.
6. A 53-year-old woman suffered a generalized seizure and was taken to the emergency department. On admission she was extremely anxious and agitated. She reported she had no history of epilepsy. Further questioning revealed that she had a long history of drug abuse, but the day before she decided to quit and ceased taking the abused drug. Withdrawal from which of the drug most likely caused the patients seizure?
7. A 48-year-old woman became agitated and visibly tremulous and showed hallucinatory behavior 1 day after being admitted to the hospital for elective surgery. She also accused the doctors and her husband of being unsympathetic and uncaring. Which of the following statements most likely explains the reason for the patient's behavior?

   a. Benzodiazepine medication given before surgery
   b. Depressive episode triggered by the operation
   c. Ethanol withdrawal
   d. Opioid medication given before surgery
   e. Halothane anesthesia used during surgery

Task 3. Answer the test questions (in the computer lab).

Lesson 20
Antiepileptic drugs. Opioid analgesics

Learning objectives are to study classifications, mechanisms of action, antimicrobial spectrum, pharmacokinetics, use, side effects and contraindications to the use of opioids and antiepileptic drugs; to study and practice prescription writing.

QUESTIONS FOR PREPARATION FOR THE LESSON

1. Antiepileptic drugs: mechanism of action, classification
   - drugs effective for partial and tonic-clonic seizures — phenytoin, benzobarbital, carbamazepine, oxcarbazepine;
   - drugs effective for partial seizures — gabapentin, pregabalin, lacosamide;
   - drugs effective for absence — ethosuximide;
   - drugs effective for absences and myoclonic seizures —clonazepam;
   - drugs with a broad spectrum of antiepileptic action — valproic acid, lamotrigine, levetiracetam, topiramate.
2. Mechanisms of action, pharmacokinetics, choice for different forms of generalized and partial epilepsy, neuropathic pain, side effects, contraindications to the use of antiepileptic drugs.
3. Principles of the treatment of epilepsy.
4. Drugs for the treatment of symptomatic convulsive seizures: features of action and use — sodium oxybutyrate, magnesium sulfate, droperidol, diazepam, phenazepam.
5. Mechanism of nociceptive sensitivity. Antinociceptive system (opioid, cannabinoid, serotonin, GABA).
6. Opioid receptors (μ, κ, δ): ligands, localization, functional significance.
7. Opium: origin, composition.
8. Opioid analgesics: neurophysiological and psychophysiological mechanism of analgesic action.
9. Classification of opioid analgesics by the effect on opioid receptors and chemical structure:

   a) full agonists

- derivatives of phenanthrene — morphine, codeine;
- piperidine derivatives — fentanyl;
- cyclohexanol derivatives — tramadol;

b) agonists with combined action

- derivatives of phenanthrene — buprenorphine, butorphanol.

10. Influence of opioid analgesics on mental functions, sleep, autonomic and endocrine functions of hypothalamus, middle brain, medulla oblongata, spinal cord reflexes, cardiovascular system and organs with smooth muscles.
11. Pharmacokinetics of opioid analgesics.
12. The use of opioid analgesics: choice for different pain syndromes, for neuroleptanalgesia, ataralgesia. Side effects and contraindications to use.
13. Acute morphine poisoning: pathogenesis, symptoms, antagonists. Mechanism of action and use of naloxone and naltrexone.
14. Chronic poisoning with opioid analgesics: mechanism of dependence, preventive measures.
15. Non-opioid analgesics — clonidine.

PRESCRIPTIONS

1. Benzobarbitalum — tablets by 0,1. TD: orally 0,1 three times a day after a meal.
2. Carbamazepine — tablets by 0,2. TD: orally 0,2—0,4 two—three times a day with a meal.
3. Acidum valproicum — tablets by 0,3; powder in vials at 0,4. TD: 0,3 three—five times a day with a meal, into the vein 0,2—0,4 in 4 ml of water for injection.
4. Morphinum — tablets by 0,01; 1% solution in ampules of 1 ml. TD: orally and subcutaneously 0,01.
5. Trimeperidinum — tablets by 0,025; 1 и 2% solution in ampules of 1 ml. TD: orally 0,025; subcutaneously 0,01—0,02.
6. Fentanylum — 0,005% solution in ampules of 1 ml, TTS (patches) at 0,0025 and 0,01. TD: into the muscles 0,000025—0,0001; into the vein 0,000025—0,0001 in 10 ml of isotonic sodium chloride solution, apply 1 patch 1 time for 3 days.

7. Tramadol — capsules by 0,05; 5% solution in ampules of 1 and 2 ml. TD: orally, into the vein, into the muscles, subcutaneously 0,05—0,1.
8. Morphine antagonists:
   - Naloxone — 0,04% solution in ampules of 1 ml. TD: into the muscles 0,0004—0,0008; into the vein 0,0004—0,0008 in 10 ml of isotonic sodium chloride solution.
   - Atropinum — 0,1% solution in ampules of 1 ml. TD: subcutaneously 0,0005.
   - Kalii permanganas — 0,05% solution, 500 ml for the gastric lavage.
   - Carbo activatus — powder. For the gastric lavage 20,0 — 30,0 dissolve in 1 liter of water.

QUESTIONS AND TASKS FOR SELF-CONTROL

Task 1. Pharmacotherapeutic questions. Write the prescriptions, justifying the choice of drugs.

1. Drug for simple and complex partial seizures.
2. Drug for psychomotor seizures.
3. Drug for tonic-clonic seizures.
4. Drug for absence seizures.
5. Drug for stopping status epilepticus.
6. Antiepileptic drug which is used as inducer of biotransformation.
7. Drug for trigeminal neuralgia.
8. Analgesic for potentiated anesthesia.
9. Drug for prevention of pain shock in trauma.
10. Analgesic for myocardial infarction.
11. Analgesic for pain in the postoperative period.
12. Analgesic for the cancer pain relief.
13. Analgesic for renal colic.
14. Drug for neuroleptanalgesia.
15. Competitive antagonist for morphine poisoning.
16. Physiological non-competitive antagonist for morphine poisoning.
17. Chemical antagonist for morphine poisoning.
18. Physical antagonist for morphine poisoning.

Task 2. After studying the theoretical material, answer the following questions:

1. What drugs have an anticonvulsant effect? Explain their mechanisms of action and use.
2. What effect do antiepileptic drugs have on the functions of sodium and calcium neuronal channels, metabolism and functions of brain mediators? Compare the mechanisms of action of antiepileptic drugs with their clinical use.
3. What antiepileptic drugs have psychotropic effects. What is the significance of psychotropic effects during epilepsy?
4. What is an aggravation of epileptic seizures? What antiepileptic drugs can cause such effect?
5. What drugs are used for neuropathic pain?
6. Dwell on potential mechanisms underlying centralized pain and emerging therapeutic interventions.
7. Is it possible to prescribe opioid analgesics for severe chronic pain? What drugs are used for chronic pain?
8. Why is it necessary to provide gastric lavage in case of morphine poisoning which was administered IV?
9. What is euphoria and dysphoria?
10. Mechanisms of opioid dependence.

Task 3.

a. Match each drug with the appropriate description.

A. Carbamazepine	1. This drug is effective in all forms of epilepsy in all age groups
B. Lamotrigine	2. This drug binds selectively to a synaptic vesicular protein (SV2A protein), altering the synaptic release of glutamate and gamma-aminobutyric acid (GABA)
C. Levetiracetam	3. This drug inhibits gamma-aminobutyric acid (GABA) reuptake in both neurons and glia, enhancing GABAergic transmission
D. Tiagabine	4. This drug inhibits glutamate release

E. Valproic acid	5. This drug affects membrane excitability by an action on voltage-dependent sodium channels

b. Match each drug with the appropriate description.

A. Buprenorphine	1. A partial agonist at μ (mu) opioid receptors and antagonist at κ (kappa) opioid receptors
B. Codeine	2. A full opioid agonist with the highest oral bioavailability used in the treatment of heroin addiction.
C. Loperamide	3. A drug with very weak opioid activity used in the treatment of diarrhea
D. Methadone	4. A weak agonist at opioid receptors which is used to treat cough
E. Naloxone	5. A drug with high affinity but no intrinsic activity at opioid receptors

Task 4. Topics for report.

1. The new antiepileptic drugs: their neuropharmacology and clinical indications
2. New approaches in the treatment of neuropathic pain.
3. TRPV1 agonist: capsaicin.

QUESTIONS AND TASKS IN CLASS

Task 1. Analyze the tasks that reflect the mechanisms and features of the action of opioids and antiepileptic drugs (the collection of graphic tasks).

Task 2. Analyze case tasks.

1. A 64-year-old man suffering from advanced heart failure was admitted to the emergency department because of extreme dyspnea over the past hour. After physical examination, a diagnosis of impending pulmonary edema was made, and an appropriate therapy was prescribed that included the intramuscular injection of morphine. Explain the actions which most likely contributed to the therapeutic effect of the drug in the patient's disorder.
2. A 39-year-old woman was admitted to the hospital because of gripping and burning abdominal pain that increased over the past 4 hours. The patient was suffering from stage 4 ovarian cancer metastatic to the

pelvis. A treatment with sustained release morphine was started. Which of the following effects on the patient's respiratory system would be expected during the first few days of therapy?

a. Stimulation of the cough reflex
b. Bronchodilation
c. Increased vital capacity
d. Decreased tidal volume
e. Increased rate of breathing

3. A 28-year-old woman was admitted unconscious to the emergency department. A friend stated that the woman used analgesic which was prescribed after multiple fractures sustained in a car accident. She had self-injected a drug approximately 45 minutes prior to admission. Vital signs were blood pressure 90/50, heart rate 40 bpm, respirations 5/min. Physical examination showed cyanosis and pinpoint pupils. What drug did the woman most likely take? Explain the symptoms of overdose.
4. A 32-year-old woman complained to her physician that two breakthrough seizures occurred last week. One month earlier the woman was diagnosed with simple partial seizure and started treatment with an antiepileptic drug. The physician increased the dose of the drug, thinking that the decreased effect was most likely because the drug is a potent enzyme inducer and can induce its own metabolism. What drug did the patient most likely take?
5. A 47-year-old woman complained to her physician of blurred and double vision. She had been suffering from a central nervous system disorder and had been receiving a drug treatment for 6 months. Physical examination showed mild hirsutism, broadening of her lips and nose, and thickening and bleeding of her gums. What drug most likely caused these adverse effects?
6. A 14-month-old baby boy exhibited jerkiness of the upper limbs for a few weeks. The jerks never caused him to fall but were repeated several dozens of times each day, including when falling asleep. An electroencephalogram showed that the jerks were combined in all instances with spike waves, and that there was an increase of jerks and spike waves when he fell asleep. What most likely caused the patient's symptoms? Which drug would be most appropriate for this boy?

Task 3. Answer the test questions (in the computer lab).

Lesson 21
Drugs for neurodegenerative diseases. Drugs for the treatment of migraine

Learning objectives are to study classifications, mechanisms of action, antimicrobial spectrum, pharmacokinetics, use, side effects and contraindications to the use of drugs for neurodegenerative diseases and for the treatment of migraine; to study and practice prescription writing.

QUESTIONS FOR PREPARATION FOR THE LESSON

1. The importance of dopamine, acetylcholine and glutamic acid in the regulation of muscle tone and mental processes. Metabolic dysfunction in Parkinson's disease and Alzheimer's disease.
2. Antiparkinsonian drugs: mechanism of action, classification (dopaminomimetics, M-cholinoblockers, antagonists of NMDA-receptors).
3. Dopaminomimetics: mechanism of action, pharmacokinetics, use, side effects, contraindications for use in Parkinson's disease
   a) levodopa, combination of levodopa with carbidopa and benserazid;
   b) MAO inhibitors type B — selegiline, rasagiline;
   c) inhibitors of catechol-*O*-methyltransferase (COMT) — entacapone;
   d) D-receptor agonists
      - ergoline agonists — bromocriptine;
      - nonergolin agonists — pramipexole.
4. M-cholinoblockers: mechanism of action, pharmacokinetics, use, side effects, contraindications for use in Parkinson's disease — trihexyphenidyl.
5. NMDA receptor antagonists: mechanism of action, pharmacokinetics, use, side effects, contraindications to use in Parkinson's disease — amantadine.
6. Principles of the treatment of Parkinson's disease and symptomatic parkinsonism.
7. Drugs for the treatment of Alzheimer's disease: mechanism of action, side effects and contraindications for use
   - precursors of acetylcholine — choline alfoscerate;

- cholinesterase inhibitors — rivastigmine, ipidacrin;
- NMDA-receptor antagonist and AMPA-receptor agonist— memantine;
- anti-amyloid treatment strategies.

8. 5-HT-receptors: localization, functions.
9. Drugs for arresting migraine attack: mechanism of action, pharmacokinetics, side effects and contraindications for use
   - ergot alkaloids — ergotamine;
   - tryptans — sumatriptan, naratriptan, eletriptan;
   - paracetamol (acetaminophen) and NSAIDs — acetylsalicylic acid, ibuprofen, diclofenac, naproxen;
   - antiemetics — metoclopramide.
10. Pharmacotherapy of migraine in the interictal state ("the period between episodes").
11. Drugs that improve cerebral circulation: mechanisms, features of action, pharmacokinetics, use, side effects and contraindications for use
    - blockers of calcium channels of cerebral vessels — cinnarizine, piracetam + cinnarizine;
    - inhibitors of phosphodiesterase cyclic nucleotides — aminophylline, vinpocetine.
12. Drugs that selectively improve cochlear blood flow — betahistine.
13. Drugs for the symptomatic treatment of spasticity and dystonia: mechanisms of action, pharmacokinetics, application, side effects and contraindications for use
    - muscle relaxants of central action — anxiolytics (diazepam), tolperisone, baclofen, tizanidine;
    - muscle relaxants with peripheral action — botulinum neurotoxin type A.

PRESCRIPTIONS

1. Levodopum by 0,25 + Carbidopum by 0,025. TD: orally 1—2 tablets two—three times a day.
2. Pramipexole — tablets by 0,00025 and 0,001. TD: orally 0,00025—0,001 three times a day.

3. Trihexyphenidyl — tablets by 0,002. TD: orally 0,001—0,004 three—four times a day.
4. Rivastigmine — capsules by 0,0015 and 0,006; TTS (patch) by 0,009. TD: orally 0,0015—0,006 two times a day with a meal, apply 1 patch 1 time a day.
5. Sumatriptan — tablets by 0,05 and 0,1. TD: orally 0,05—0,1 once.
6. Vinpocetine — tablets by 0,005; 0,5% solution in ampules of 2 ml. TD: orally 0,005—0,01 three times a day, into the vein TD 0,01—0,02 in 1000 ml of isotonic sodium chloride solution dropwise.
7. Metoprolol — tablets by 0,05—0,1; 0.1% solution in ampoules of 5 ml. TD: orally 0,05—0,1 one or two times a day; into the vein 0,002 — 0,005 in 10 — 20 ml of 5% glucose solution slowly.
8. Aminophyllinum — tablets at 0,15; 2,4% solution in ampules at 10 ml. TD: orally 0,15 one—three times a day; into the vein 0,12—0,24 in 20 ml of isotonic sodium chloride solution.
9. Metoclopramide — tablets at 0,01; 0,5% solution in ampules of 2 ml. TD: orally 0,01 three times a day before a meal; into the muscles 0,01 one—two times a day; into the vein 0,01 in 10 ml of isotonic sodium chloride solution.

QUESTIONS AND TASKS FOR SELF-CONTROL

Task 1. Pharmacotherapeutic questions. Write the prescriptions, justifying the choice of drugs.

1. Combination of drugs for the treatment of Parkinson's disease.
2. Drug that causes accumulation of dopamine in the brain for the treatment of Parkinson's disease.
3. Dopamine agonist for the treatment of Parkinson's disease.
4. Drug for Parkinson's disease treatment which rarely causes dyskinesia.
5. Drug for Parkinson's disease treatment which has neuroprotective effect.
6. M-anticholinergic drug for the treatment of Parkinson's disease.
7. Drug that reduces tremor for the treatment of Parkinson's disease.
8. Drug for drug-induced parkinsonism.
9. Selective inhibitor of acetylcholinesterase in the brain for treatment of Alzheimer's disease.
10. Drug that improves memory and attention in Alzheimer's disease.

11. Drug for the treatment of senile dementia.
12. Selective 5HT—receptor agonist for migraine attacks.
13. Drug for the management of vomiting in migraine.
14. Drug for the treatment of migraine in the attack-free interval.
15. Drug for the treatment of ischemic stroke.
16. Drug for the treatment of chronic cerebrovascular insufficiency.
17. Drug for hearing loss of vascular origin.
18. Drug for the treatment of traumatic brain injury.

Task 2. After studying the theoretical material, answer the following questions:

1. Name the types of dopamine receptors. Where are they located and how do they function? Consider the effects of antiparkinsonian drugs on D-receptors.
2. Compare the efficacy and toxicity of levodopa and D-receptor agonists.
3. What drugs are used for the treatment of drug-induced parkinsonism? Why?
4. There is an opinion that smokers have a lower risk of Alzheimer's disease. Is it true?
5. Why does the full opening of ion channels, regulated by NMDA receptors, depend on the function of AMPA receptors? What is long-term potentiation?
6. It is known that in Alzheimer's disease, in addition to drugs that affect the effects of mediators of the central nervous system, glucocorticoids and NSAIDs also have a therapeutic effect. Tell about the possible mechanism of action of these pharmacological groups for Alzheimer's disease.
7. What types of 5-HT receptors are known? Where are they located and how do they function? What medications are used for migraines which affect 5-HT receptors?
8. Why does sumatriptan have advantages over ergotamine as a therapeutic agent in a migraine attack?
9. Name the drugs which selectively dilate the cerebral vessels. What is the reason for their selective action?
10. What drugs have a neuroprotective effect? What is antiexitotoxic effect?

Task 3.

a. Match each drug with the appropriate description.

A. Trihexyphenidyl	1. A central muscarinic receptor blocker
B. Entacapone	2. A metabolic precursor of dopamine
C. Levodopa	3. An *N*-methyl-D-aspartate (NMDA) receptor blocker used in Alzheimer disease
D. Memantine	4. A selective monoamine oxygenase B (MAO B) inhibitor
E. Selegiline	5. A peripheral inhibitor of catechol-*O*-methyltransferase (COMT)

b. Match each drug with the appropriate description.

A. Sumatriptan	1. Triptan which is given subcutaneously, intranasally, or orally
B. Aspirin	2. A drug which binds to 5-HT_1 receptors, α receptors, and dopamine receptors
C. Frovatriptan	3. The longest-acting triptan, with a half-life of more than 24 hours
D. Ergotamine	4. A weak organic acid that irreversibly acetylates (and, thus, inactivates) cyclooxygenase

Task 4. Topics for report.

1. Huntington disease: definition, treatment.
2. Amyotrophic lateral sclerosis (ALS): definition, treatment.
3. Famous people who suffered from migraines.
4. New approaches for the treatment of Alzheimer's disease.
5. Current approaches to the treatment of Parkinson's disease.

QUESTIONS AND TASKS IN CLASS

Task 1. Analyze the tasks that reflect the mechanisms and features of the action of drugs for the treatment of neurodegenerative diseases and migraine (the collection of graphic tasks).

Task 2. Analyze case tasks.

1. A 62-year-old man complained to his physician of facial grimacing, lip smacking, and rocking of the trunk that occurred 1 to 2 hours after taking his prescribed medication. The man, who suffered from Parkinson disease, had been receiving an antiparkinson drug for 3 years. What is a type of adverse effect in this patient? Which drug most likely caused the adverse effects reported by the patient?
2. A 78-year-old man had been showing increasing memory impairment and recognition deficits over the past 2 years. Recently, he became disoriented and confused at night. Physical examination revealed an alert person oriented to place with no focal neurologic deficits. His physician prescribed a drug that might help to slow the progression of his symptoms. What is a disease presented in the patient? What drug would be appropriate for this patient?
3. A 63-year-old woman complained to her physician of frequent palpitations. The woman, recently diagnosed with Parkinson disease, had been receiving levodopa/carbidopa for 3 weeks. Subsequent exams led to the diagnosis of sinus tachycardia likely due to the antiparkinson therapy. Which of the following actions most likely mediate the adverse effect reported by the patient?
   a. Activation of cardiac dopamine receptors
   b. Decreased acetylcholine release from cholinergic terminals
   c. Activation of cardiac β receptors
   d. Blockade of cardiac M_2 receptors
4. A 64-year-old man with Parkinson disease complained of periods of a few minutes of complete immobility, followed by a sudden switch to involuntary movements, such as twitching, nodding, and jerking. The patient's current medications included levodopa/carbidopa. To reduce these rapid fluctuations, the neurologist reduced the daily dose of levodopa/carbidopa and added a drug. What type of phenomenon is presented in this patient? Which drug was most likely prescribed?
5. A 30-year-old man presented to the clinic with a 2-month history of right-side head pain recurring on a weekly basis. His headaches were usually preceded by unformed ashes of light, bilaterally, and were associated with nausea, vomiting, and photophobia. The headaches were not relieved by aspirin or ibuprofen and usually lasted all day unless he was able to sleep. A drug acting on which of the following

receptors would be most appropriate to stop the migraine attack in this patient?

a. Beta-2 adrenergic
b. GABAergic
c. M_1 cholinergic
d. 5-HT $_{1B/1D}$ serotonergic
e. Alpha-2 adrenergic
f. D_1 dopaminergic

6. A 59-year-old man with a body mass index of 42 and a long history of poorly controlled hypertension was recently diagnosed with migraine headaches. Which of the following antimigraine drugs would be contraindicated in this patient?

a. Aspirin
b. Acetaminophen
c. Ergotamine
d. Propranolol

Task 3. Answer the test questions (in the computer lab).

Lesson 22
Antipsychotic, anxiolytic and sedative agents

Learning objectives are to study classifications, mechanisms of action, antimicrobial spectrum, pharmacokinetics, use, side effects and contraindications to the use of antipsychotics, anxiolytics and sedative agents; to study and practice prescription writing.

QUESTIONS FOR PREPARATION FOR THE LESSON

1. Psychotropic drugs: classification, the history of creation.
2. Schizophrenia: positive and negative symptoms.
3. Antipsychotic agents: chemical structure, mechanism of antipsychotic and sedative action.
4. Influence of antipsychotic agents on vegetative functions (hypothermic, antiemetic, hypotensive action, changes in hormone secretion, blockade of M-cholinergic receptors).
5. Classification, mechanisms and features of the action, pharmacokinetics of antipsychotics:
   a) First generation (typical):
      - derivatives of phenothiazine — chlorpromazine, levomepromazine, pericyazine, thioridazine, perphenazine, trifluoperazine, fluphenazine;
      - derivatives of butyrophenone — droperidol, haloperidol;
      - derivatives of substituted benzamide — sulpiride;

   b) Second generation (atypical):
      - derivatives of benzodiazepine — clozapine, quetiapine, olanzapin;
      - benzisoxazole derivatives — risperidone;
      - derivatives of substituted benzamide — amisulpride;
      - derivatives of imidazolidinone — sertindole.
6. The use of antipsychotic drugs in psychiatry, anesthesiology, internal diseases.
7. Side effects of antipsychotic drugs and methods for their correction, contraindications for use.
8. Acute chlorpromazine poisoning: pathogenesis, symptoms, treatment.

9. Structure, functions and localization of GABA-receptors. The participation of benzodiazepine receptors, σ1-receptors, MT-receptors in the mechanism of action of anxiolytics.
10. Anxiolytics: mechanism of action.
11. Anxiolytics: classification, mechanism of action, pharmacokinetics, use, side effects, contraindications for use
    - benzodiazepine derivatives —diazepam, alprazolam, medazepam;
    - modified benzodiazepine — tofizopam;
    - anxiolytics with another chemical structure —c.
12. Acute poisoning with anxiolytics of the benzodiazepine group: pathogenesis, symptoms, treatment.
13. Chronic poisoning with anxiolytics: mechanisms of addiction, prevention of drug addiction.
14. Sedatives: mechanism of action, differences from anxiolytics.

PRESCRIPTIONS

1. Droperidole — 0.25% solution in ampules of 5 ml and 10 ml. TD: into the muscles 0,0025; into the vein 0,005 in 20 ml 5% glucose solution slowly.
2. Clozapine — tablets by 0,025 and 0,1. TD: orally 0,05—0,2 two—three times a day.
3. Diazepam — tablets by 0,005; 0,5% solution in ampules of 2 ml. TD: orally 0,005 one—three times a day; into the muscles 0,01; into the vein 0,01 in 20 ml isotonic sodium chloride solution.
4. Tofisopam — tablets by 0,05. TD: orally 0,05 two times a day in the first half of the day.
5. Flumazenil — 0,01% solution in ampules of 5 ml. TD: into the vein 0,0005, if necessary, the injections are repeated to DD 0,002.

QUESTIONS AND TASKS FOR SELF-CONTROL

Task 1. Pharmacotherapeutic questions. Write the prescriptions, justifying the choice of drugs.

1. Drug for psychomotor agitation.
2. Drug for the course treatment of schizophrenia.
3. Drug for neuroleptanalgesia.

4. Drug for synergistic anesthesia.
5. Drug for controlled hypothermia.
6. Drug for malignant hyperthermia.
7. Antipsychotic agent which is used in shock complex therapy.
8. Drug for the course of treatment of schizophrenia which is resistant to antipsychotics of the first generation.
9. Drug for the treatment of generalized anxiety disorder.
10. Drug for post-traumatic stress disorder.
11. Anxiolytic for anxiety without drowsiness effect.
12. Drug for phobias.
13. Drug for ataralgesia.
14. Drug for convulsions.
15. Drug for the treatment of spasticity.
16. Drug for alcohol withdrawal syndrome.
17. Drug for the treatment of status epilepticus.
18. Competitive antagonist for anxiolytic poisoning.

Task 2. After studying the theoretical material, answer the following questions:

1. Impact on which receptors underlie the antipsychotic and sedative effects of antipsychotics?
2. Indicate what effects of antipsychotics are due to their a) dopamine-blocking activity, b) adrenergic blocking activity, c) effect on 5-HT receptors.
3. What are behavior correctors? When are they prescribed?
4. Offer the ways to correct the side effects of antipsychotic drugs that do not reduce their main therapeutic effect. What kind of antagonism underlies such interaction?
5. What antipsychotics rarely cause parkinsonism and hyperprolactinemia? Why?
6. What antipsychotic agent can be prescribed for tardive dyskinesia, which occurred after long-term use of haloperidol?
7. What effect is common for antipsychotic and anxiolytic drugs?
8. Antianxiety, anticonvulsant, sedative, hypnotic, and muscle relaxant effects of anxiolytics have a common mechanism. What is this mechanism?

9. What is the difference between peripheral muscle relaxants and anxiolytics for the myorelaxation?

Task 3.

a. Match each drug with the appropriate description.

A. Clozapine	1. A typical antipsychotic drug which can cause obstructive jaundice
B. Fluphenazine	2. An atypical antipsychotic drug which is effective in treatment-resistant group of patients
C. Haloperidol	3. An antipsychotic drug with high potency
D. Chlorpromazine	4. An antipsychotic from phenothiazine class which does not cause obstructive jaundice

b. Match each drug with the appropriate description.

A. Midazolam	1. Benzodiazepine with long (24—48h) duration of action used as anxiolytic, muscle relaxant and anticonvulsant
B. Lorazepam	2. An ultrashort-acting drug which is used as intravenous anaesthetic
C. Diazepam	3. A short-acting (12—18 h) drug which is used as hypnotic
D. Buspirone	4. A medium-acting (24 h) drug which is used as anxiolytic
E. Alprazolam	5. A partial agonist at 5-HT_{1A} receptors which is used to treat generalized anxiety disorders

Task 4. Topics for report.

1. History of psychopharmacology.
2. Animal models of schizophrenia.
3. Future developments: modafinil as antipsychotic drug.
4. Measurement of anxiolytic activity: animal models of anxiety and test on humans.
5. Functions of σ1-receptors.

QUESTIONS AND TASKS IN CLASS

Task 1. Analyze the tasks that reflect the mechanisms and features of action of antipsychotic, anxiolytic and sedative agents (the collection of graphic tasks).

Task 2. Analyze case tasks.

1. A 17-year-old boy presented with brief episodes of protruding tongue, grimacing, and spasmodic torticollis on day 2 after admission to the psychiatric emergency department. The patient was brought there by the police because of assaultive behavior toward his mother. He struck her after a heavy drinking bout because he thought she was about to kill him with a knife. A drug treatment was started to control his assaultive behavior, and he received three intramuscular injections over 24 hours. Which drug most likely caused the adverse effects reported by the patient? What adverse effect is presented in this patient?
2. A 39-year-old man, a resident in a psychiatric unit because of disorganized schizophrenia, presented with profound lack of motivation, remarkably blunted affect, paucity of speech, and psychomotor retardation. He had been hospitalized three times since his diagnosis, and had been treated with haloperidol, chlorpromazine, and risperidone but had only a partial response to each medication. What psychotropic drug would be most appropriate to try at this stage and why?
3. A 24-year-old woman complained to her physician of amenorrhea of 2 months' duration and of a white discharge from her breasts during the past week. The woman had been on haloperidol and paroxetine for 3 months to treat a schizoaffective disorder. She was medication-compliant, and her illness was well controlled. Explain the mechanism which was most likely responsible for the patient's symptoms?
4. A 33-year-old woman was brought to the emergency department with increased agitation and confusion. Physical examination revealed a temperature of 40°C (104°F), pulse of 125 bpm, labile blood pressure, profuse diaphoresis, sialorrhea, and muscle rigidity. The woman, recently diagnosed with schizophrenia, had started a therapy a few days previously. What adverse effect is presented in this patient? Which drug most likely caused the patient's syndrome?

5. A 41-year-old man was admitted to a psychiatric hospital because of worsening of his psychosis. The man was recently diagnosed with paranoid schizophrenia and had been treated with risperidone without success. A new treatment was started. One week later, a blood test gave the following results:
   - White blood cell count: 1200/mm3 (normal 4500−11,000/mm3)
   - Neutrophils 12% (normal 54−62%)
   - Red blood cell count: 4.3 million/mm3 (normal 4,0−5,5 million/mm3)
   - Platelet count: 145,000/mm3 (normal 150,000−400,000/ mm3)
   - Hemoglobin (Hb): 15 g/dL (normal >12 g/dL)

   What drug did the patient most likely receive as the new treatment? What is the specific adverse effect caused by this drug?
6. A 56-year-old homeless alcoholic man was brought to the emergency department by police, who found him wandering in the street. The man was nauseated, tremulous, and hallucinating. He stated he was out of money and unable to buy his usual daily amount of whiskey. What would be an appropriate drug to treat the acute alcohol withdrawal of this patient?

Task 3. Answer the test questions (in the computer lab).

Lesson 23
Antidepressants, psychostimulants, nootropic drugs

Learning objectives are to study classifications, mechanisms of action, antimicrobial spectrum, pharmacokinetics, use, side effects and contraindications to the use of antidepressants, psychostimulants, nootropic drugs; to study and practice prescription writing.

QUESTIONS FOR PREPARATION FOR THE LESSON

1. Antidepressants: general characteristics, spectrum and mechanism of psychotropic action.
2. Antidepressants: classification, chemical structure, mechanism of action, indications, side effects and contraindications for use
   a) nonselective monoamine reuptake inhibitors
      - tricyclic antidepressants — amitriptyline, imipramine;
      - tetracyclic antidepressants — maprotiline;
      - antidepressants with another chemical structure — venlafaxine, duloxetine;

   b) selective serotonin reuptake inhibitors — paroxetine, sertraline, fluvoxamine, fluoxetine;
   c) MAO inhibitors
      - irreversible inhibitors — phenelzine, nialamide;
      - reversible inhibitors — moclobemide;

   d) atypical antidepressants — mirtazapine, tianeptine, trazodone, agomelatine.
3. Lithium drugs: mechanism of action, use, side effects and contraindications for use — lithium carbonate.
4. Psychostimulants: characteristic, classification.
5. Neurophysiological mechanism of action of psychomotor stimulants: influence on the brain, emotional-motivational response, motor skills.
6. The influence of psychomotor stimulators on psychophysiological processes: memory, attention, the quality of mental work.
7. Psychomotor stimulators: mechanism of action, use, side effects and contraindications
   - derivatives of sidnonimine — mesocarb.

8. Natural sources, chemical structure, spectrum and mechanism of psychostimulating action of caffeine; influence of caffeine and methylxanthines (theophylline, theobromine) on functions of the cardiovascular system, kidneys, digestive system; use, side effects, contraindications to the use of methylxanthines.
9. Acute and chronic poisoning with amphetamine and caffeine: pathogenesis, symptoms, treatment.
10. Psychostimulants-adaptogens: origin, active substances, mechanisms, features of action, application
    - products of plant origin — drugs of rhodiola rosea, levsea, eleutherococcus, aralia, ginseng;
11. Nootropics (neurometabolic stimulants): mechanism of action, application, side effects, contraindications to use, differences from psychostimulants.
    - GABA derivatives — gamma-aminobutyric acid, aminophenylbutyric acid, nicotinylgamma-aminobutyric acid;
    - piracetam.
12. Analeptics: general characteristic, classification by mechanism of action and influence on various parts of the central nervous system
    - direct stimulants of the respiratory center — caffeine;
    - analeptic with reflex action (N-cholinomimetics) — cytisine varenicline;
    - analeptics with direct and reflex action — camphor, nikethamide.
13. Use, side effects and contraindications of analeptics.

PRESCRIPTIONS

1. Sertraline — tablets by 0,05 and 0,1. TD: orally 0,025—0,2 once a day.
2. Coffeinum — tablets by 0,1 and 0,2; 10 and 20% solution in ampules of 1 and 2 ml. TD: orally 0,1—0,2 two—three times a day in the first half of the day; subcutaneously 0,1—0,2.
3. Pyracetam — capsules by 0,4; coated tablets by 0,8; 20% solution in ampules of 5 ml. TD: orally 0,4—0,8 three times a day; into the vein 1,0—2,0 in 250 ml 5% glucose solution 1—2 times a day.
4. Norepinephrinum — 0,2% solution in ampoules of 1 ml. TD: into the vein 0,004—0,008 in 1 000 ml of 5% glucose solution dropwise.

QUESTIONS AND TASKS FOR SELF-CONTROL

Task 1. Pharmacotherapeutic questions. Write the prescriptions, justifying the choice of drugs.

1. Drug for the treatment of bipolar affective disorder.
2. Drug for somatization depression.
3. Drug for depression in combination with pain syndrome.
4. Drug for panic attacks.
5. Psychostimulant for asthenia.
6. Physiological antagonist for acute alcohol intoxication.
7. Drug for migraine attacks.
8. Drug for consequences of traumatic brain injury (TBI).
9. Drug for coma.
10. Drug with the awakening effect for the termination of anesthesia.
11. Drug for chronic fatigue syndrome.
12. Drug for dizziness.
13. Drug for vascular collapse, with central effect.
14. Drug for cardiovascular collapse with peripheral effect.
15. Drug for chronic arterial hypotension.
16. Cardiotonic drug for heart failure.
17. Drug for the prevention of pressure ulcers.

Task 1. After studying the theoretical material, answer the following questions:

1. What is “neuroplasticity”? How does it change with depression and under the influence of antidepressants?
2. Which antidepressants have a multitarget effect? How to evaluate this action — as a medical or adverse effect?
3. Name antidepressants with additional sedative or psychostimulant effects. Why should these effects be considered when prescribing antidepressants?
4. What is the role of σ1-receptors in the mechanism of antidepressant action?
5. What is the purpose to prescribe psychostimulants-adaptogens for diabetes, immunodeficiency states, cancer?

6. Explain the mechanism of action of nootropic drugs in violation of cerebral circulation; vertigo; chronic fatigue syndrome. Why are nootropic drugs ineffective in healthy people?
7. What nootropic drugs can be prescribed to reduce cognitive disorders in a patient with epilepsy?

Task 3.

a. Match each drug with the appropriate description.

A. Amitriptyline	1. A drug with pronounced anticholinergic properties
B. Fluoxetine	2. A nonselective monoamine oxidase inhibitor
C. Phenelzine	3. An active metabolite of this drug has a half-life of about 10 days
D. Selegiline	4. A selective monoamine oxidase inhibitor type A
E. Trazodone	5. A serotonin 5-HT_{2A} presynaptic receptor blocker

b. Match each drug with the appropriate description.

A. Amphetamine	1. A naturally occurring xanthine derivative, increasing alertness and producing agitation
B. Caffeine	2. A psychostimulant which acts by releasing monoamines from nerve terminals in the brain
C. Piracetam	3. A nootropic drug in the racetams group which has neuroprotective and anticonvulsant properties and is reported to improve neural plasticity

Task 3. Topics for report.

1. Theories of depression.
2. Future antidepressant drugs.
3. N-cholinomimetics for smoking cessation.
4. Functions of purine receptors.
5. Brain stimulation therapies.

QUESTIONS AND TASKS IN CLASS

Task 1. Analyze the tasks that reflect the mechanisms and features of action of antidepressants, psychostimulants, nootropic drugs (the collection of graphic tasks).

Task 2. Analyze case tasks.

1. A 25-year-old woman visited a psychiatrist because she felt very anxious when she had to eat or drink in public. She acknowledged that her ideas of being watched by others were irrational, but she could not get beyond them. She also realized that alcohol helped her cope with her anxiety, and she had started drinking two or three glasses of brandy every day. After further questioning, a preliminary diagnosis was made, and cognitive behavioral therapy was prescribed, together with a pharmacological treatment. Which of the following drugs would be appropriate for this patient?
   a. Diazepam
   b. Zolpidem
   c. Bupropion
   d. Haloperidol
   e. Paroxetine
2. A 56-year-old woman with a long history of major depressive disorder was brought unconscious to the emergency department after her husband discovered she had taken several pills of amitriptyline in a suicide attempt. Which symptoms did the patient most likely show? Describe poisoning with tricyclic antidepressants.
3. A 53-year-old woman with a long history of depression was admitted to the hospital because of agitation, insomnia, and tremors. She had been taking fluoxetine, lorazepam, and mirtazapine for several months. The doses of fluoxetine and mirtazapine had just been increased. Physical examination showed a confused patient with hyperhidrosis, hyperreexia, and myoclonus but without focal neurologic deficits. Vital signs were blood pressure 105/60 mm Hg, heart rate 130 bpm, respirations 32/min, body temperature 39,8°C (103,8°F). Qualitative plasma tests for alcohol, opioids, benzodiazepines, and tricyclic antidepressants were negative. An electrocardiogram indicated sinus tachycardia. A brain computed tomography scan was normal. Which

disorder most likely caused the patients signs and symptoms? Indicate therapy for this case.

4. A 36-year-old woman presented at an outpatient psychiatric clinic complaining of extreme lethargy and depressed mood for the past 5 weeks. On interview she also reported an intense fear of being in confined spaces, and she carefully avoided elevators and traveling by airplane. Her psychiatric history indicated two similar episodes in the past, treated, respectively, with fluoxetine and venlafaxine, but with negligible results. After further questioning, a diagnosis of depression with atypical features was made. Which drug would be appropriate for the patient?
5. A 30-year-old woman was brought to a psychiatric hospital by her parents because she had been in bed most of the day for the last 2 weeks. The woman was admitted to the hospital 4 months ago because of an acute manic episode and was discharged on valproic acid with a favorable response. On questioning, she said she discontinued her therapy 2 week ago because she felt cured, but now she admitted she was depressed most of the time and wanted to die. The patient was dismissed from the hospital 1 week later with an appropriate maintenance therapy. Which drug would be appropriate for the patient at this time?

Task 3. Answer the test questions (in the computer lab).

Lesson 24
Final class about drugs affecting the central nervous system

Learning objectives are to check skills in prescription writing; to check and fix knowledge about the mechanism of action, classification, pharmacokinetics, use, side effects of agents, drug poisoning in the frame of topics which have been studied.

QUESTIONS FOR PREPARATION FOR THE FINAL LESSON

1. Inhalation anesthetic drugs: classification, mechanism of action, stages of anesthesia.
2. Liquid (gas-forming) inhalation anesthetic agents: mechanism of action, effects on vegetative functions and metabolism.
3. Non-inhalation anesthetic agents: classification, mechanism of action, use, side effects, contraindications to use.
4. Acute ethanol poisoning: pathogenesis, symptoms, treatment.
5. Hypnotic drugs: classification, mechanism of action, side effects, contraindications to use.
6. Treatment of insomnia. The choice of sleeping pills for different types of insomnia.
7. Acute and chronic hypnotic poisoning.
8. Antiepileptic drugs: classification, mechanism of action, side effects, contraindications to use.
9. Opioid analgesics: opioid receptors, mechanism of analgesic action, classification.
10. Use, side effects and contraindications to the use of opioid analgesics.
11. Acute and chronic opioid analgesic poisoning.
12. Antiparkinsonian drugs: mechanism of action, classification, side effects.
13. Mechanism of action, side effects, contraindications of M-anticholinergics and NMDA-receptor antagonists used in Parkinson's disease.

14. Mechanism of action, side effects and contraindications to the use of drugs for the treatment of Alzheimer's disease.
15. Mechanism of action, side effects and contraindications to the use of drugs for the treatment of migraine.
16. Psychotropic drugs: principles of action, classification, use.
17. Antipsychotics: classification, chemical structure; mechanism of action and use.
18. Anxiolytics: classification; mechanism of action, use and side effects, contraindications to use.
19. Acute and chronic anxiolytic poisoning.
20. Antidepressants: classification; mechanism of action.
21. Antidepressants — monoamine reuptake inhibitors: classification, mechanism of action, use, side effects, contraindications to use.
22. Antidepressants — MAO inhibitors: classification, mechanism of action, use, side effects, contraindications to use.
23. Psychostimulants: classification; mechanism of action, use, side effects.
24. Caffeine: the origin, mechanism action, use, side effects, contraindications to the use.
25. Analeptic: classification, mechanisms of action, use, side effects, contraindications to use.

PRESCRIPTIONS

Prescribe: propofol, zolpidem, flumazenil, benzobarbital, carbamazepine, valproic acid, morphine, fentanyl, tramadol, naloxone, levodopa+carbidopa, pramipexole, rivastigmine, sumatriptan, vinpocetine, droperidol, clozapine, diazepam, sertraline, caffeine, piracetam.

PHARMACOTHERAPEUTIC QUESTIONS

1. Drug for non-inhalation anesthesia.
2. Drug for the treatment of presomnia.
3. Drug for neuroleptanalgesia.
4. Drug for the course of treatment of epilepsy.
5. Drug for stopping the status epilepticus.
6. Drug for trigeminal neuralgia.
7. Analgesic for the prevention of shock in case of injury.

8. Analgesic for myocardial infarction.
9. Drug for the treatment of Parkinson's disease.
10. Drug for the treatment of Alzheimer's disease.
11. Drug for the treatment of migraine.
12. Drug for relieving psychomotor excitement.
13. Drug for the course of treatment of schizophrenia.
14. Antipsychotic agent used in complex shock therapy.
15. Drug for anxiety.
16. Drug for depression.
17. Drug for asthenia.
18. Drug which stimulates respiratory center in case of poisoning.

CONTROL TASK

Answer the questions, reflecting the mechanisms and features of action of drugs affecting the central nervous system (a computer-based test).

Lesson 25
Cardiotonic and antiarrhythmic drugs

Learning objectives are to study classifications, mechanism of action, antimicrobial spectrum, pharmacokinetics, use, side effects and contraindications to the use of cardiotonic and antiarrhythmic drug; cardiac glycoside toxicity; to study and practice prescription writing.

QUESTIONS FOR PREPARATION FOR THE LESSON

1. Characteristics of cardiac glycosides. Cardiac glycoside-containing plants.
2. Pharmacodynamics of cardiac glycosides: mechanism of action, influence on the heart contraction and on the conduction system of the heart.
3. Effect of cardiac glycosides on hemodynamics in normal condition and in heart failure; diuretic action.
4. Pharmacokinetics of cardiac glycosides, classification:
   a) medium polarity and lipophilicity — digoxin;
   b) polar water-soluble — strophanthin-K (ouabain).
6. Mechanism of action and pharmacokinetics of digoxin.
7. Indications, side effects and contraindications to the use of digoxin,
8. Glycoside intoxication (transitional and toxic stages): pathogenesis, symptoms, treatment. Digoxin immune Fab.
9. Nonsteroidal cardiotonic drugs: mechanism of action and the use of levosimendan.
10. Antiarrhythmics: classification
    a) Class I — sodium channel blockers
       - IA — drugs that prolong the effective refractory period (ERP) — procainamide;
       - IB — drugs that reduce ERP — lidocaine;
       - IC — drugs that have a multidirectional impact on ERP, — propafenone;
    b) Class II — β-adrenoblockers — propranolol, atenolol, metoprolol, esmolol;

c) Class III — potassium channel blockers prolonging ERP — amiodarone, sotalol;

d) Class IV — calcium channel blockers — verapamil.

11. Unclassified antiarrhythmic drugs
    - adenosine;
    - potassium and magnesium asparaginate.
12. Mechanism of action, pharmacokinetics of antiarrhythmic agents; choice for different forms of supraventricular and ventricular arrhythmias, side effects and contraindications to use. Arrhythmogenic effect of antiarrhythmic drugs.
13. Antiarrhythmic effect of drugs used to treat bradycardia — atropine.

PRESCRIPTIONS

1. Digoxinum — tablets by 0,00025; 0,025% solution in ampules of 1 ml. TD: orally 0,000125—0,00025 one—two times a day; into the vein 0,00025 in 10—20 ml 5% glucose solution slowly.
2. Procainamide — tablets by 0,25; 10% solution in ampules of 5 ml. TD: orally 0,25—0,5 every 4 hours; into the vein 0,1—0,5 in 20 ml 5% glucose solution slowly.
3. Lidocainum — 2% solution in ampules of 10 ml. TD: into the vein 0,05—0,1 in 10 ml of isotonic sodium chloride solution slowly, then dropwise in 500 ml of isotonic sodium chloride solution to DD 2.0.
4. Amiodarone — tablets by 0,2; 5% solution in ampules of 3 ml. TD: orally 0,2—0,4 two times a day before a meal; into the vein 0,25—0,5 in 250 ml 5% glucose solution dropwise.
5. Verapamil — coated tablets by 0,04 and 0,08; 0,25% solution in ampules of 2 ml. TD: orally 0,04—0,08 three — four times a day; into the vein 0,005—0,01 in 100 ml of isotonic sodium chloride solution slowly.
6. Metoprolol — tablets by 0,05 — 0,1; 0,1% solution in ampoules of 5 ml. TD: orally 0,05 — 0,1 one or two times a day; into the vein 0,002 — 0,005 in 10—20 ml of 5% glucose solution slowly.
7. Atropinum — 0,1% solution in ampoules of 1 ml. TD: subcutaneously, into the muscles 0,00025—0,0005 once to two times a day.

QUESTIONS AND TASKS FOR SELF-CONTROL

Task 1. Pharmacotherapeutic questions. Write the prescriptions, justifying the choice of drugs.

1. A drug for chronic heart failure.
2. A drug which is given by injection into a vein for chronic heart failure.
3. Cardiac glycoside for atrial fibrillation.
4. Drug arresting hypokalemia in the glycoside toxicity.
5. Chemical antagonist for glycoside toxicity.
6. Drug for arrhythmia in the glycoside toxicity.
7. Drug for sinus tachycardia.
8. Adrenergic blocking agent for atrial fibrillation.
9. Calcium channel blocking agent for atrial fibrillation.
10. Drug for paroxysmal supraventricular tachycardia treatment.
11. Potassium drug for ventricular tachycardia treatment.
12. Drug for arrhythmia during halothane anesthesia.
13. Drug for thyrotoxic atrial fibrillation
14. Drug for arrhythmia in a patient with arterial hypertension.
15. Drug for arrhythmia in a patient with angina.
16. Drug for arrhythmia with myocardial infarction.
17. Drug for sinus bradycardia.
18. Drug for atrioventricular block.

Task 2. After studying the theoretical material, answer the following questions:

1. What is the difference between cardiotonic drugs and cardiac stimulants?
2. Why, despite the ability to increase the heart contractions, do cardiac glycosides not improve blood flow in the organs of healthy people?
3. What mechanisms of action on electrophysiological processes in the heart are common for antiarrhythmic drugs?
4. Why do antiarrhythmic drugs, both prolonging and shortening ERP, prevent circulation of the excitation wave in the myocardium?
5. Why are IB class antiarrhythmic drugs effective only for ventricular arrhythmias? Why do they not violate conductivity?
6. What antiarrhythmic drugs have a therapeutic effect only in supraventricular arrhythmias? Why?

7. Verapamil and nifedipine block L-type of calcium channels. Why is only verapamil used as an antiarrhythmic agent?
8. Why, despite the good absorption in the intestine, do propranolol and verapamil have a low bioavailability when taken orally?

Task 3.

a. Match each drug with the appropriate description.

A. Amiodarone	1. An antiarrhythmic drug which blocks L-type pf calcium channel
B. Verapamil	2. This drug acts on acetylcholine-sensitive K+ channels
C. Adenosine	3. This drug blocks inactivated Na+ channels and is the most effective antiarrhythmic agent for both supraventricular and ventricular arrhythmias
D. Quinidine	4. This drug blocks both β receptors and K+ channels
E. Sotalol	5. A class I antiarrhythmic agent (Ia) in the heart. It is a stereoisomer of quinine, originally derived from the bark of the cinchona tree

b. Match each drug with the appropriate description.

A. Digitoxin	1. This drug can cause peripheral vasodilation by blocking phosphodiesterase type 3
B. Digoxin	2. This drug can increase the synthesis of cyclic adenosine monophosphate (cAMP) in the heart
C. Dobutamine	3. A cardiac glycoside with longer half-life than digoxin
D. Milrinone	4. A drug which inhibits the Na^+-K^+-ATPase membrane pump

Task 4. Topics for report.

1. New antiarrythmyc drugs: vernakalant hydrochloride.
2. Dronedarone is an amiodarone-like compound.
3. Arrhythmogenic effect of antiarrhythmic drugs.
4. Digoxin immune Fab.

QUESTIONS AND TASKS IN CLASS

Task 1. Analyze the tasks that reflect the mechanisms and features of the action of cardiotonic and antiarrhythmic drugs (the collection of graphic tasks).

Task 2. Analyze case tasks.

1. A 78-year-old man was admitted to the hospital because of dyspnea, a nonproductive cough, and fever. The man had been receiving an antiarrhythmic drug for 2 months to treat refractory supraventricular tachycardia. A chest X-ray showed diffuse bilateral infiltrates. Bacterial, fungal, and viral cultures were negative. Which drug most likely caused the patients pulmonary disorder?
2. A 54-year-old woman was admitted to the hospital because of an episode of dizziness and near-syncope. Her medical history was significant for urinary tract infection, presently treated with ciprofloxacin. A few days earlier, she was diagnosed with atrial fibrillation and started a treatment with sotalol. An electrocardiogram strip recorded by a Holter monitor during another episode of near-syncope clarified the diagnosis. From which disorder did the patient most likely suffer?
3. A 65-year-old man was brought to the emergency department in acute distress. He was agitated, incoherent, disoriented in time and space, and seemed to be hallucinating. The patient had been suffering from severe chronic cardiac failure for 2 years, and his wife reported that she had found an empty bottle of digoxin tablets near her husbands bed. Vital signs were blood pressure 100/50 mm Hg, heart rate 45 bpm. An emergency treatment was instituted, and a drug was given intravenously. Which of the following drugs was most likely administered?

   a. Lidocaine
   b. Atropine
   c. Phenytoin
   d. Potassium chloride
   e. Digoxin immune Fab
   f. Amiodarone
4. A 61-year-old alcoholic man was admitted to the hospital with a 2-day history of epigastric pain associated with nausea and vomiting. The man

had been suffering from systolic heart failure for 1 year, and his disease was well controlled with captopril, furosemide, and digoxin. Pertinent serum data on admission were K+ 2.8 mEq/L, creatinine 3.2 mg/dL. An electrocardiogram showed a heart rate of 65 bpm with occasional premature ventricular contractions and runs of bigeminy. What would be an appropriate therapeutic adjustment for this patient?

Task 3. Answer the test questions (in the computer lab).

Lesson 26
Antianginal drugs. Lipid-lowering agents

Learning objectives are to study classifications, mechanism of action, antimicrobial spectrum, pharmacokinetics, use, side effects and contraindications to the use of antianginal drugs and lipid-lowering agents; to study and practice prescription writing.

QUESTIONS FOR PREPARATION FOR THE LESSON

1. Antianginal drugs: classification by the effect on the imbalance between the need for oxygen in the myocardium and the delivery of oxygen; medical significance.
2. Mechanism of action, pharmacokinetics, clinical use of antianginal drugs:
   a) organic nitrates
      - nitroglycerin
      - isosorbide dinitrate
      - isosorbide mononitrate

   b) molsidomine, nicorandil;
   c) calcium channel blockers
      - phenylalkylamine derivatives — verapamil;
      - 1,4-dihydropyridine derivatives
        generation I — nifedipine;
        generation II — nitrendipine, felodipine;
        generation III — amlodipine, lacidipine, lercanidipine;
      - benzothiazepine derivatives types — diltiazem.

3. Mechanism of action, pharmacokinetics, clinical use of drugs which reduce myocardial oxygen demand:
   a) β-adrenoblockers
      - nonselective β-adrenoblockers — propranolol;
      - cardioselective β_1-adrenoblockers — atenolol, bisoprolol, metoprolol;
      - β-adrenoblockers with additional vasodilating action — nebivolol;

   b) bradycardic agents (selective sinus node If channel inhibitors) — ivabradine.
4. Nitrite and nitrate poisoning: pathogenesis, symptoms, treatment.

5. Drugs that have cardioprotective action — trimetazidine, meldonium.
6. Lipid-lowering agents: mechanism of action, medical significance, classification
   - statins (3-hydroxy-3-methylglutaryl-coenzyme A reductase inhibitors) — atorvastatin, lovastatin, pravastatin, rosuvastatin, simvastatin, fluvastatin;
   - fibrates — gemfibrozil, fenofibrate;
   - nicotinic acid;
   - drugs that reduce absorption of cholesterol in the intestines — ezetemib;
7. Mechanism of action, pharmacokinetics, drugs of choice for different forms of hyperlipidemia, side effects, contraindications for the use of lipid-lowering drugs.

PRESCRIPTIONS

1. Nitroglycerinum — tablets by 0,0005; 1% oil solution in capsules by 0,0005 and 0,001. TD: sublingual 0,0005—0,001 (crush the capsule with teeth)
2. Isosorbide mononitrate — tablets by 0,02 and 0,04; modified-release capsules by 0,05. TD: orally 0,02—0,04 two times a day in the first half of the day (tablets); 0,05 once a day (capsules).
3. Nifedipine — tablets and capsules by 0,01 and 0,02. TD: orally 0,01—0,04 one—two times a day.
4. Rosuvastatine — tablets by 0,005 and 0,02. TD: 0,005—0,02 once a day during dinner.
5. Acidum nicotinicum — tablets by 0,05; coated tablets by 0,5, 1% solution in ampoules of 1 ml. TD: orally 0,05—0,1 three times a day; for the treatment of atherosclerosis 0.5 once a day in the morning after a meal; into the vein 0.01 in 10 ml of 5% glucose solution.
6. Metoprolol — tablets by 0,05 — 0,1; 0,1% solution in ampoules of 5 ml. TD: orally 0,05 — 0,1 one or two times a day; into the vein 0,002 — 0,005 in 10 — 20 ml of 5% glucose solution slowly.
7. Verapamil — coated tablets by 0,04 and 0,08; 0,25% solution in ampules of 2 ml. TD: orally 0,04—0,08 three—four times a day; into the vein 0,005—0,01 in 100 ml of isotonic sodium chloride solution slowly.

QUESTIONS AND TASKS FOR SELF-CONTROL

Task 1. Pharmacotherapeutic questions. Write the prescriptions, justifying the choice of drugs.

1. Drug for arresting angina.
2. Capsule for arresting angina.
3. Drug for the course treatment of stable angina.
4. Drug for course treatment of unstable angina.
5. Drug for myocardial infarction.
6. Drug for the treatment of IHD with thyrotoxicosis.
7. Drug for heart failure.
8. Open calcium channels blocking agent for the IHD treatment.
9. Inactivated calcium channels blocking agent for the IHD treatment.
10. Cardioselective β-adrenoceptor blocking agent for the IHD treatment.
11. Drug for the treatment of IHD with arrhythmia.
12. Statin drug for the treatment of atherosclerosis.
13. 3-hydroxy-3-methyl-glutaryl-coenzyme A reductase inhibitor for the treatment of atherosclerosis.
14. Inhibitor of lipolysis for the treatment of atherosclerosis.
15. Vitamin for the treatment of atherosclerosis.
16. Drug for hypercholesterolemia.
17. Drug for hypertriglyceridemia.
18. Drug for mixed hyperlipidemia.

Task 2. After studying the theoretical material, answer the following questions:

1. Consider mechanisms of decreased myocardial oxygen demand. What are the groups of antianginal drugs and how do they cause this effect?
2. What is a coronary steal syndrome? What drugs can cause it?
3. What antianginal agents have the greatest bioavailability — nitroglycerin with prolong action, isosorbide dinitrate or isosorbide mononitrate? Why?
4. Why does the long-term use of nitrates lead to tolerance and when is molsidomine tolerance less pronounced?
5. What drugs cause dilation of blood vessels with the participation of nitric oxide?
6. Name advantages of ivabradine.

7. Meldonium inhibits γ-butyrobetaine-hydroxylase, which converts γ-butyrobetaine to carnitine, trimetazidine inhibits the mitochondrial β-oxidation enzyme of long-chain fatty acids — 3-ketoacyl-CoA-thiolase. Why do these drugs have a cardioprotective effect? For what purpose are they used in the complex therapy of cardiovascular diseases?
8. What stages of cholesterol metabolism are affected by lipid-lowering agents?
9. What is a "pleiotropic action"? Identify the pleiotropic effects of statins and fibrates. Are they related to hypolipidemic action?

Task 3.

a. Match each antianginal drug with the appropriate description.

A. Isosorbide mononitrate	1. Extended released nitrate for chronic use
B. Nicardipine	2. This drug has no therapeutic effect on variant angina
C. Nitroglycerin	3. This drug has a good transdermal bioavailability
D. Metoprolol	4. This drug has high affinity for calcium channels of cerebral vessels
E. Verapamil	5. This drug blocks L-type Ca^{2+} channels in heart

b. Match each lipid-lowering drug with the appropriate description.

A. Cholestyramine	1. This drug can sometimes cause hypertriglyceridemia
B. Ezetimibe	2. Facial flushing is the most common adverse effect of this drug
C. Gemfibrozil	3. This drug prevents intestinal absorption of cholesterol
D. Niacin	4. This drug activates a nuclear transcription receptor
E. Lovastatin	5. HMG-CoA reductase inhibitor

Task 4. Topics for report.

1. Functions of PPAR receptors
2. Bempedoic acid (ETC-1002): ATP citrate lyase inhibitor
3. PCSK9 inhibitors: a new era of lipid lowering therapy.

QUESTIONS AND TASKS IN CLASS

Task 1. Analyze the tasks that reflect the mechanisms and features of action of antianginal and lipid-lowering drugs (the collection of graphic tasks).

Task 2. Analyze case tasks.

1. A 47-year-old man complained to his physician that he experienced mild angina attacks during exertion. The patient, recently diagnosed with exertional angina, had started a therapy with a transdermal nitroglycerin preparation 2 weeks previously. He carefully applied a new patch every morning immediately after removing the old one. Anginal attacks had disappeared completely during the first week of therapy but were back thereafter. Explain the reason for his angina episodes.
2. A 54-year-old man complained to his physician of palpitations, facial flushing, and vertigo. The man had been suffering from gastroesophageal reflux disease for 3 years. Two week earlier, he was diagnosed with exertional angina and started the prescribed therapy. Which drug most likely caused the patients symptoms?
3. A 50-year-old woman was admitted to the hospital with a 3-week history of early morning chest pain that caused her to awaken from sleep. The pain lasted 10 to 15 minutes and frequently radiated to her left arm. An exercise tolerance test failed to elicit precordial pain. A diagnosis of variant angina was made, and she was discharged from the hospital with a prescription for nifedipine. Which of the following actions most likely mediated the therapeutic effect of the drug in the patient's disease?

   a. Decreased preload and afterload
   b. Decreased myocardial contractility
   c. Increased heart rate
   d. Decreased coronary vascular tone

4. A 45-year-old man complained to his physician of muscle aches, soreness, and weakness. The patient had been suffering from duodenal ulcer for 2 years, from familial hypercholesterolemia for 5 years, and from open-angle glaucoma for 1 year. Current therapy included famotidine and sucralfate for ulcer, lovastatin for hyperlipidemia, and timolol for glaucoma. A urinalysis showed myoglobinuria. Which drug

most likely caused this and what type of disorder presented in a patient?

5. During a routine follow-up visit, a 52-year-old man was found to have the following lab results: alanine aminotransferase 120 U/L (normal 8−20 U/L), aspartate aminotransferase 108 U/L (normal 8−20 U/L). The man had been discharged from the hospital after an acute myocardial infarction 2 months earlier and was on an appropriate postdischarge therapy such as bisoprolol, rosuvastatin, isosorbide mononitrate. Which drug most likely caused the lab results?

Task 3. Answer the test questions (in the computer lab).

Lesson 27
Diuretics

Learning objectives are to study classifications, mechanism of action, antimicrobial spectrum, pharmacokinetics, use, side effects and contraindications to the use of diuretics; to study and practice prescription writing.

QUESTIONS FOR PREPARATION FOR THE LESSON

1. Diuretics: mechanism of action, classifications by the site of the action in the nephron; strength, influence on acid-base balance of blood, excretion of potassium and calcium ions.
2. Mechanism of action:
   - diuretics which increase filtration in the glomeruli (dimethylxanthines), — aminophylline;
   - diuretics that inhibit reabsorption in the proximal tubules
     inhibitors of carbonic anhydrase — acetazolamide;
   - diuretics that inhibit reabsorption in the loop of nephron
     osmotic diuretics — mannitol;
   - diuretics that inhibit reabsorption in the ascending loop of Henle
     loop (potent) diuretics — furosemide, torasemide;
   - diuretics that inhibit reabsorption in distal convoluted tubules
     thiazides — hydrochlorothiazide;
     thiazide-like diuretics — indapamide;
   - diuretics that inhibit reabsorption in distal convoluted tubules and collecting ducts
   - potassium-sparing diuretics:
     antagonists of aldosterone — spironolactone, eplerenone;
     blockers of sodium channels — triamterene.
3. Clinical uses of diuretics.
4. Use of diuretics for glaucoma, epilepsy, heart failure and hypertension.
5. Side effects and contraindications to diuretics.

PRESCRIPTIONS

1. Mannitolum — 20% solution in bottles 500 ml. TD: into the vein in form of bolus preventive dose — 0,5 g/kg, therapeutic dose — 1—1,5 g/kg.
2. Furosemidum — tablets by 0,04; 1% solution in ampules of 2 ml. TD: orally 0,04 one—two times a day; into the muscles 0,02—0,04 one—two times a day; into the vein 0,02—0,04 in 20 ml of isotonic sodium chloride solution.
3. Torasemide — tablets by 0,005 and 0,01. TD: orally 0,005—0,01 one—two times a day.
4. Hydrochlorothiazide — tablets by 0,025. TD: orally 0,025—0,05 one—two times a day for 3—7 days, then break for 3—4 days.
5. Indapamide — dragee by 0,0025. TD: orally 0,0025 in the morning before a meal.
6. Spironolactone — tablets by 0,025. TD: orally 0,025 two—four times a day.
7. Aminophyllinum — tablets at 0,15; 2,4% solution in ampules at 10 ml. TD: orally 0,15 one—three times a day; into the vein 0,12—0,24 in 20 ml of isotonic sodium chloride solution.

QUESTIONS AND TASKS FOR SELF-CONTROL

Task 1. Pharmacotherapeutic questions. Write the prescriptions, justifying the choice of drugs.

1. Diuretic for acute renal failure.
2. Diuretic for chronic renal failure.
3. Diuretic for the prevention of renal ischemia.
4. Diuretic for the acute attack of glaucoma.
5. Diuretic for a non-traumatic swelling of the brain.
6. Diuretic that improves renal blood flow in the renal artery spasm
7. Diuretic for forced diuresis.
8. Diuretic for heart failure.
9. Diuretic for hypertensive crisis.
10. Potent diuretic for the course treatment of arterial hypertension.
11. Thiazide diuretic for the course treatment of arterial hypertension.
12. Thiazide-like diuretic for course treatment of arterial hypertension.

13. Diuretic for Nephrogenic Diabetes Insipidus.
14. Diuretic for patient with cirrhosis and ascites.
15. Diuretic for hypercalcemia.
16. Diuretic for the treatment of hypocalcemia.
17. Diuretic for the treatment of hypokalemia.
18. Diuretic for hyperaldosteronism.

Task 2. After studying the theoretical material, answer the following questions:

1. What is the difference between the simport, antiport of ions in the apical membrane of nephron and similar types of transport in the basement membrane?
2. What diuretic can be used for central sleep apnea?
3. Why is mannitol a drug of choice for the prevention and treatment of acute renal failure?
4. Why can't mannitol be used for brain swelling due to a skull injury, meningitis, encephalitis?
5. What diuretics are used for the treatment of glaucoma? Why?
6. What diuretics are used for heart failure?
7. Why are diuretics the drugs of choice for arterial hypertension?
8. It is known that the diuretic action of potassium-sparing agents is moderate. What is the clinical value of this group of diuretics?
9. Identify the mechanisms of the cardioprotective action of spironolactone. With the participation of what receptors does this effect take place?
10. Why is the onset of spironolactone action 2-3 days, and the onset of triamterene action – 2-4 hours after administration?

Task 3.

a. Match each diuretic with the appropriate description.

A. Acetazolamide	1. This drug inhibits Na+ reabsorption in the proximal tubule
B. Eplerenone	2. This drug inhibits the synthesis of new Na+ channels in the collecting duct

	3.
C. Ethacrynic acid	4. This drug causes an initial extracellular volume expansion in normal subjects
D. Indapamide	5. This drug increases the renal reabsorption of Ca2+
E. Mannitol	6. This drug blocks Na+ transport channels
F. Spironolactone	7. This drug is the most likely to cause deafness

b. Match each lipid-lowering drug with the appropriate clinical use.

A. Acetazolamide	1. Clinically, this drug is a mainstay of antihypertensive medication
B. Spironaloctone	2. The diuretic of choice in reducing extracellular volume in heart failure
C. Indapamide	3. This drug is a mainstay of treatment for patients with increased intracranial pressure
D. Furosemide	4. A drug which is used in the prophylaxis of acute mountain sickness
E. Mannitol	5. This drug is particularly effective in clinical situations associated with secondary hyperaldosteronism

Task 4. Topics for report.

1. Ethnic differences in response to diuretics.
2. Pleiotropic effects of diuretics.
3. Cardioprotective effects of spironolactone.

QUESTIONS AND TASKS IN CLASS

Task 1. Analyze the tasks that reflect mechanisms and features of action of diuretics (the collection of graphic tasks).

Task 2. Analyze case tasks.

1. A 66-year-old woman suffering from systolic cardiac failure was brought to the emergency department because of a sudden onset of extreme dyspnea. She presented with cyanosis, tachypnea, hyperpnea, restlessness, anxiety, and a sense of suffocation. Cough was prominent and produced pink-tinged, frothy sputum. Pulse was thready and fast (120 bpm), blood pressure 80/45 mm Hg, and rales were audible at the

lung bases. Which drug was most likely included in the immediate medical treatment of this patient?

2. A 54-year-old alcoholic man was admitted to the emergency department with a 2-week history of nausea, vomiting, and lower abdominal cramps. Physical examination revealed an afebrile, jaundiced, and cachectic male in moderate distress. The abdomen appeared very tense with prominent veins, and 2+ ascites was noted by shifting dullness and a fluid wave. Pertinent serum values on admission were Na+ 144 mEq/L (normal 136−145 mEq/L); K+ 2,9 q/L (normal 3,−5,0 mEq/L); bicarbonate 34 mEq/L (normal 22−28 Eq/L); albumin 2,3 g/dL (normal 3,3−4,8 mEq/L). What diuretics would be the drug of choice for this patient?
3. A 75-year-old woman with hypertension is being treated with a thiazide. Her blood pressure responds well and reads at 120/76 mm Hg. After several months on the medication, she complains of being tired and weak. An analysis of the blood indicates low values for which of the following?

   a. Calcium
   b. Glucose
   c. Potassium
   d. Sodium

4. A new diuretic is being studied in human volunteers. Compared with placebo, the new drug increases urine volume, increases urinary Ca^{2+}, increases plasma pH, and decreases serum K^{+}. If this new drug has a similar mechanism of action to an established diuretic, it probably:

   a. Blocks the NaCl cotransporter in the DCT;
   b. Blocks aldosterone receptors in the CT;
   c. Inhibits carbonic anhydrase in the PCT;
   d. Inhibits the Na+/K+/2Cl— cotransporter in the TAL;
   e. Acts as an osmotic diuretic.

Task 3. Answer the test questions (in the computer lab).

Lesson 28
Drugs affecting the blood pressure

Learning objectives are to study classifications, mechanism of action, antimicrobial spectrum, pharmacokinetics, use, side effects and contraindications to the use of drugs affecting blood pressure; to study and practice prescription writing.

QUESTIONS FOR PREPARATION FOR THE LESSON

1. Antihypertensive drugs: mechanism of action; classification.
2. Antihypertensive drugs: mechanism of action, pharmacokinetics, use, side effects, contraindications
   a) drugs reducing the excitability of the vasomotor center and sympathetic tone
      - central α_2-adrenomimetics — clonidine, methyldopa;
      - I_1-imidazoline receptor agonists — moxonidine, rilmenidine;

   b) adrenergic blockers
      - α_1-adrenoblockers — prazosin, doxazosin;
      - β-adrenoblockers — propranolol, atenolol, metoprolol, bisoprolol;
      - α, β-adrenoblockers — carvedilol;

   c) calcium channel blockers
      - phenylalkylamine derivatives — verapamil;
      - 1,4-dihydropyridine derivatives
        generation I — nifedipine;
        generation II — nitrendipine, felodipine;
        generation III — amlodipine, lacidipine, lercanidipine;
      - benzothiazepine derivatives types — diltiazem.

   d) arterial and venous vasodilators — sodium nitroprusside.
3. The use of diuretics for the treatment of arterial hypertension.
4. Drugs affecting functions of the renin-angiotensin system: mechanism of action, pharmacokinetics, use, side effects, contraindications
   a) antagonists of renin — aliskiren;
   b) inhibitors of angiotensin-converting enzyme (ACE)
      - ACE inhibitors containing sulfhydryl group — captopril;

- ACE inhibitors containing carboxyl group — lisinopril, perindopril, ramipril, trandolapril, enalapril;
- ACE inhibitors containing sulfhydryl and carboxyl groups (cardioselective)— zofenopril;
- ACE inhibitors containing phosphoryl group — fosinopril;

c) AT_1-receptor blockers — losartan, valsartan, irbesartan, olmesartan medoxomil, eprosartan.

5. Drugs of choice for the treatment of hypertension (first line drugs — β-adrenoblockers, 3rd generation of calcium channel blockers, ACE inhibitors, AT_1-receptor blockers, thiazides and thiazide-like diuretics).
6. Rational combinations of antihypertensive drugs.
7. Drugs for the treatment of hypertensive crisis — clonidine, short-acting nifedipine, magnesium sulfate, captopril, enalaprilate, furosemide.
8. Drugs for the treatment of pulmonary hypertension — antagonist of endothelin receptors bosentan;
9. Drugs increasing blood pressure: classification, mechanism of action, use, side effects and contraindications

a) drugs for the treatment of collapse and shock

- analeptics — caffeine, niketamide;
- drugs that increase cardiac output and peripheral vascular resistance — epinephrine, ephedrine, dopamine;
- drugs that increase peripheral vascular resistance — norepinephrine, phenylephrine;

b) drugs for long-term therapy of arterial hypotension

- psychostimulants-adaptogens — rhodiola, ginseng;
- adrenomimetics — phenylephrine.

PRESCRIPTIONS

1. Amlodipine — tablets by 0,005 and 0,01. TD: 0,005—0,01 once a day.
2. Captopril — tablets by 0,025. TD: 0,025 sublingual.
3. Enalapril — tablets by 0,005 and 0,01. TD: orally 0,005—0,01 once a day.
4. Losartan — tablets by 0,05 and 0,1. TD: orally 0,05—0,1 once a day.

5. Metoprolol — tablets by 0,05—0,1; 0,1% solution in ampoules of 5 ml. TD: orally 0,05—0,1 one or two times a day; into the vein 0,002—0,005 in 10—20 ml of 5% glucose solution slowly.
6. Nifedipine — tablets and capsules by 0,01 and 0,02. TD: orally 0,01—0,04 one—two times a day.
7. Furosemidum — tablets by 0,04; 1% solution in ampules of 2 ml. TD: orally 0,04 one—two times a day; into the muscles 0,02—0,04 one—two times a day; into the vein 0,02—0,04 in 20 ml of isotonic sodium chloride solution.
8. Hydrochlorothiazide — tablets by 0,025. TD: orally 0,025—0,05 one—two times a day for 3—7 days, then break for 3—4 days.
9. Indapamide — dragee by 0,0025. TD: orally 0,0025 in the morning before a meal.
10. Norepinephrinum — 0.2% solution in ampoules of 1 ml. TD: into the vein 0.004—0.008 in 1 000 ml of 5% glucose solution dropwise.
11. Coffeinum — tablets by 0,1 and 0,2; 10 and 20% solution in ampules of 1 and 2 ml. TD: orally 0,1—0,2 two—three times a day in the first half of the day; subcutaneously 0,1—0,2.

QUESTIONS AND TASKS FOR SELF-CONTROL

Task 1. Pharmacotherapeutic questions. Write the prescriptions, justifying the choice of drugs.

1. Drug with central action for arresting of hypertensive crisis.
2. Calcium channel blocking agent for arresting of hypertensive crisis.
3. ACE inhibitor for the treatment of hypertensive crisis.
4. Diuretic for the treatment of hypertensive crisis.
5. Drug for the treatment of arterial hypertension which is accompanied by tachycardia.
6. Drug for the treatment of arterial hypertension which is accompanied by artery spasm.
7. Drug for the treatment of arterial hypertension with angina pectoris.
8. Drug for the treatment of patients suffering from arterial hypertension with concomitant bronchial asthma.

9. Drug for the treatment of patients suffering from arterial hypertension, complicated by heart failure.
10. Drug for the treatment of high renin essential hypertension.
11. Drug for the treatment of isolated systolic arterial hypertension.
12. Cardioprotective drug for the treatment of arterial hypertension.
13. Cardioselective β-adrenergic blocking agent for the treatment of arterial hypertension.
14. Drug for the treatment of arterial hypertension with resistance to ACE inhibitors.
15. Drug with central action for arresting of circulatory collapse.
16. Drug with peripheral action for arresting of circulatory collapse.
17. Analeptic drug for chronic arterial hypotension.
18. Calcium channel blocker for the treatment of hypertension.

Task 1. After studying the theoretical material, answer the following questions:

1. What drugs are prescribed for patients with arterial hypertension with increased cardiac output; increased vascular resistance; increased activity of renin and angiotensin II?
2. Why is clonidine used only for the treatment of hypertensive crisis, and not for long-term therapy of hypertension? What medications that reduce the excitability of the vasomotor center can be used for a long time? Why?
3. In what forms of arterial hypertension is it preferable to prescribe α-adrenoblockers? In which cases are β-adrenoreceptors the drugs of choice? Why?
4. What is the difference between β-adrenoblockers and calcium channel blockers? What do they have in common?
5. What is the difference between the derivatives of 1,4-dihydropyridine of 1^{st}, 2^{nd} and 3^{rd} generations? What are the indications (clinical uses) for each generation?
6. Which ACE inhibitors act as active molecule, and which are prodrugs?
7. What is the most common form of target organ damage associated with hypertension? Which groups of antihypertensive drugs have

organoprotective properties and improve functions of target organs in case of hypertension?

8. What is special about the pharmacokinetics and mechanism of action of zofenopril which makes it the drug of choice for the treatment of myocardial infarction and heart failure?
9. Identify the mechanism of antioxidant, antiatherosclerotic, antiplatelet, endothelium-protective effects of drugs that affect the function of the renin-angiotensin system.
10. In what cases do AT_1 receptor blockers have advantages over ACE inhibitors?
11. Consider the mechanisms of hypotensive action of diuretics. Choose diuretics for the treatment of arterial hypertension, evaluate their efficacy and safety with long-term use.

Task 3.

a. Match each antihypertensive drug with the appropriate description.

A. Aliskiren	1. Nitric oxide is the active metabolite of this drug
B. Losartan	2. Angiotensin-converting enzyme inhibitor
C. Enalapril	3. A drug which blocks angiotensin AT_1 receptors
D. Nifedipine	4. A calcium channel blocker
E. Nitroprusside	5. A competitive inhibitor of renin

b. Match each drug which increases blood pressure with the appropriate clinical use.

A. Epinephrine	1. The immediate metabolic precursor of norepinephrine, can activate α- and β adrenergic receptors
B. Dopamine	2. A direct-acting, synthetic adrenergic drug that binds primarily to α_1 receptors
C. Phenylephrine	3. A drug which causes a decrease in fatigue and increased mental alertness as a result of stimulating the cortex and other areas of the brain
D. Caffeine	4. Direct-acting agonists bind to adrenergic receptors on effector organs without interacting with the presynaptic neuron

Task 4. Topics for report.

1. Hypertension: classification, pathogenesis.
2. Functions of ET and AT receptors.
3. Pleiotropic effects of ACE-inhibitors.
4. Rational and irrational combinations of antihypertensive drugs.

QUESTIONS AND TASKS IN CLASS

Task 1. Analyze the tasks that reflect the mechanisms and features of action of drugs affecting blood pressure (the collection of graphic tasks).

Task 2. Analyze case tasks.

1. A 65-year-old man was admitted to the emergency department because of restlessness, apprehension, tremor, sweating, and tachycardia. Vital signs on admission were blood pressure 190/100 mm Hg, pulse 110 bpm, respirations 18/min. History revealed that the patient had been taking a thiazide diuretic and losartan for 3 months for stage 2 hypertension. However, his blood pressure was still not well controlled, and recently his physician had added a third drug to the therapeutic regimen. Because the patient was experiencing daytime somnolence and dry mouth, he decided to discontinue the newly prescribed medication the day before admission. Which drug was most likely the new drug that the patient decided to stop taking?
2. A 67-year-old man complained to his physician of a dry, disturbing cough. In addition, he noted that food seemed to have lost its flavor. The man was recently diagnosed with stage 2 essential hypertension and had started a multidrug treatment 1 week earlier. Which drug most likely caused the patient's signs and symptoms?
3. A 40-year-old male has recently been diagnosed with hypertension due to pressure readings of 163/102 and 165/100 mm Hg. He also has diabetes that is well controlled with oral hypoglycemic medications. Which is the best initial treatment regimen for treatment of hypertension in this patient? Explain the choice.
   a. Felodipine
   b. Furosemide
   c. Lisinopril
   d. Lisinopril and hydrochlorothiazide
   e. Metoprolol

4. A 53-year-old man was brought to the emergency department after suffering crushing substernal pain for the past hour. Vital signs on admission were blood pressure 88/50, pulse 115 bpm, respirations 30/min. Further exams led to the diagnosis of cardiogenic shock due to myocardial infarction, and therapy was started that included an intravenous infusion of an appropriate drug. Which of the following molecular actions most likely mediated the therapeutic effectiveness of the drug in this patient? What drugs are responsible for this mechanism?
   a. Activation of phospholipase A_2
   b. Increased synthesis of inositol triphosphate (IP_3) and diacylglycerol (DAG)
   c. Increased synthesis of cyclic adenosine monophosphate (cAMP)
   d. Increased synthesis of cyclic guanosine monophosphate (cGMP)
   e. Opening of ligand-gated Na^+-channels
5. A 33-year-old man was brought to the emergency room after a car accident. Upon admission, the patient was lucid but completely paralyzed, with loss of all sensation and reflex activity below the thorax. Vital signs were blood pressure 80/40 mm Hg, heart rate 42 bpm, respirations 36/min. A preliminary diagnosis of spinal shock, due to spinal cord injury, was made, and an intravenous infusion of an appropriate drug was started. Which drug was most likely administered?

Task 3. Answer the test questions (in the computer lab).

Lesson 29
Drugs affecting the blood system

Learning objectives are to study classifications, mechanism of action, antimicrobial spectrum, pharmacokinetics, use, side effects and contraindications to the use of drugs affecting the blood system; to study and practice prescription writing.

QUESTIONS FOR PREPARATION FOR THE LESSON

1. Blood substitutes: classification, composition, mechanism of action, indications:
   a) hemodynamic blood substitutes (plasma replacement substances)
      - natural colloids — human albumin;
      - synthetic colloids

        dextran-based drugs — dextran [50—70 kDa], dextran [35—45 kDa]

        gelatin-based drugs (16—30 kDa) — gelatin;

        hydroxyethylated starch-based drugs (200—450 kDa) — hydroxyethyl starch (HES);

   b) blood substitutes with detoxification action

      polyvinylpyrrolidone-based preparations (PVP) — povidone [8 kDa] (Haemodes).
2. Regulators of water-salt and acid-base equilibrium — polyion salt solutions based on sodium chloride, sodium acetate, sodium bicarbonate, potassium chloride, sodium acetate + sodium chloride, sodium hydrocarbonate + sodium chloride + potassium chloride, glucose + sodium citrate + sodium chloride + potassium chloride.
3. Parenteral nutrition medications: composition, indications
   - glucose solution;
   - amino acid solutions — amino acids for parenteral nutrition + minerals;
   - fat emulsions.
4. Erythropoiesis stimulants for iron deficiency anemia: natural sources of iron, mechanism of action, indications, side effects, contraindications to the use of iron drugs
   a) iron supplements for oral administration
      - ferrous (Fe^{2+}) sulfate;

- ferrous sulfate + ascorbic acid, folic acid, cyanocobalamin, serine;
- ferrous chloride;
- ferrous gluconate;
- ferrous fumarate;
- Fe^{3+} protein succinylate;
- Fe^{3+}-hydroxide polymaltose complex;

b) iron oxide preparations (Fe^{3+}) for injections
- into the muscles — Iron(III)-hydroxide polymaltose complex;
- into the vein — Iron [III] sucrose complex.

5. Acute iron poisoning: pathogenesis, symptoms, treatment — deferoxamine, sodium calcium edetate.
6. Erythropoiesis stimulants for macrocytic anemia: natural sources, chemical structure, pharmacokinetics, mechanism of action, use, side effects of cyanocobalamin and folic acid.
7. Hematopoietic growth factors: mechanism of action, indications for use, side effects
   a) erythropoietin drugs
      - short-acting — epoetin alfa, epoetin beta;
      - long-acting — darbepoetin alfa, epoetin beta (methoxypolyethylene glycol);

   b) drugs which stimulate leukopoiesis
      - granulocyte-macrophage colony-stimulating factor (GM-CSF)— molgramostim;
      - granulocyte colony-stimulating factor — filgrastim, pegfilgrastim, lenograstim;

   c) thrombopoietin receptor agonists — eltrombopag.
8. Hemostatic agents: origin, mechanism of action, use, side effects, contraindications
   a) coagulants for local use — hemostatic collagen sponge
   b) coagulants with resorptive action
   - drugs of vitamin K — sodium menadione bisulfite;
   - drugs containing blood coagulation factors
     coagulation factor VII — eptac alpha,
     coagulation factor VIII — octocog alpha,
     blood coagulation factor IX — nonacog alpha;
   - calcium drugs — calcium chloride;

c) drugs that reduce permeability of vascular wall, — etamzilat, ascorbic acid.

9. Antiplatelet agents: classification, mechanism of action, pharmacokinetics, use, side effects, contraindications
   - platelet receptor blockers
   - P2Y12 platelet inhibition — ticlopidine, prasugrel, clopidogrel, cangrelor;
   - glycoprotein IIb/IIIa receptor antagonists — eptifibatide, abciximab;
   - thromboxane A_2 synthesis blockers — acetylsalicylic acid;
   - antiplatelet agents that increase the content of adenosine and cAMP in platelets — dipyridamole, pentoxifylline.
10. Mechanism of action, indications of drugs that increase the elasticity of red blood cells — pentoxifylline.
11. Anticoagulants: mechanism of action, classification (direct and indirect action).
12. Direct acting anticoagulants: the history of the discovery (D. McLean, U.G. Howell), chemical structure, mechanism of action, pharmacokinetics, use
    - selective thrombin inhibitors — dabigatran;
    - selective inhibitors of the factor Xa — rivaroxaban;
    - heparin sodium;
    - low molecular weight heparin — nadroparin calcium, enoxaparin sodium;
    - drugs with heparin-like action — sulodexid, fondaparinux sodium.
13. Warfarin as indirect anticoagulant: mechanism of action, pharmacokinetics, use.
14. Side effects of anticoagulants, measures for their prevention. Antagonists of anticoagulants (protamine sulfate, menadione sodium bisulfite, ascorbic acid). Contraindications to the use of anticoagulants.
15. Drugs affecting fibrinolysis: mechanism of action, use, side effects, contraindications to use
    - non-fibrin-specific agents — streptokinase, urokinase;
    - fibrin-specific agents — prourokinase, alteplase, tenecteplase;
    - inhibitors of fibrinolysis — aminocaproic acid, tranexamic acid, aprotinin.

PRESCRIPTIONS

1. «Haemodes» — official solution in bottles of 100, 200, 400 ml. TD: into the vein 200—400 ml dropwise.
2. «Sorbifer durules» — official drug in coated tablets (0,32 mg ferrous sulphate and 0,06 ascorbic acid). TD: orally 1 tablet 2 times a day 1 hour before a meal.
3. Cyanocobalaminum — 0,01 and 0,02% solution in ampules of 1 ml. TD: subcutaneously, into the muscles 0,0001—0,0002 once in 2 days.
4. Menadioni natrii bisulfis — tablets by 0,015; 1% solution in ampules of 1 ml. TD: orally 0,015 one—two times a day; into the muscles 0,01—0,015.
5. Acidum acetylsalicylicum — tablets by 0,1. TD: orally 0,1 once a day after a meal.
6. Heparinum natrium — vials of 5 ml (1 ml − 5 000 Units). TD: subcutaneously 5 000—10 000 Units four—six times a day; into the vein 20 000—30 000 Units it 1 000 ml isotonic sodium chloride solution dropwise.
7. Warfarin — tablets by 0,0025. TD: orally 0,0025 two times a day during 4 days, then 0,0025 once a day in the morning.
8. Deferoxamine — powder in vials of 0,5. TD: into the muscles 1,0 (dissolve the content of the vial in 5 ml water for injection); into the vein 20—60 mg/kg in 250 isotonic sodium chloride solution dropwise.
9. Calcii chloridum — 5—10% solution for oral use; 10% solution in ampoules of 5 and 10 ml. TD: orally 0,5—1,0 three times a day 30 minutes before a meal, drink a glass of water; into the vein 0,5—1,0 slowly.

QUESTIONS AND TASKS FOR SELF-CONTROL

Task 1. Pharmacotherapeutic questions. Write the prescriptions, justifying the choice of drugs.

1. Drug for acute blood loss.
2. Drug for treatment of shock.
3. Drug with detoxification effect for poisoning.
4. Drug with detoxification effect for peritonitis.
5. Drug for the treatment of iron deficiency anemia.

6. Drug for the treatment of macrocytic anemia.
7. Drug for the treatment of neurological diseases.
8. Drug for hepatitis.
9. Drug for the treatment of hemorrhagic syndrome.
10. Drug for the management bleeding associated with anticoagulants of indirect action.
11. Drug for the treatment of angina.
12. Drug for the treatment of ischemic stroke.
13. Drug for secondary prevention of IHD.
14. Drug for hearing impairment in vascular disorders.
15. Drug for myocardial infarction.
16. Drug for disseminated intravascular coagulation (DIC)
17. Drug for the treatment of thrombophlebitis.
18. Antidote for iron poisoning.

Task 2. After studying the theoretical material, answer the following questions:

1. Name the factors that increase and decrease the bioavailability of iron.
2. Why are erythropoietin drugs often prescribed together with iron drugs? In what types of anemia do erythropoietin drugs not have a therapeutic effect and why?
3. It is known that clopidogrel is a prodrug, which is converted to the active metabolite 2-oxaclopidogrel with the participation of the isoenzyme 2C19. Explain why clopidogrel increases the risk of thrombosis of implanted coronary artery stents in patients with an allelic variant of the CYP2C19 * 2 gene with myocardial infarction, and, in patients with a variant of the CYP2C19 * 17 gene, clopidogrel increases the risk of bleeding.
4. Why does warfarin at a dose of 5 mg/day cause bleeding in patients with persistent atrial fibrillation, carriers of CYP2C9 * 3 more often than in those with the genotypes of CYP2C9 * 1 and CYP2C9 * 2?
5. Acetylsalicylic acid inhibits the synthesis of thromboxane A2 and prostacyclin. Why does acetylsalicylic acid have a pronounced antiplatelet effect?
6. Why do indirect anticoagulants have a therapeutic effect after a long latent period? How does blood coagulation change during the first 24—48 hours after the use of this drugs?

7. Why is streptokinase contraindicated in patients who have had streptococcal infection? What thrombolytic agents can be prescribed for such patients?

Task 3.

a. Match each hemostatic drug with the appropriate description

A. Abciximab	1. This drug binds noncompetitively to glycoprotein IIb/IIIa receptor complex
B. Alteplase	2. An orally administered drug that directly inhibits thrombin
C. Aminocaproic acid	3. This drug blocks the conversion of plasminogen to plasmin
D. Dabigatran	4. This drug catalyzes the conversion of plasminogen into active plasmin
E. Prasugrel	5. This drug produces irreversible blockade of platelet adenosine diphosphate P2Y receptors

b. Match each hematopoietic drug with the appropriate description

A. Cyanocobalamin	1. This drug is used to prevent transfusional iron overload
B. Deferoxamine	2. An endogenous compound synthesized by the kidney in response to hypoxia
C. Erythropoietin	3. This drug is absorbed through the distal ileum by a process of receptor-mediated endocytosis
D. Folic acid	4. Deficiency of this vitamin leads to megaloblastic anemia (large-sized red blood cells), which is caused by diminished synthesis of purines and pyrimidines

Task 4. Topics for report.

1. Iron: recommended intake, benefits, and food sources.
2. New oral anticoagulants.
3. New antiplatelet drugs.
4. Direct oral anticoagulants versus warfarin.

QUESTIONS AND TASKS IN CLASS

Task 1. Analyze the tasks that reflect the mechanisms and features of action of drugs affecting blood system (the collection of graphic tasks).

Task 2. Analyze case tasks.

1. A 30-year-old woman presented to her family physician complaining of black, tarry stools. The woman had a prosthetic valve replacement 4 months earlier for severe aortic stenosis secondary to rheumatic disease and had been receiving daily oral anticoagulant therapy since then. Physical examination revealed subconjunctival hemorrhage and bruises on her arms and legs. Which drug most likely caused the patient's signs and symptoms?
2. A 65-year-old man developed sudden dyspnea and chest pain 2 days after surgery to remove a gastric carcinoma. Physical examination revealed an anxious man in severe respiratory distress with the following vital signs: temperature 37,5°C (99,5°F (), pulse 120 bpm, blood pressure 90/50 mm Hg, respirations 28 breaths/min. A computed tomography scan showed complete obstruction of a branch of the left pulmonary artery. Make diagnosis and prescribe appropriate treatment for this patient.
3. A 65-year-old man was seen at a clinic because of muscle weakness, emotional instability, burning of the tongue, and alternating constipation and diarrhea. Physical examination showed a pale man with red tongue, loss of vibratory sense in the lower extremities, and ataxia. Pertinent blood values were red blood cell count 3,4×106/mm3 (normal, male 4,3−5,9×10^6/mm3), mean corpuscular volume 110 fL (normal 80−100 fL), vitamin B_{12} 96 pg/mL (normal > 280 pg/mL), serum ferritin 250 ng/mL (normal 30−300 ng/mL). Make diagnosis. Which drug would be most appropriate for this patient?
4. A 2-year-old boy was brought to the emergency department after suffering two episodes of brownish vomit containing pills, followed by

a large hematemesis. The mother, who was pregnant, suspected her son had ingested several tablets of her medication. Physical examination showed a lethargic and cyanotic child complaining of abdominal pain. Vital signs were blood pressure 80/50 mm Hg (normal for 2 years 100/65 mm Hg), pulse 130 bpm (normal for 2 years 115 bpm) respirations 30/min (normal at 2 years 24/min). Laboratory values indicated severe metabolic acidosis. Make diagnosis. Prescribe treatment for this patient.

Task 3. Answer the test questions (in the computer lab).

Lesson 30
Final class about drugs affecting the major organs and systems

Learning objective is to check skills in prescription writing; to check and fix knowledge about the mechanism of action, classification, pharmacokinetics, use, side effects of agents, drug poisoning in the frame of the topics which have been studied.

QUESTIONS FOR PREPARATION FOR THE FINAL LESSON

1. Mechanism of cardiotonic action, classification, pharmacokinetics of cardiac glycosides.
2. The effect of cardiac glycosides on the heart rate, conduction system, hemodynamics and kidney functions; use, contraindications to use.
3. Glycoside intoxication: stages, pathogenesis, symptoms, treatment.
4. Antiarrhythmic drugs class I: mechanism of action, use, side effects, contraindications to use.
5. Antiarrhythmic drugs of classes II and III: mechanism of action, use, side effects, contraindications to use.
6. Antianginal drugs: mechanism of action, classification, use.
7. Nitrates: mechanism of action, pharmacokinetics, use, side effects, contraindications to use. Mechanism of action of molsidomine.
8. Lipid-lowering agents: mechanism of action, classification.
9. Statins: mechanism of action, use, side effects, contraindications to use.
10. Diuretics: mechanism of action, classification.
11. Methylxanthines, carbonic anhydrase inhibitors and osmotic diuretics: mechanism of action, use, side effects, contraindications to use.
12. Loop diuretics: mechanism of action, use, side effects, contraindications to use.
13. Thiazides and thiazide-like diuretics: mechanism of action, use, side effects, contraindications to use.
14. Potassium-sparing diuretics: mechanism of action, use, side effects, contraindications to use.

15. The choice and mechanism of action of diuretics for glaucoma, heart failure and arterial hypertension.
16. Antihypertensive drugs: mechanism of action; requirements for antihypertensive drugs; classification.
17. Antihypertensive agents that reduce the excitability of the vascular center: mechanism of action, use, side effects, contraindications to the use.
18. α-Adrenergic blockers: classification, mechanism of action, use, side effects, contraindications to use.
19. β-Adrenergic blockers: classification, mechanism of action, use in cardiology, side effects, contraindications to use.
20. Calcium channel blockers: classification, mechanism of action, use, side effects, contraindications to use.
21. ACE inhibitors: classification, mechanism of action, use, side effects, contraindications to use.
22. AT_1-receptor blockers: mechanism of action, use, side effects, contraindications to use.
23. Iron drugs: natural sources of iron, metabolism of iron; mechanism of action, use, side effects, contraindications to the use.
24. Acute iron poisoning: stages, pathogenesis, symptoms, treatment.
25. Vitamin B_{12}: natural sources of vitamin B_{12}, chemical structure, pharmacokinetics, mechanism of action, use.
26. Folic acid: natural sources, mechanism of action, use.
27. Hemostatic agents: classification, mechanism of action, use, side effects.
28. Antiplatelet agents: classification, mechanism of action, use, side effects, contraindications to use.
29. Heparin: origin, chemical structure, mechanism of action, use, side effects, contraindications to use.
30. Indirect anticoagulants: mechanism of action, use, side effects, contraindications to use.
31. Indirect anticoagulant poisoning: pathogenesis, symptoms, treatment.

32. Thrombolytic agents: classification, mechanism of action, use, side effects, contraindications to use.

PRESCRIPTIONS

Prescribe: digoxin, lidocaine, amiodarone, verapamil, nifedipine, amlodipine, nitroglycerin, isosorbide mononitrate, rosuvastatin, mannitol, furosemide, indapamide, spironolactone, captopril, enalapril, hemodez, sorbifer durules*, cyanocobalamin, menadione sodium bisulfite, acetylsalicylic acid as an antiplatelet drug, heparin, warfarin.

PHARMACOTHERAPEUTIC QUESTIONS

1. Drug for chronic heart failure.
2. Drug for atrial fibrillation.
3. Drug for ventricular extrasystoles.
4. Drug for the course treatment of ischemic heart disease.
5. Drug for stopping an attack of angina.
6. Drug for myocardial infarction.
7. Drug for atherosclerosis.
8. Diuretic for renal failure.
9. Diuretic for non-traumatic swelling of the brain.
10. Diuretic for the course treatment of arterial hypertension.
11. Diuretic for the correction of hypokalemia.
12. Calcium channel blocker for the treatment of arterial hypertension.
13. ACE inhibitor for the treatment of arterial hypertension.
14. Drug for hypertensive crisis.
15. Drug with detoxification effect in case of poisoning.
16. Drug for the treatment of iron deficiency anemia.
17. Drug for the treatment of macrocytic anemia.
18. Antiplatelet drug for the treatment of thrombophlebitis.

CONTROL TASK

Answer the questions, reflecting the mechanisms and features of action of drugs affecting the major organs and systems (a computer-based test).

Lesson 31
Immunotropic, antiallergic agents. Nonsteroidal anti-inflammatory drugs and medications for the treatment of gout.

Learning objectives are to study classifications, mechanism of action, antimicrobial spectrum, pharmacokinetics, use, side effects and contraindications to the use of drugs affecting the blood system; to study and practice prescription writing.

QUESTIONS FOR PREPARATION FOR THE LESSON

1. Structure and functions of the immune system. Cell mediated and humoral immunity, specific and nonspecific protective factors, mediators of immunity.
2. Primary and secondary immunodeficiency states: etiology, pathogenesis, clinical picture, principles of pharmacological correction.
3. Immunostimulants: classification, mechanism of action, pharmacokinetics, indications and contraindications to use, side effects
   a) non-selective stimulants of leukopoiesis and tissue regeneration — methyluracil;
   b) drugs of colony-stimulating factors — lenograstim, molgramostim, filgrastim, pegfilgrastim;
   c) interleukin drugs — interleukin-1 beta, interleukin-2;
   d) interferon drugs and inducers of its synthesis
      - recombinant interferon alfa, interferon alfa-2a, interferon alfa-2b, peginterferon alfa-2a, peginterferon-alpha-2b;
      - interferon beta;
      - interferon gamma;
      - inducers of interferon synthesis (interferonogenes)— dipyridamole, meglumine acridone acetate, tylorone;
4. Classification of allergic reactions.
5. Immunosuppressants: classification, mechanism of action, pharmacokinetics, indications and contraindications to use, side effects
   a) nonselective immunosuppressants
      - cytostatic agents and antimetabolites — azathioprine, mercaptopurin;
      - glucocorticoids — prednisolone, methylprednisolone,

dexametazone, betamethasone;

b) selective immunosuppressants

- inhibitors of lymphocyte proliferation and activation
  inhibitors of calcineurin — cyclosporin, tacrolimus;
  inhibitor of purine synthesis — mycophenolic acid and its salts;
  T-cell division inhibitor (mTOR kinase inhibitor) — sirolimus;
  inhibitors of dihydroorotate dehydrogenase (DHODH) — leflunomide;
- monoclonal antibodies against immunocompetent cells, their receptors and lymphokines
  chimeric monoclonal antibodies to tumor necrosis factor α-infliximab;
  human monoclonal antibodies to tumor necrosis factor-α-adalimumab, golimumab;
  a PEGylated Fab fragment against tumor necrosis factor — certolizumab;
  hybrid human type 2 receptor to tumor necrosis factor-α-etanercept;
  the hybrid extracellular domain of human CTLA-4 — abatacept;
  monoclonal antibodies to the interleukin-2 receptor — basiliximab
  humanized monoclonal antibodies to interleukin-6 — tocilizumab;
  chimeric monoclonal antibodies to the CD20 antigen of B lymphocytes — rituximab.

6. Allergic reactions of immediate type. Biological role of histamine. Localization and functions of H-receptors.
7. Antiallergic agents: classification, mechanism of action, pharmacokinetics, indications and contraindications for use, side effects.

a) drugs preventing mast cell degranulation

- ketotiphen;
- glucocorticoids — beclomethasone, budesonide, fluticasone;

b) H_1- receptor blockers

- generation I — diphenhydramine, clemastin, mebhydroline, promethazine, chloropyramine;
- generation II — loratadine, cetirizine;
- generation III — desloratadine, levocetirizine;

8. Nonsteroidal anti-inflammatory drugs (NSAIDs): classification,

mechanism of action, pharmacokinetics, indications for use
- salicylates — acetylsalicylic acid;
- pyrazole derivatives — metamizole sodium;
- derivatives of indole acetic acid — indomethacin;
- derivatives of phenyl alkanoic acids — diclofenac, aceclofenac, ibuprofen, ketoprofen;
- oxicam — piroxicam, lornoxicam, meloxicam;
- drugs containing a sulfonamide group — nimesulide, celecoxib, etoricoxib;
- derivatives of pyrrolizine carboxylic acid — ketorolac.

9. Classification of NSAIDs by selectivity to isoenzymes of cyclooxygenase. Advantages and disadvantages of selective inhibitors of cyclooxygenase-2 — meloxicam, nimesulide, celecoxib, etoricoxib.
10. Mechanism of anti-inflammatory and immunotropic action of NSAIDs. Use of NSAIDs for rheumatic diseases, arthritis and other inflammatory diseases.
11. Mechanism of analgesic and antipyretic action of NSAIDs and paracetamol, use in pain syndromes and fever.
12. Adverse effects and contraindications to the use of NSAIDs and paracetamol.
13. Antigout agents: mechanism of action, pharmacokinetic, use for the relief of an acute attack and treatment, side effects, contraindications to the use
    - agents that reduce inflammation caused by urates — colchicine, NSAIDs (diclofenac, aceclofenac, lornoxicam);
    - uric acid-lowering drugs — allopurinol, febuxostat.

PRESCRIPTIONS

1. Diphenhydramine — tablets by 0,03 and 0,05; 1% solution in ampules of 1 ml. TD: orally 0,03—0,05 one—three times a day; into the muscles 0,01.
2. Loratadine — tablets by 0,01. TD: orally 0,01 once a day.
3. Paracetamol — tablets by 0,25 and 0,5; 2,5% suspension in bottles of 100 ml; suppositories rectal by 0,25. TD: orally 0,125—0,5; rectally 0,25.
4. Diclofenac — tablets by 0,025; 2,5% solution in ampules of 3 ml; 1% gel in tubes of 20.0; TTS (patches) at 0,025. TD: orally 0,05 two—three

times a day after a meal; into the muscles 0,075 one—two times a day; apply 1 patch 1 time a day.

5. Meloxicam — tablets by 0,015; 1% solution in ampules of 1,5 ml. TD: orally 0,0075—0,015; into the muscles 0,015 once a day.
6. Prednisolonum — tablets by 0,005; 2,5% solution in ampules of 1 ml; 0,5% ointment in tubes of 10,0 and 20,0; 0.5% solution in vials of 5 ml (eye drops). TD: orally 0,005—0,02 once a day in the morning with a meal; into the vein 0,05—0,15 in 500 ml of 5% glucose solution dropwise.
7. Calcii chloridum — 5—10% solution for oral use; 10% solution in ampoules of 5 and 10 ml. TD: orally 0,5 — 1,0 three times a day 30 minutes before a meal, drink a glass of water; into the vein 0,5—1,0 slowly.

QUESTIONS AND TASKS FOR SELF-CONTROL

Task 1. Pharmacotherapeutic questions. Write the prescriptions, justifying the choice of drugs.

1. Drug which potentiates analgesic effect of anesthetics in postoperative pain.
2. Drug for combination therapy of hyperthermia.
3. Hormonal drug for systemic diseases of connective tissue.
4. Immunosuppressant for the treatment of rheumatoid arthritis.
5. Immunosuppressant which is used for organ transplantation.
6. Drug for the treatment and prevention of allergic bronchitis.
7. Drug with anti-inflammatory effect for the treatment of bronchial asthma.
8. Drug for the treatment of dermatosis (itchy skin).
9. Antihistamine that does not have a sedative effect for the treatment of drug allergy.
10. Anti-allergic drug that reduces vascular permeability for the treatment of exudative diathesis.
11. Drug for emergency treatment of anaphylactic shock.
12. Antipyretic with fever.
13. Anti-inflammatory drug for the treatment of rheumatism.
14. Anti-inflammatory drug for the treatment of osteoarthritis.
15. Anti-inflammatory drug for gout.
16. Analgesic with local action for injury.

17. Analgesic with local action for low back pain.
18. Drug for injection for low back pain.

Task 2. After studying the theoretical material, answer the following questions:

1. Pros and cons for the use of interferon drugs and interferon inducers in the chronic infection process.
2. What is the best way — to prescribe antibiotics and immunity stimulants sequentially or in combinations for the treatment of infectious diseases?
3. What is the difference between the immunosuppressive effect of cytostatic drugs and glucocorticoids?
4. Explain the term "selective immunosuppressants".
5. Consider the mechanism of action of selective immunodepressants, for example, effects of tacrolimus, arranging them in a logical sequence:
   - binding to specific intracellular protein FKBP 12;
   - calcineurin blockade with tacrolimus complex — FKBP 12 protein;
   - violation of calcium-dependent transcription of lymphokine genes;
   - disruption by cytotoxic lymphocytes of interleukin production and presentation of interleukin receptors;
   - inhibition of proliferation and interaction of cytotoxic lymphocytes;
   - termination of the graft rejection reaction.
6. For what type of allergic reactions are H_1-receptor blockers the most effective?
7. In what cases can sedative effect of antihistamine drugs be useful?
8. Discuss the differences between antihistamine drugs of generations I, II, and III. Why do antihistamine drugs of generation II have a prolonged (up to 12—24 h) action?
9. Consider side effects of NSAIDs which depend on impaired prostaglandin synthesis. Why do meloxicam, nimesulide, and celecoxib have less pronounced ulcerogenic effects?
10. What mechanism of the anti-inflammatory action of NSAIDs has pathogenetic significance in rheumatic diseases?

11. Consider the peripheral and central mechanisms of the analgesic action of NSAIDs and paracetamol. Why does only paracetamol have a central effect?
12. It is known, fever is a protective reaction of the body. Is it necessary to use antipyretic during fever?
13. Why does colchicine have an anti-inflammatory effect only in case of gout?

Task 3.

a. Match each antihistamine drug with the appropriate description

A. Diphenhydramine	1. An antihistamine drug with pronounced sedative properties
B. Levocetirizine	2. A histamine receptor antagonist which may cause paradoxical hyperactivity in young children
C. Promethazine	3. An antihistamine drug without sedative properties

b. Match each NSAID with the appropriate description

A. Aspirin	1. The analgesic effect of this drug is primarily mediated by central impairment of pain transmission
B. Celecoxib	2. A selective inhibitor of cyclooxygenase-2
C. Indomethacin	3. An irreversible inhibitor of cyclooxygenase in platelet
D. Piroxicam	4. This drug can inhibit both cyclooxygenase and phospholipase A_2
E. Acetaminophen	5. The long half-life of this drug (more than 50 hours) permits once-daily dosing

c. Match each immunomodulating drug with the appropriate description

A. Azathioprine	1. A specific inhibitor of inosine monophosphate dehydrogenase
B. Basiliximab	2. This drug binds to the CD25 α chain of the interleukin-2 receptor on activated T lymphocytes

C. Mycophenolate mofetil	3. A prodrug that is converted into mercaptopurine in the body

d. Match each drug with the appropriate description

A. Azathioprine	1. An antimalarial drug used in rheumatoid arthritis
B. Infliximab	2. A monoclonal antibody that binds to CD20 B lymphocytes
C. Hydroxychloroquine	3. A monoclonal antibody that binds to tumor necrosis factor-α
D. Rituximab	4. This drug can inhibit the synthesis of inosinic acid

Task 4. Topics for report.

1. Paracetamol metabolism in children and adults.
2. Toll-like receptors (TLRs): functions. Drugs targeting Toll-like receptors.
3. Combination drug therapies for immunosuppression in transplantation.
4. The role and choice criteria of antihistamines in allergy management.

QUESTIONS AND TASKS IN CLASS

Task 1. Analyze the tasks that reflect the mechanisms and features of action of immunomodulating, antiallergic, antigout agents and NSAIDs (the collection of graphic tasks).

Task 2. Analyze case tasks.

1. A 65-year-old man had been recently diagnosed with osteoarthritis. Six months ago, the patient suffered from peptic ulcer disease that healed after triple antiulcer therapy. Which nonsteroidal anti-inflammatory drugs would be the most appropriate for this patient?
2. A 21-year-old woman suffering from seasonal allergic conjunctivitis was admitted to the hospital. A physician decided to start a treatment with eye drops of azelastine, a second-generation histamine H_1 antagonist. Second-generation H_1 antagonists are used locally in the conjunctiva instead of first-generation H_1 antagonists. Explain the choice of drug.

3. A 44-year-old woman was in the coronary unit after a heart transplant performed 2 weeks earlier. Pertinent blood test results were white blood cell count $1{,}2\times10^3/mm^3$ (normal $4{,}5-11{,}0\times10^3/mm^3$), platelets $40{,}000/mm^3$ (normal $150{,}000-400{,}000/mm^3$). Which of the following drugs most likely caused these findings?

   a. Cyclosporine
   b. Dobutamine
   c. Dopamine
   d. Azathioprine
   e. Fluorouracil

4. A 53-year-old man who underwent liver transplantation for advanced biliary cirrhosis had been receiving immunosuppression treatment with prednisone and cyclosporine. Despite the therapy, a liver biopsy still showed rejection 14 days after surgery. Which of the following drugs could be substituted for cyclosporine to treat this case of cyclosporine resistant rejection?

   a. Aldesleukin
   b. Celecoxib
   c. Tacrolimus
   d. Fluorouracil

5. A 43-year-old man suffering from rheumatoid arthritis complained to his physician that his joint pain had increased recently despite current naproxen and hydroxychloroquine therapy. The patient was otherwise healthy, and his past medical history was unremarkable. Which drug would be appropriate to add to the patient's therapy at this time?

Task 3. Answer the test questions (in the computer lab).

Lesson 32
Acute drug poisoning

Learning objectives are to study treatment of acute poisoning; repeat pathogenesis, symptoms of poisoning and antidotes.

QUESTIONS FOR PREPARATION FOR THE LESSON

1. Acute poisoning: characteristics, causes.
2. The use of antagonism for the treatment of poisoning (physical, chemical, physiological indirect, direct — competitive and noncompetitive).
3. The principles of management of acute drug poisoning:
   a) measures and drugs to reduce the absorption and resorptive action of the poison
      - in case of skin damage — washing and decontamination;
      - with inhalation — lung hyperventilation;
      - during injection intake — ice, vasoconstrictor agents, application of a harness;
      - by ingestion — adsorbents, emetics, laxatives with an osmotic effect, drugs for chemical neutralization of the poison in the gastrointestinal tract;

   b) drugs that reduce the concentration of poison in the blood and tissues and eliminate its effect on target organs
      - antidote therapy — chemical and physiological antagonists;
      - detoxification therapy — blood substitution and disinfection solutions, glucose, ascorbic acid;

   c) measures accelerating the excretion of poison from the body, — forced diuresis, hemodialysis, hemosorption, peritoneal dialysis;
   d) symptomatic treatment — anti-shock drugs, drugs to eliminate pain syndrome, seizures, hyperthermia, respiratory disorders, cardiovascular disorders; correction of water-electrolyte and acid-base balance.
4. Pathogenesis, symptoms and treatment of drug poisonings: indirect anticoagulants, atropine, barbiturates, cholinesterase inhibitors (organophosphates), insulin, iodine, acids, clonidine, cocaine,

morphine, a mushroom, nitrates, iron preparations, cardiac glycosides, hypnotics and anxiolytics of the benzodiazepine group, alkalis, ethanol.

POISONINGS (SYMPTOMS AND TREATMENT)

Indirect anticoagulants (warfarin)

Symptoms: weakness, headache, multiple hemorrhages on the conjunctiva, other mucous membranes, skin, cough with blood, containing traces of blood; nasal, uterine, gastric and intestinal bleeding, vomiting with blood, hemarthrosis, hematuria.

Treatment: gastric lavage (activated charcoal), sodium menadione bisulfite; calcium chloride, glucose and ascorbic acid into the vein

Atropine

1st stage: disorientation, hallucinations, delusions, clonic-tonic seizures, frequent breathing, hyperthermia, dilation of the pupils, photophobia, paralysis of accommodation (cycloplegia), dryness and hyperemia of the skin and mucous membranes, rash, dryness and burning in the mouth and throat, athonia, swallowing disorder, water phobia, tachycardia, arrhythmia, urinary retention and defecation.

Treatment: gastric lavage (activated carbon), neostigmine methylsulfate, droperidol or diazepam.

Stage 2: loss of consciousness, inhibition of reflexes, rare breathing, coma.

Treatment: gastric lavage (activated carbon), neostigmine methylsulfate; glucose and sodium bicarbonate into the vein.

Barbiturates

Symptoms: apathy, ataxia, sleep, passing into coma, type of anesthesia, hypothermia, depression of tendon reflexes, pathological reflexes, decreased muscle tone, pupillary constriction (hypoxia — extension), rare, shallow breathing, periodic breathing, Cheyne—Stokes respiration, pulmonary edema, pneumatic mania, decreased blood pressure, congestive heart failure, anuria.

Treatment: gastric lavage (activated charcoal, sodium bicarbonate), sodium bicarbonate in vein, furosemide, hemodes, pyracetam, norepinephrine, ceftazidim.

Cholinesterase inhibitors (organophosphates)

1st stage: psychomotor agitation, disorientation, tonic-clonic convulsions, tremor of head and hands, generalized fasciculations, pupillary constriction, spasm of accommodation, profuse sweating, difficulty breathing (laryngospasm, bronchospasm), tachycardia or bradycardia, increased or decreased blood pressure, salivation, nausea, vomiting, abdominal pain, diarrhea, involuntary urination and defecation.

Stage 2: rare shallow breathing, paralysis of the respiratory muscles, pulmonary edema, bradycardia, vascular collapse, coma.

Treatment: gastric lavage (activated charcoal, sodium bicarbonate), atropine, trimedoxime bromide, droperidol or diazepam, ceftazidime.

Insulin

Symptoms of hypoglycemic come: anxiety, feeling of fear, weakness, dizziness, feeling of hunger, trembling of the limbs, heartbeat, profuse saliva and sweating; hypoglycemic coma — loss of consciousness, tonic-clonic seizures, increased tendon reflexes and skeletal muscle tone, pallor and cyanosis of skin, cold sweat, tachycardia, increased blood pressure.

Treatment: 50—75 ml of 40% glucose solution and ascorbic acid in a vein, epinephrine.

Symptoms of diabetic coma: hyperglycemia, glycosuria, metabolic acidosis, loss of consciousness, depression of tendon reflexes, reduced skeletal muscle and eyeball tone, dryness and hyperemia of the skin, constriction of the pupils, deep noisy breathing, smell of acetone in exhaled air, tachycardia, low blood pressure.

Treatment: 10 Units of insulin soluble human genetically engineered in 100 ml of isotonic sodium chloride solution into the vein as a bolus every hour under the control of plasma glucose level; potassium and magnesium asparaginate into the vein.

Cocaine

1st stage: euphoria, anxiety, headache, hallucinations, delirium, hyperthermia, increased tendon reflexes, tremor, tonic-clonic seizures, pale face, dilation of the eyes, frequent breathing, tachycardia, arrhythmia, increased blood pressure.

Treatment: gastric lavage (activated carbon), diazepam.

Stage 2: depression of tendon reflexes, muscle atony, rare superficial breathing, vascular collapse, coma.

Treatment: gastric lavage (activated charcoal).

Morphine

Symptoms: euphoria, loss of pain sensitivity, sleep, hypothermia, tonic-clonic seizures, increased tendon reflexes, pupillary constriction, rare, shallow breathing, Cheyne—Stokes respiration, bronchospasm, pulmonary edema, low blood pressure, coma.

Treatment: gastric lavage (activated carbon, potassium permanganate), naloxone, piracetam, caffeine, atropine.

Iron drugs

Symptoms: vomiting and diarrhea with blood, abdominal pain, cyanosis, tonic-clonic seizures, tachycardia, vascular collapse, metabolic acidosis, hemolysis, coma.

Treatment: gastric lavage (activated charcoal, sodium bicarbonate), deferoxamine; sodium bicarbonate into a vein, prednisolone, norepinephrine, hemodez.

Cardiac glycoside

Transitional stage

Symptoms: headache, fear, hallucinations, muscle weakness, blurred vision, xanthopsia (objects appear in yellow or green), anorexia, nausea, vomiting, abdominal pain, bradycardia, increased blood pressure.

Toxic stage

Symptoms: ventricular extrasystole, supraventricular and ventricular paroxysmal tachycardia, pre-cardiac fibrillation, atrioventricular and intraventricular blockades, heart failure.

Treatment: gastric lavage (activated charcoal), potassium and magnesium asparaginate and lidocaine into the vein, digoxin immune Fab.

Hypnotics, anxiolytics of the benzodiazepine

Symptoms: weakness, drowsiness, hallucinations, speech disorders, nystagmus, inhibition of tendon reflexes, decreased muscle tone, rare

superficial breathing, cyanosis, arrhythmia, decreased blood pressure, loss of consciousness, coma.

Treatment: gastric lavage (activated charcoal), flumazeni, caffeine, norepinephrine, and furosemide.

Ethanol

Symptoms: sleep, coma, hypothermia, reduction of tendon reflexes and muscle tone, dilation of the pupils, rare surface breathing, the smell of alcohol in the exhaled air, cyanosis, pulmonary edema, a weak frequent pulse, collapse.

Treatment: gastric lavage (sodium bicarbonate), naloxone, piracetam, norepinephrine; potassium and magnesium asparaginate, furosemide.

Amanita

Symptoms: delirium, hallucinations, tonic-clonic seizures, miosis, accommodation spasm, facial flushing, profuse sweating, bronchospasm and bronchorea, bradycardia, decreased blood pressure, excessive salivation, nausea, abdominal pain, diarrhea, diarrhea.

Treatment: gastric lavage (activated charcoal), atropine, diazepam.

Nitrates

Symptoms: severe weakness, dizziness, headache, hyperemia, then cyanosis of the skin and mucous membranes, frequent breathing, orthostatic reduction of blood pressure, collapse, vomiting, methemoglobinmia.

Treatment: gastric lavage (activated charcoal), norepinephrine; 1% methylthioninium chloride solution (0,1 ml/kg body weight), ascorbic acid and glucose into the vein.

Alkali

Symptoms: burns to the lips, mouth, esophagus and stomach, sharp pain, severe thirst, drooling, vomiting and diarrhea with blood, shock, rare shallow breathing, anuria (liquefactive necrosis).

Treatment: gastric lavage (activated charcoal, acetic acid or citric acid), morphine, atropine, prednisolone; glucose into a vein, norepinephrine, hemodez, ceftazidime.

Iodine

Symptoms: burning and pain in the mouth, behind the sternum and abdomen, brown lips and tongue, nausea, vomiting of blue masses with blood, diarrhea with blood, swelling of the larynx, loss of consciousness, rare shallow breathing, weak frequent pulse, decreased blood pressure, anuria.

Treatment: gastric lavage (activated charcoal, sodium thiosulfate), prednisone; sodium thiosulfate and sodium bicarbonate into a vein, morphine, atropine, hemodez, norepinephrine.

Strong acids

Symptoms: burns of the lips, tongue and face, sharp pain in the mouth, behind the sternum and abdomen, hoarseness, spasm and swelling of the larynx, asphyxiation, drowsiness, vomiting of blood, weak rapid pulse, decreased blood pressure, metabolic acidosis, hemolysis, hematuria, anuria (coagulative necrosis).

Treatment: gastric lavage (activated charcoal, protein, milk), magnesium oxide, morphine, atropine, prednisolone; glucose and sodium bicarbonate in a vein, hemodez, ceftazidime.

Lesson 33
Combination drug therapy, drug incompatibility

Learning objectives are to study types and mechanisms of drug incompatibility. Using the knowledge of pharmacokinetics and pharmacodynamics, to study how to determine the rationality of combination drug therapy.

QUESTIONS FOR PREPARATION FOR THE LESSON

1. Types of drug interactions:
   - synergism (summarized, potentiated);
   - antagonism (physical, chemical, physiological);
   - types of physiological antagonism (indirect, direct competitive and non-competitive, partial).
2. Pharmaceutical and pharmacological incompatibility of drugs.
3. Relative and absolute incompatibility. Methods for correcting the relative incompatibility.
4. Pharmacokinetic incompatibility: interaction of drugs during absorption, distribution, biotransformation and excretion.
5. Pharmacodynamic incompatibility: interaction of drugs as a result of synergism, antagonism.

QUESTIONS AND TASKS FOR SELF-CONTROL

Task 1. After studying the theoretical material, answer the questions.

1. What is polypragmasy and what significance does it have in modern pharmacotherapy?
2. How does bioavailability of drugs change when they are used together with drugs that strengthen or suppress intestinal motility? How can we explain the change in bioavailability? Name the pharmacological groups of drugs that affect intestinal motility.
3. In what cases can the competition of two drugs for plasma proteins binding be beneficial? Give examples.
4. Name inductors and inhibitors of biotransformation.

5. How does the excretion of drugs change weak acids and bases with increasing and decreasing urine pH? Name the drugs that can acidify and alkalize urine.
6. What is potentiated anesthesia? What drugs are used for potentiated anesthesia?
7. It is known, that anxiolytics without directly affecting the function of GABA receptors potentiate the effects of drugs that activate GABA receptors. Explain this effect. What is the type of this interaction?
8. Name bactericidal and bacteriostatic antibiotics. Is it rational to use bactericidal and bacteriostatic antibiotics together?
9. Could antagonism between drugs be desirable? Give examples.

Task 2. Assess the results and medical significance of the pharmacokinetic drug interaction.

Mechanism of action	Drug		Result of interaction
	A	B	
	Aluminum phosphate	Diclofenac	
	Ascorbic acid	Platyfillin	
	Acetylsalicylic acid	Phenytoin	
	Ferrous sulfate	Doxycycline	
	Metoclopramide	Digoxin	
Competition for binding to plasma proteins	Ketoprofen	Warfarin	
Interaction during biotransformation	Carbamazepine	Propranolol	
	Rifampicin	Verapamil	
Interaction during excretion	Acetazolamide	Sulfonamides	
	Sodium bicarbonate	Lidocaine	
	Calcium chloride	Naproxen	
	Ascorbic acid	Morphine	
	Benzylpenicillin	Furosemide	

Task 3. Assess the results and medical significance of the pharmacodynamic interaction of drugs.

Drug combinations	Undesirable consequences of interactions
Metoprolol + verapamil (into the vein)	
Suxamethonium iodide + neostigmine methylsulfate	
Halothane + epinephrine	
Amitriptyline + Metocynia iodide	
Digoxin + acetazolamide	
Nifedipine + Calcium chloride	
Warfarin + Amoxicillin	
Oxacillin + doxycycline	
Gentamicin + Furosemide	

Task 4. Specify the therapeutic value of the pharmacodynamic interaction of drugs. In what cases and for what diseases are combinations of drugs in the table below used for?

Drug combinations	Therapeutic effects and clinical use
Levothyroxine sodium + potassium iodide	
Bupivacaine + epinephrine	
Salmeterol + fluticasone	
Dinitrogen oxide + cisatracuria besylate	
Fentanyl + droperidol	
Haloperidol + trihexyphenidyl	
Digoxin + potassium and magnesium asparaginate	
Hydrochlorothiazide + triamteren	

Enalapril + hydrochlorothiazide	
Lisinopril + amlodipine	
Simvastatin + ezetimibe	
Metformin + glibenclamide	
Piperacillin + sulbactam	
Sulfamethoxazole + trimethoprim	
Isoniazid + pyridoxine	

QUESTIONS AND TASKS IN CLASS

Task 1. Analyze the case tasks.

1. A patient was presented to a physician complaining to incoordination of movements, stiffness and tremor of the extremities. The man had schizophrenia and had been receiving sedative antipsychotic (neuroleptic) drug. To eliminate these side effects, the doctor prescribed a combination of drugs containing levodopa. After his admission, adverse reactions did not diminish, hallucinations and nonsense resumed. What can explain the side effects of an antipsychotic agent? Why did levodopa not have a therapeutic effect and contributed to the exacerbation of schizophrenia? What drug should be prescribed instead of levodopa?
2. A patient with periodontitis during antibiotic treatment developed diarrhea as a result of pseudomembranous colitis. The doctor prescribed loperamide, but the patient's condition worsened. What antibiotic can cause this side effect? Why does loperamide make the patient worse?
3. A 60-year-old patient suffering from osteoarthritis with severe pain, hypertension and chronic heart failure was admitted to the hospital. On the recommendation of a doctor, he took perindopril and hydrochlorothiazide. To reduce the pain, he took diclofenac daily. How can you evaluate such combination therapy?

EXAM PRESCRIPTION

1. *Adrenomimetics:* norepinephrine, fenoterol.
2. *Adrenergic blocking agents*: metoprolol.
3. *M-cholinomimetics and cholinesterase inhibitors:* pilocarpine, neostigmine methylsulfate.
4. *M-cholinergic blocking agents:* atropine.
5. *Local anesthetics:* lidocaine.
6. *Hypnotic drugs:* zolpidem.
8. *Antiepileptic drugs:* carbamazepine, valproic acid.
9. *Opioid analgesics and their antagonists:* morphine, naloxone.
10. *Antiparkinsonian drugs:* levodopa + carbidopa.
11. *Drugs for the treatment of migraine:* sumatriptan.
12. *Psychotropic drugs:* droperidol, diazepam, sertraline, caffeine, pyracetam.
13. *Drugs affecting the functions of the respiratory system:* bromhexin, aminophylline.
14. *Cardiac glycosides:* digoxin.
15. *Antiarrhythmic drugs:* lidocaine, amiodarone.
16. *Calcium channel blockers:* verapamil, nifedipine, amlodipine.
17. *Antianginal drugs:* nitroglycerin, isosorbide mononitrate.
18. *Diuretics:* furosemide, indapamide.
19. *ACE inhibitors:* captopril, enalapril.
20. *Drugs that improve cerebral circulation*: vinpocetine.
21. *Drugs affecting the functions of digestive system:* omeprazole, metoclopramide, drotaverine.
22. *Stimulators of blood formation*: sorbifer durules*, cyanocobalamin.
23. *Drugs that affect blood coagulation:* menadioni sodium bisulfite, sodium heparin, warfarin.
24. *Drugs affecting myometrium*: oxytocin.
25. *Hormonal and antihormonal agents:* levothyroxine sodium, tiamazol, insulin soluble human genetically engineered, glibenclamide, metformin, prednisone.
26. *NSAIDs:* diclofenac.
27. *Antiallergic drugs:* loratadine, calcium chloride.
28. *Antiseptics:* potassium permanganate, nitrofural.
29. *Antibiotics:* amoxicillin + clavulanic acid, ceftazidim, rifampicin, azithromycin.

30. *Drugs for the treatment of tuberculosis:* isoniazid.
31. *Fluoroquinolones:* ciprofloxacin.
32. *Antiviral drugs:* acyclovir, oseltamivir.
33. *Antiparasitic drugs:* metronidazole.
34. *Drugs for the treatment of poisoning:* sodium hydrogencarbonate, magnesium oxide, glucose, trimedoxime bromide, flumazenil, deferoxamine, sodium thiosulfate.

PHARMACOTHERAPEUTIC QUESTIONS

1. Drug for stopping vascular collapse.
2. Drug for the treatment of glaucoma.
3. Drug g for myasthenia.
4. Drug g for infiltration anesthesia.
5. Drug for the treatment of insomnia.
6. Drug for the treatment of epilepsy.
7. Analgesic for the prevention of shock in case of injury.
8. Drug for the treatment of Parkinson's disease.
9. Drug for the treatment of migraine.
10. Drug for the relief of psychomotor excitation.
11. Drug for the treatment of anxiety.
12. Drug for the treatment of depression.
13. Drug for the treatment of asthenia.
14. Drug for the treatment of bronchial asthma.
15. Drug for heart failure.
16. Drug for atrial fibrillation.
17. Drug for angina.
18. Drug for myocardial infarction.
19. Drug for the course of treatment of hypertension.
20. Drug for the treatment of hypertensive crisis.
21. Drug for ischemic stroke.
22. Drug for the treatment of peptic ulcer.
23. Drug for intestinal atony.
24. Drug for the treatment of anemia.
25. Drug for the treatment of thrombophlebitis.
26. Drug for the treatment of renal colic.
27. Drug for stimulation of labor.
28. Drug for the treatment of diabetes.
29. Drug for the treatment of hypothyroidism.

30. Drug for the treatment of thyrotoxicosis.
31. Drug for the treatment of rheumatism.
32. Drug for the treatment of allergic diseases.
33. Drug for washing wounds.
35. Drug for the treatment of pneumonia.
36. Drug for the treatment of sepsis.
37. Drug for the treatment of dysentery.
38. Drug for the treatment of tuberculosis.
39. Drug for the treatment of flu.
40. Drug for the treatment of herpes.
41. Drug for the treatment of trichomoniasis.

EXAM QUESTIONS

GENERAL PHARMACOLOGY

1. Pharmacology: objectives, research methods and position in the system of medical sciences. Pharmacokinetics and pharmacodynamics.
2. Enteral route of administration of medicines: medical significance, advantages, disadvantages.
3. First-pass elimination and enterohepatic circulation: medical significance, examples of drugs which have the first-pass elimination or enterohepatic circulation.
4. Parenteral route of administration of drugs (under the skin, into the muscles, into the vein): features, medical significance.
5. Parenteral route of administration of drugs (intra-arterial, subarachnoid injections, epidural, inhalation, application to the epithelial surfaces): features, medical significance.
6. Absorption of drugs, types of transport of drugs through the biological membranes, factors influencing absorption. Bioavailability: medical significance; factors that affect bioavailability.
7. Biological barriers and their permeability for drugs (capillary wall, BBB (Blood-brain barrier), placental barrier).
8. Distribution of drugs in organs and tissues: factors affecting distribution. Volume of distribution.
9. Biotransformation of medicines: the concept of endobiotics and xenobiotics, biological significance, enzymes of bio-transformation of xenobiotics and types of reactions.
10. Drug clearance, types of clearance, factors that affect clearance. (Kinetic metabolism, reaction of drug metabolism: phase I and phase II)
11. Pharmacological effect, primary pharmacological reaction, receptors. Types and mechanisms of interaction of agonists and antagonists with receptors.
12. Localization, classification and functions of receptors.
13. Selectivity of drugs. Principles for classification of drugs.

14. Design and optimization of dosage regimen.
15. Cumulation: mechanism of development, medical significance.
16. Tolerance, tachyphylaxis: mechanism of development, medical significance.
17. Drugs of abuse, addiction, dependence: mechanisms of development, medical significance.
18. Individual variation of drug response: ethnicity, age, diseases, genetic factors.
19. Synergy of medicines: types, mechanisms of interaction, medical significance.
20. Antagonism of medicines: types, mechanisms of interaction, medical significance.

DRUGS AFFECTING AUTONOMIC NERVOUS SYSTEM

1. Types of peripheral nerves. Types of neurotransmitters.
2. Localization, structure and functions of adrenergic synapses.
3. Adrenoreceptors: types, localization, functions.
4. Epinephrine: mechanisms and features of action, indications, side effects.
5. α-Adrenergic agonists: classification, mechanisms and features of action, indications, side effects.
6. β-Adrenergic agonists: mechanisms of action, indications, side effects.
7. α-Adrenergic antagonists: classification, mechanism and characteristics of action, uses, side effects.
8. β-Blockers: classification, mechanisms of antiarrhythmic and antianginal actions, side effects.
9. β-Blockers: mechanisms of antihypertensive action, therapeutic use, side effects.
10. Localization, structure and functions of cholinergic synapses.
11. Cholinergic receptors: types, localization, functions.
12. The muscarinic agonists: classification, mechanisms and features of action, therapeutic use, side effects.

13. Cholinesterase inhibitors: classification, mechanisms, actions, indications and side effects.
14. Antimuscarinic drugs: classification; mechanisms and features of action, the use in ophthalmology, side effects
15. Acute atropine poisoning: stages, pathogenesis, symptoms, management.
16. Non-depolarizing muscle relaxants: classification, mechanisms and features of action, synergists and antagonists, indications, side effects.
17. Depolarizing muscle relaxants: mechanisms of action, synergists, indications, side effects.
18. Organophosphates overdose: symptoms, pathogenesis, management.

DRUGS AFFECTING THE MAJOR ORGANS AND SYSTEMS.

1. Antitussives and expectorants: classification, mechanisms and features of action, indications, side effects.
2. Bronchodilators: classification, mechanisms of action, treatment of bronchial asthma and other broncho-obstructive syndrome, side effects.
3. Cardiac glycosides: mechanisms of action on the heart rate, the conductive system of the heart, hemodynamics and renal function. Indications.
4. Glycoside intoxication (Digitalis Toxicity): stages, pathogenesis, symptoms, management.
5. Antiarrhythmic agents of class I: mechanisms of action, indications, side effects.
6. Antiarrhythmic agents of classes II, III and IV: mechanisms of action, indications, side effects.
7. Calcium channel blockers: classification, mechanisms of action, indications, side effects.
8. Nitrates: mechanisms and features of action, use, side effects.
9. Lipid-lowering agents: principles of action, classification. Mechanisms of action, indications, side effects of statins.
10. Diuretics: mechanisms of action, classification.
11. The carbonic anhydrase inhibitors and osmotic diuretics: mechanisms and features of action, uses, side effects.

12. Loop diuretics, thiazides and thiazide-like diuretics: mechanisms and features of action, indications, side effects.
13. Potassium-sparing diuretics: mechanisms and features of action, use, side effects.
14. ACE inhibitors: mechanisms of action, indications, side effects.
15. AT_1-receptor blockers: mechanisms of action, indications, side effects.
16. Antiemetic agents: classification, mechanisms and principles of action, indications, side effects.
17. Drugs that reduce gastric acidity: classification, mechanisms and features of action, indications, side effects.
18. Laxatives: classification, mechanisms of action, use, side effects.
19. Drugs affecting the uterus: classification, mechanisms and features of action, indications, side effects.
20. Antiplatelet agents: classification, mechanisms and features of action, indications, side effects.
21. Heparin: origin, chemical structure, mechanisms and features of action, indications, side effects.
22. Low molecular weight heparins: mechanisms and features of action, indications, side effects.
23. Warfarin: mechanisms and features of action, indications, side effects.
24. Thrombolytic drugs: mechanisms of action, therapeutic use, adverse effects.
25. Fibrinolytic agents: classification, mechanisms of action, clinical use, side effects.
26. Iron drugs: metabolism of iron, classification, mechanisms of action, clinical use, side effects.
27. Cyanocobalamin (Vitamin B_{12}): oral metabolism, clinical uses, side effects
28. Drugs for diabetes mellitus type 1: insulin and insulin analogues.
29. Drugs for diabetes mellitus type 2: classification, mechanisms of action, adverse effects.

ANTI-INFLAMMATORY AND ANTI-ALLERGY AGENTS

1. Antihistamines: classification, mechanisms and features of action, use, side effects.
2. Mechanisms of action and indications of anti-inflammatory action of NSAIDs.
3. Mechanisms of analgesic and antipyretic action of NSAIDs and paracetamol (acetaminophen). Side effects.
4. Glucocorticoids: classification, mechanisms of anti-inflammatory, immunosuppressive and anti-allergic actions, therapeutic use, adverse effects.

DRUGS AFFECTING CENTRAL NERVOUS SYSTEM

1. Anesthesia. Stages of anesthesia, classification of anesthetics.
2. Inhalation anesthetics: common features, drugs, mechanisms of action, adverse effects.
3. Intravenous anesthetics: drugs, features of anesthesia, effects, adverse effects, influence on autonomic functions and metabolism.
4. Ethanol: mechanism of action, effects, use.
5. Acute ethanol poisoning: pathogenesis, symptoms, treatment.
6. Sleeping pills: classification, mechanisms of action, influence at the stage of sleep, use, side effects, contraindications.
7. Antiepileptic drugs: classification, mechanisms of action, side effects, contraindications.
8. Opioid analgesics: opioid receptors, mechanisms of analgesic action, classification.
9. Use, side effects and contraindications to opioid analgesics.
10. Anxiolytics: mechanism of action, GABA-receptors, side effects, uses.
11. Benzodiazepine toxicity: symptoms, treatment.
12. Drug for Parkinson’s disease: principles of action (dopamine, dopaminergic pathways), classification.
13. Mechanisms of the action, side effects, indications and contraindications to dopaminomimetics used in Parkinson's disease.

14. Mechanisms of the action, side effects, indications and contraindications to antimuscarinic and NMDA receptor antagonists used in Parkinson's disease.
15. Mechanisms of the action, side effects of drugs for the treatment of Alzheimer's disease.
16. Mechanisms, features of the action, side effects of drugs for the treatment of migraine.
17. Antipsychotic drugs: classification, first-generation (typical) drugs, mechanisms of antipsychotic and sedative action, therapeutic use.
18. Antipsychotic drugs: classification, second-generation (atypical) drugs, mechanisms of antipsychotic and sedative action, therapeutic use.
19. Antidepressants: tricyclic antidepressants (TCAs) and selective serotonin reuptake inhibitors (SSRIs), mechanisms of action, indications, side effects.
20. Antidepressants — MAO inhibitors: classification, mechanisms and features of action, use, side effects, contraindications for use.
21. CNS stimulants: classification; mechanisms and features of action, indications, side effects.
22. Local anaesthetics: classification; mechanisms and features of action, indications, side effects.

ANTIMICROBIAL, ANTIVIRAL DRUGS

1. Classification of antibiotics by the mechanism of action.
2. Mechanism of bacterial resistance to antibiotics, methods of control and preventions of resistance.
3. Penicillins. Mechanism of action, antibacterial spectrum, classification, therapeutic use, resistance, adverse effects.
4. Cephalosporins. Mechanism of action, antibacterial spectrum, classification, therapeutic use, resistance, adverse effects.
5. Carbapenems. Mechanism of action, antibacterial spectrum, classification, therapeutic use, resistance, adverse effects.
6. Tetracyclines. Mechanism of action, antibacterial spectrum, classification, therapeutic use, resistance, adverse effects.

7. Aminoglycosides. Mechanism of action, antibacterial spectrum, classification, therapeutic use, resistance, adverse effects.
8. Macrolides. Mechanism of action, antibacterial spectrum, classification, therapeutic use, resistance, adverse effects.
9. Quinolones. Mechanism of action, antibacterial spectrum, classification, therapeutic use, resistance, adverse effects.
10. Sulfonamides. Mechanism of action, antibacterial spectrum, classification, therapeutic use, resistance, adverse effects.
11. Antimycobacterial drugs (Drugs used to treat tuberculosis). Mechanisms of action, classification, therapeutic use, resistance, adverse effects.
12. Antifungal drugs. Classification, antifungal spectrum, therapeutic use, resistance, adverse effects.
13. Antiviral drugs for the treatment of herpes virus infection. Mechanisms of action, classification, therapeutic use, adverse reactions
14. Antiviral drugs for the treatment of HIV. Mechanisms of action, classification, therapeutic use, adverse effects.
15. Interferons. Mechanisms of action, classification, therapeutic use, adverse effects.
16. Antiseptics. Classification, mechanisms of action, therapeutic and practice use, resistance, adverse effects.

DRUGS THAT REGULATE METABOLIC PROCESSES

1. Vitamin A and E: natural sources and metabolic significance of the vitamins, use. Hypervitaminosis A.
2. Vitamin D: natural sources and metabolic significance of the vitamin, its hormonal functions, use. Hypervitaminosis D.
3. The vitamins B_1 and B_6: the natural sources and metabolic significance of the vitamins, use.
4. Vitamins B_2 and nicotinic acid: the natural sources and metabolic significance of the vitamin, use.
5. Vitamin C: the natural sources and metabolic significance of the vitamin, use.

6. Drugs of Anterior Pituitary Hormones: mechanisms and features of action, use, side effects.
7. The hormones of the posterior lobe of the pituitary gland: mechanisms and features of action, use, side effects.
8. Drugs of thyroid hormones and antithyroid agents: mechanisms and features of action, use, side effects.

ANSWERS

Lesson 5. General pharmacology. Pharmacokinetics

Task 3

a. 1C, 2E, 3D, 4A, 5B

b. 1C, 2D, 3E, 4B, 5A

Case tasks

1. Correct answer is e. The Henderson-Hasselbalch equation predicts that a weak acid will be more nonionized, and therefore more lipid soluble, when pKa is greater than pH. Because the pH of the stomach lumen is less than 2, ibuprofen, an acid drug with a pK_a of 4,8, will be mainly nonionized in the gastric lumen and will readily penetrate the gastric mucosal cell membranes. Inside the mucosal cells, however, the pH is about 7, and the drug will become mainly ionized because now the pKa is less than the pH. Consequently, the concentration gradient of the nonionized, lipid-soluble form will remain high, and the drug will continue crossing cell membranes. At equilibrium, the concentration of the nonionized moiety of the drug will be the same on both sides, but the concentration of the ionized moiety inside the cell can be 15 to 20 times higher than that in the gastric lumen, as the ionized moiety is "trapped" inside the cell (ion-trapping mechanism). Therefore, the total drug concentration inside the cell will be high.
2. One half of the dose is eliminated in the first two hours so its elimination half-life equals two hours. With the passage of each half-life the amount in the body (or in the blood) will decrease to 50% of a former level. Thus, at 6 hours after administration, three half-lives have passed: 1) 200 mg to 100 mg, 2) 100 mg to 50 mg, and 3) 50 mg to 25 mg.
3. At 6 h after IV injection (which corresponds to two half-lives of the drug), the plasma level is 5 mg/L. Extrapolating back to zero time, "doubling" plasma level for each half-life results in an initial plasma level at zero time (C_0) = 5 mg/L × 2 × 2 = 20 mg/L.

   Dose = C_0 x Vd

   = 20 mg/L × 10 L

   = 200 mg
4. As a result of hypoalbuminemia, the free pharmacologically active fraction of warfarin increased in the patient.
5. Correct answer is 80. The volume of distribution (Vd) of a drug is independent of the dose. In fact, Vd = D × F/Cp0, where D = dose, F = fraction absorbed, and Cp_0 = plasma concentration at time 0. If the dose is increased by a certain proportion,

the plasma concentration will also be increased by the same proportion, and the Vd will remain the same.

6. Correct answer is 60. The dose of a drug can be calculated using the equation Dose = Vd × Cp0/F , where Vd = volume of distribution, Cp_0 = plasma concentration at time 0, and F = fraction absorbed. Because the Vd of the obese patient is twice the Vd of a normal-weight person, the dose must be doubled to 60 mg to achieve the same plasma concentration.

Lesson 6. General pharmacology. Pharmacodynamics

Task 3

a. 1D, 2A, 3B, 4C, 5E

b. 1B, 2C, 3D, 4E, 5A

Case tasks

1. A drug interaction is defined as synergistic when the response elicited by combined drugs is greater than the combined responses of the individual drugs. In other words, the response elicited by the drug combination is more than simply additive. In the present case, the effects of the individual drugs are bacteriostatic, whereas the effect of the combined drugs is more than an additive bacteriostatic effect (by definition, a bactericidal effect is greater than a bacteriostatic effect). The interaction is therefore defined as synergism.
2. Chemical antagonism is said to occur when a drug combines chemically with the drug to be antagonized, making that drug pharmacologically inactive, as in the present example. A chemical antagonist does not act on receptors or on the pharmacokinetics of the drug to be antagonized.
3. Potentiation. Although benzodiazepines are no longer first-line agents for generalized anxiety disorder, they are still used when other drugs are poorly tolerated or ineffective, as most likely occurred in this case. Potentiation occurs when a drug enhances the effect of another drug but is devoid of that effect when given alone. Cimetidine is devoid of sedative effects but can increase the sedative effect of diazepam by inhibiting hepatic metabolism of diazepam metabolism.
4. Correct answer is d. Potency of a drug refers to the dose of that drug needed to obtain a given effect. Because 10 mg of morphine is needed to get an analgesic effect equal to that given by 0,3 mg of buprenorphine, morphine is less potent than buprenorphine. Efficacy refers to the maximal effect produced by a drug. By definition, partial agonists have a maximal efficacy lower than that of full agonists. Because morphine is a full agonist and buprenorphine a partial agonist at the same receptor, buprenorphine is less effective than morphine.
5. Correct answer is d. Opiates exhibit pharmacodynamic tolerance, which can be defined as the decreased responsiveness to the action of a drug whose concentration at the site of action remains the same. The most common

mechanism underlying pharmacodynamics tolerance is receptor down-regulation; a decrease in receptor density.

6. Characterize effects of the drugs:
   a. Withdrawal syndrome
   b. Withdrawal syndrome
   c. Rebound syndrome

Lesson 7. Vitamins, drugs for bone disorders

Task 3

a. 1A, 2E, 3D, 4C, 5B

b. 1D, 2C, 3B, 4A, 5E, 6F

Case tasks

1. The main cause is hemeralopia ("night blindness"). It is based on vitamin A (retinol) hypovitaminosis. Retinol is part of the rhodopsin sticks pigment, which provides twilight vision and dark adaptation. In this case, patient does not receive enough vitamin A (malnutrition) or it is not absorbed (endogenous causes — pancreatitis). Also, the development of hemeralopia is affected by the lack of vitamins PP and B_2.
2. The described symptoms are retinol vitamin deficiency (vitamin A) associated with inadequate dietary intake. It is binding to the cytosolic receptors (retinol-binding proteins), after which vitamin A penetrates into the nucleus. In the nucleus, it causes a repression, thereby regulating the biosynthesis of certain proteins (membrane glycoproteins). Retinol stimulates cell proliferation, epithelialization and prevents keratinization of the epithelium. In retinol vitamin deficiency the skin becomes dry, the papular rash appears. The conjunctiva becomes dry, thick and wrinkled (xerophthalmia).
3. Cholecalciferol. The patient's signs and symptoms, together with the lab results, suggest that he was suffering from rickets, a disease that can affect children. Dark-skinned are at greater risk, because skin pigmentation blocks ultraviolet irradiation needed for synthesis of vitamin D. Rickets is due to vitamin D deficiency, which in turn causes deficient mineralization of epiphyseal cartilage and osteoid matrix. Vitamin D deficiency tends to cause hypocalcemia. When this occurs, parathyroid hormone (PTH) production is increased. Thus, the serum level of calcium is restored to nearly normal, but hypophosphatemia persists (due to PTH-mediated increase in renal secretion of phosphate), and mineralization of bone is impaired. The elevated alkaline phosphatase reflects the increased osteoblast activity. Cholecalciferol (vitamin D_3) supplementation with adequate calcium and phosphate intake is the standard therapy for rickets.
4. Bisphosphonates in bones are often retained for months or years, and a single injection of zoledronate can be effective for up to 1 year in the treatment of osteoporosis. The reason for this exceptionally long duration of action is because

these drugs are incorporated into the hydroxyapatite crystals of bone in place of pyrophosphate, thus altering the structure of the crystal. When bisphosphonates are released from resorbed bone mineral, they cause apoptosis of the osteoclasts, thus reducing the rate of bone resorption and decreasing the net bone loss that characterizes osteoporosis.

Lesson 8. Hormonal and antihormonal drugs

Task 3

a. 1A, 2C, 3B

b. 1A, 2D, 3B, 4C

Case tasks

1. Hypoglycemia due to alcohol consumption. The patient's signs (unconsciousness, sweating, hypothermia, tachycardia, and tonic-clonic seizure) and his history (alcoholic and insulin treatment) indicate that he was suffering from hypoglycemic coma. Hypoglycemia often occurs in alcoholics, likely due to a combination of starvation and impaired liver gluconeogenesis. In this case, the insulin treatment most likely made the patient even more sensitive to the hypoglycemic effects of alcohol, thus precipitating the hypoglycemic coma.
2. Metabolic conditions may be the result of recent injuries, or they may be the cause of altered consciousness leading to the traumatic event, as in this patient. Most likely the girl had undetected diabetes that led to her involvement in the accident. The marked hyperglycemia, glycosuria, and ketosis indicate that the patient has diabetic ketoacidosis and therefore must receive intravenous (IV) regular insulin at once. A latent diabetes can lead to hyperosmolar coma, which should be treated with IV regular insulin. However, the patient was not unconscious, and the ketotic bodies in the urine indicate that the most likely diagnosis is diabetic ketoacidosis.
3. Addison disease is a progressive hypofunctioning of the adrenal cortex. Mineralocorticoid deficiency results in increased excretion of Na^+ and decreased excretion of K^+, whereas glucocorticoid deficiency contributes to postural hypotension and causes severe insulin sensitivity. Gluconeogenesis is impaired, and hypoglycemia results. Decreased blood cortisol causes increased pituitary adrenocorticotropic hormone (ACTH) production and increased blood β-lipotropin, which has melanocyte-stimulating activity. Both ACTH and β-lipotropin cause hyperpigmentation of the skin and mucous membranes characteristic of Addison disease. The rational pharmacotherapy of the disease is to provide both mineralo- and glucocorticoid treatment. Fludrocortisone is preferred over aldosterone because of its long duration of action and its powerful salt —retaining activity. It is the only drug used for mineralocorticoid supplementation. Cortisol or a synthetic steroid are used for glucocorticoid supplementation.

4. Dexamethasone. The patient's signs and symptoms indicate that she was suffering from Cushing syndrome, most likely due to high-dose glucocorticoid therapy. Polymyositis is a chronic autoimmune disease of unknown cause characterized by inflammatory and degenerative changes in the muscles. High-dose glucocorticoid is usually the treatment of choice. Drugs with high potency and negligible salt-retaining activity, such as dexamethasone, are commonly the preferred agents.
5. The patient's signs and symptoms indicate that she was most likely suffering from hypothyroidism, and lab results confirmed that the disorder was due to Hashimoto thyroiditis. In most cases, high levels of antibodies to thyroid peroxidase are diagnostic for this disease. Hashimoto thyroiditis is likely the most common cause of hypothyroidism in North America. The treatment usually requires lifelong replacement therapy with thyroid hormones such as levothyroxine.

Lesson 9. Drugs affecting functions of adrenergic synapses

Task 3

a. 1B, 2C, 3D, 4E, 5A

b. 1C, 2A, 3D, 4E, 5B

Case tasks

1. The shock due to the spinal cord injury is vasodilatory (also called neurogenic or distributive shock), which occurs because the injured sympathetic nervous system fails to maintain the arteriolar tone. Drugs with α_1-adrenergic activity such as norepinephrine, phenylephrine, and dopamine are used to restore the arteriolar tone, thus counteracting the decreased blood pressure.
2. Norepinephrine usually causes a reflex bradycardia in patients with intact innervation of the heart for the following reason: the increase in blood pressure due to activation of α_1-receptors activates baroreceptors located in the carotid sinus and aortic arch (baroreceptors are stretch receptors). This increases the ring rate to the nucleus of the tractus solitaries in the medulla, which in turn increases its ring to the vagal motor neurons (dorsal motor neuron and nucleus ambiguus). When this vagal excitation is strong enough, it can overcome the norepinephrine-induced tachycardia due to activation of cardiac β receptors; therefore, bradycardia ensues.
3. Historically, the presence of diabetes was a contraindication for β-blockade, due to the adverse effects on insulin release and blunting of hypoglycemia-associated tachycardia. However, diabetics comprise a large portion of infarct patients, and many studies have found that patients treated with β-blockers following myocardial infarction experience a 30 to 35% reduction in mortality. Therefore, β-blockers can be given to diabetic patients, but they must carefully control their sugar levels. In fact, hypoglycemia-associated tachycardia can be blunted by β-blockers, depriving the patient of an important diagnostic sign.

4. The patient was most given a nonselective β-blocker propranolol (antagonizes both β_1 and β_2 receptors) that made her asthma worse due to β_2 antagonism. An alternative is to prescribe a cardioselective (antagonizes only β_1) β-blocker that does not antagonize β_2 receptors in the bronchioles. For example, metoprolol is a cardioselective β-blocker.

Lesson 10. Drugs affecting functions of cholinergic synapses (M, N-cholinomimetics, M-cholinomimetics, cholinesterase inhibitors, M-cholinoblockers)

Task 3

a. 1A, 2B, 3D, 4C, 5E

b. 1B, 2D, 3A, 4C

Case tasks

1. By inhibiting cholinesterase, neostigmine increases acetylcholine availability in the synaptic cleft of cholinergic fibers. This can increase the activity of both sympathetic and parasympathetic ganglia supplying the heart and can activate muscarinic M_2 receptors, which are the most abundant acetylcholine receptors in the sinoatrial (SA), atrium, and atrioventricular (AV) nodes. This activation in turn opens acetylcholine-sensitive K^+-channels, increasing the hyperpolarization of SA and AV cardiac fibers. The final result is a negative chronotropic and dromotropic effect.
2. The history and the patient's symptoms and signs indicate that he was most likely suffering from organophosphate poisoning. Serious poisoning from organophosphate pesticides is rare today because of enforced occupational health and safety standards, but mild poisoning is still surprisingly common.
3. The patient's signs and symptoms are consistent with the diagnosis of muscarine poisoning. High concentrations of muscarine are presented in various species of Inocybe and Clitocybe mushrooms. The symptoms of muscarine intoxication start within 1 hour after the ingestion and are all attributable to activation of muscarinic receptors.
4. The patient's symptoms, signs, and history indicate that he was most likely poisoned by black berries of deadly nightshade (*Atropa belladonna*), a plant containing antimuscarinic alkaloids (mainly atropine and scopolamine). Antimuscarinic syndrome is due to competitive blockade of muscarinic receptors all over the body. Physostigmine is an anticholinesterase inhibitor that can cross the blood−brain barrier, increasing the availability of acetylcholine both in the central nervous system and in the periphery. Although theoretically a cholinesterase inhibitor would be the ideal therapy for antimuscarinic poisoning, physostigmine can have dangerous central nervous system effects. Therefore, it is

used only in patients with dangerous hyperthermia or severe tachycardia, as in this case.

5. Organophosphate overdose. Atropine is always used to treat poisoning by cholinesterase inhibitors, because it is able to counteract both the central and peripheral symptoms of acetylcholine excess.
6. A. Physostigmine-induced sweating. Physostigmine is a cholinesterase inhibitor, and therefore it can increase the availability of acetylcholine at cholinergic neuroeffector junctions. Activation of M_3 receptors in sweat glands promotes sweating. By blocking M_3 receptors, atropine can counteract this action.

Lesson 11. Drugs affecting functions of cholinergic synapses (N-cholinomimetics, ganglionic blocking agents, muscle relaxants). Drugs affecting afferent innervation (local anesthetics, astringents, adsorbents and irritating agents)

Task 3

a. 1A, 2B, 3E, 4C, 5D

b. 1C, 2B, 3D, 4A

Case tasks

1. Drowsiness is the most frequent complaint that results from central nervous system (CNS) actions of local anesthetics and is usually an early sign of a high plasma level of the drug. CNS effects of lidocaine are common when the drug is administered systemically as an antiarrhythmic or when a sufficient concentration of the drug can reach the general circulation after being given locally for local anesthesia, as was most likely in this case.
2. e. Local anesthetics are weak bases; all but benzocaine have a pK_a in the range of about 7,7 to 9,4. Therefore, they are mainly water-soluble at the physiological pH of the extracellular fluid. However, only the small, lipid soluble portion of the drug can cross the nerve membrane. The extracellular fluid of the infected tissues has a lower pH due to the increased concentration of lactic acid. The lipid solubility of the drug will be even lower, and less drug will be available for diffusion into the nerve fibers.
3. Cisatracurium is a neuromuscular blocking drug that has the unique property of being inactivated primarily by a form of spontaneous breakdown also known as Hoffmann elimination. Because of this, it does not exhibit an increase in half-life in patients with compromised hepatic or renal function, and it is therefore the agent of choice under these conditions, as in the present case.
4. Blepharospasm is spasm of muscles around the eye that causes involuntary blinking and eye closing. Injection of botulinum toxin in to the eyelid muscle is often the preferred treatment (the effects of each treatment last about 3 months).

The most common adverse effect is eyelid ptosis (up to 20% of cases), which represents an unwanted extension of the pharmacological effect.

5. The patient's signs and symptoms indicate that he most likely took a high dose of cocaine. Formication ("Bugs are crawling under my skin"), stereotyped behavior, and paranoid delusions, together with signs of sympathetic overactivity (hypertension and tachycardia), are classic symptoms of cocaine overdose.

Lesson 13. Drugs affecting the functions of respiratory system and myometrium

Task 3

a. 1C, 2A, 3B, 4E, 5D

b. 1B, 2D, 3A, 4C, 5E

Case tasks

1. Systemic corticosteroids are given in cases of severe asthma exacerbation for two main reasons:

   a. They improve the responsiveness of β_2 receptors.
   b. They inhibit many phases of the inflammatory responses.

   The anti-inflammatory activity of corticosteroids is delayed for 4 to 6 hours after administration. However, the restoration of responsiveness to endogenous catecholamines, as well as to exogenous β_2-agonists, occurs within 1 hour of glucocorticoid administration in severe chronic asthmatics. This restoration is therefore the main potential benefit of intravenous administration of corticosteroids to a patient with severe asthma exacerbation under treatment with β_2-agonist

2. Theophylline. The antiasthmatic action of theophylline seems to result from both bronchodilating and nonbronchodilating actions. The inhibition of phosphodiesterase 4 (PDE4) in smooth muscle most likely explains the bronchodilating activity. Proposed nonbronchodilating mechanisms involve inhibition of PDE4 in inflammatory cells, which most likely reduces the release of inflammatory cytokines and enhances histone deacetylation (acetylation of histone is needed for activation of inflammatory gene transcription).

3. Dextromethorphan. Dextromethorphan is a stereoisomer of a levorphanol derivative, has lost the analgesic, sedative, and addictive properties of the parent compound but is an effective cough suppressant with potency nearly equal to that of codeine. The drug can be an appropriate cough suppressant in asthmatic patients. Codeine is the most commonly used cough suppressant but is not indicated in asthmatic patients because opioids can cause respiratory depression even when given in subanalgesic doses. This respiratory depression does not occur with dextromethorphan.

4. Oral triamcinolone. Oral steroids are usually administered to treat severe asthma that is not controlled by other antiasthmatic drugs. Corticosteroids have potent anti-inflammatory activity, and although they are not direct bronchodilators, they can relieve bronchial obstruction by improving the responsiveness of β_2 receptors to β_2-agonists.
5. Benzonatate. Benzonatate suppresses the cough reflex through peripheral action and has no abuse potential. Dextromethorphan, an opioid derivative, and codeine, an opioid, both have abuse potential.

Lesson 14. Drugs affecting the functions of digestive system

Task 3

a. 1A, 2C, 3E, 4D, 5B

b. 1E, 2A, 3B, 4C, 5D

Case tasks

1. Because magnesium hydroxide tends to cause diarrhea, and aluminum hydroxide tends to cause constipation, a combination of the two can have a balanced effect on intestinal motility without any loss of antacid effectiveness.
2. Correct answer is e. Metoclopramide is a dopamine D_2-receptor antagonist, a serotonin 5-HT_3-receptor antagonist, and a serotonin 5-HT_4-receptor agonist. In the enteric nervous system, all of these molecular actions seem to contribute to the final effect that is related to an increased activity of cholinergic motor neurons. In this way, the drug exerts a prokinetic effect; that is, it increases the lower esophageal sphincter tone and enhances transit in the upper digestive tract. It has negligible effects on gastric secretion or motility of the large intestine. In addition, the blockade of D_2-receptors and 5-HT_3-receptors in the chemoreceptor trigger zone can explain the antiemetic activity of the drug.
3. NaHCO3. All antacids can cause metabolic alkalosis, due to the spared endogenous bicarbonate that is secreted in the stomach under prostaglandin E_2 control. In addition, exogenous bicarbonate is readily and completely absorbed; therefore, the risk of metabolic alkalosis is higher than that of calcium, magnesium, and aluminum salts that have an oral bioavailability less than 30%.
4. Correct answer is d. When diarrhea is experienced with the use of laxatives, the laxative should be discontinued until resolution of the diarrhea. A diet rich in fiber and abundant fluid intake usually helps to normalize the intestine.
5. Omeprazole. It is appropriate to treat this patient with a proton-pump inhibitor (PPI) to reduce acid production and promote healing.

Lesson 15. Antiseptic, disinfectant, antifungal, antiparasitic drugs

Task 3

a. 1A, 2B, 3D, 4C

b. 1A, 2D, 3C, 4B

c. 1D, 2B, 3A, 4C, 5F, 6E

Case tasks

1. Voriconazole is the drug of choice for aspergillosis. Studies have found it to be superior to other regimens including amphotericin B.
2. The symptoms and other findings for this patient are consistent with neurocysticercosis. Albendazole is the drug of choice for the treatment of this infestation.
3. Correct answer is e. The patient's signs, symptoms, and X-ray suggest a systemic mycosis. Lab results confirm the diagnosis of systemic candidiasis, which accounts for about 80% of major systemic fungal infections. Amphotericin B, antifungal azoles, and echinocandins are first-line agents for systemic candidiasis.
4. Correct answer is c. The patient's symptoms and lab results suggest that she was suffering from vulvovaginal candidiasis, the most common opportunistic mycosis of the genital tract in women taking oral contraceptives. Other predisposing factors are pregnancy, menstruation, diabetes mellitus, and use of broad-spectrum antibiotics, corticosteroids, or immunosuppressive drugs. Budding yeast cells and pseudohyphae of *Candida albicans,* the most common *Candida* species causing candidiasis, can be detected by microscopic examination of biologic specimens. Local therapy of vulvovaginal candidiasis includes azoles and nystatin. Cure rates for uncomplicated vulvovaginal candidiasis are 80 to 95% with topical or oral azoles and 70 to 90% with nystatin.
5. Praziquantel. The patient's symptoms indicate that he was most likely suffering from adverse effects of praziquantel. This drug is the first-line agent for most trematode and cestode infections. Although serious adverse effects of the drug are rare, minor adverse effects are common and usually subside in 1 or 2 days.
6. Alkali poisoning. Treatment: alkalis can be neutralized with mild vinegar, lemon or orange juice; morphine and atropine — PC, prednisolone, glucose, norepinephrine, and hemodez — IV; ceftazidime — IM.
7. Iodine poisoning. Treatment: gastric lavage (activated charcoal, protein, milk), sodium bicarbonate and sodium thiosulfas — IV, ceftazidime — IM.

Lesson 16. Antibiotics and anticancer drugs

Task 3

a. 1E, 2 D, 3A, 4B, 5C

b. 1D, 2A, 3C, 4E, 5 B

Case tasks

1. Correct answer is d**.** The patient's history and clinical presentation suggest that the man is suffering from infective endocarditis. He appears chronically ill and

represents the typical patient with subacute disease. He has mitral valve prolapse, which is the predominant defect in infective endocarditis, and he also exhibits several peripheral manifestation of infective endocarditis, including hemorrhages in the hands and feet. The gram-positive bacteria most commonly involved in infective endocarditis are streptococci and staphylococci. Streptococci of the viridans group are the principal cause of endocarditis in an abnormal heart valve (which is present in this case), and they reach the bloodstream typically after dental trauma. The temporal relationship between the dental procedure and the onset of symptoms makes it the most obvious cause of the disease. Most viridans streptococci are sensitive to penicillins and cephalosporins. Single-drug regimens include high-dose penicillin G or ceftriaxone for 2 to 4 weeks. When empirical therapy is needed, the guidelines suggest high dose penicillin G plus an aminoglycoside, as in this case. This is a synergistic combination that can achieve bactericidal activity against resistant streptococcal species.

2. The patient's symptoms and physical examination suggest the diagnosis of acute otitis media, one of the most common infectious diseases afflicting infants and children. The main bacteria causing otitis media in children are *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis*. Most clinicians advocate a stepped approach to the antimicrobial therapy, which involves initial treatment with amoxicillin or trimethoprim-sulfamethoxazole. If this regimen does not reduce symptoms within 3 days, amoxicillin/ clavulanate or cefuroxime or ceftriaxone should be substituted for the initial therapy, as was done in this case. Potassium clavulanate is a β-lactamase inhibitor that blocks many, but not all, β lactamase enzymes, protecting amoxicillin from inactivation by β-lactamase-producing bacteria.
3. The predominant organisms causing nosocomial pneumonia are aerobic gram-negative bacilli, including *Klebsiella pneumoniae*, *Escherichia coli*, *Proteus mirabilis*, and *Pseudomonas aeruginosa*. The most frequent and best characterized pathogen is *Klebsiella pneumoniae*, which causes Friedlander pneumonia, a disease that can have a fulminant course and a mortality rate of about 50%, despite the availability of effective antibiotics. In this case, the typical appearance of the sputum (a homogeneous mixture of blood and mucus resembling currant jelly) and the results of lab tests and X-ray suggest Friedlander pneumonia. Cephalosporins are drugs of first choice against *Klebsiellae*. However, due to the seriousness of the disease, most authorities suggest the use of an aminoglycoside together with a cephalosporin.
4. Tetracycline absorption is impaired by some cations (Ca^{2+}, Mg^{2+}, Fe^{2+}, Al^{3+}) because tetracyclines can chelate these cations, forming a complex that cannot permeate the intestinal wall. Therefore, products that contain a large amount of these cations (e.g., milk and dairy products, antacids, and iron and zinc supplements) must not be administered with tetracyclines.
5. Azithromycin is highly effective as an oral agent in the management of pharyngitis caused by gram-positive cocci and may necessitate only a short course

of therapy. In patients who have marked hypersensitivity to penicillins, it is inappropriate to use a cephalosporin, even though cefaclor is active against common oropharyngeal pathogens. Doxycycline should not be used in children. One must assume that complete cross-allergenicity exists between different members of the penicillin class of antibiotics, and, in any case, penicillin G is not usually given orally because of its lability in gastric acid. Vancomycin would need parenteral administration, and this antibiotic should be reserved for more serious bacterial infections.

Lesson 17. Sulfonamides, quinolones, antituberculosis, antiviral, antimalarial drugs

Task 3

a. 1E, 2A, 3B, 4C, 5D

b. 1D, 2A, 3B, 4C

Case tasks

1. Oseltamivir is the best choice since it is administered orally and not associated with resistance.
2. Correct answer is c. The primary goal of highly active antiretroviral therapy is to delay the emergence of resistance, as mutations conferring resistance to one drug do not necessarily confer resistance to other drugs. An additional benefit of the combination therapy is to decrease the risk of toxicity associated with any one of the agents, as the drugs have different toxicity profiles.
3. The signs and symptoms of the patient are most likely due to ethambutol-induced optic neuritis, a serious adverse effect of the drug that is dose- and duration-related. Because of this, periodic visual acuity testing is desirable during ethambutol therapy. Recovery is usually, but not always, complete when the drug is discontinued.
4. The symptoms of the patient and the lab results indicate that she was most likely suffering from isoniazid-induced hepatitis, which is the most frequent major toxic effect of isoniazid. It occurs in about 1% of patients and can lead to potentially fatal multilobular necrosis. The risk increases with age and in alcoholics, as in this case.
5. The patient most likely received trimethoprim-sulfamethoxazole, a drug combination frequently used to treat urinary tract infection. The patient's signs and symptoms (tiredness, dark urine) suggest that she was suffering from acute hemolytic anemia, a disease that can develop in persons with congenital deficiency of glucose-6-phosphate dehydrogenase when given oxidant chemicals. Glucose-6-phosphate dehydrogenase is a key enzyme in reduction reactions, and these reactions appear to be essential for maintenance of cellular integrity. A deficiency of this enzyme results in an exaggerated sensitivity to the hemolytic effect of certain oxidant drugs such as sulfonamides, antimalarials, and certain nonsteroidal anti-inflammatory drugs.

6. Resistance to chloroquine is now very common in many areas of Africa. Mefloquine has strong schizonticidal activity and is effective against many chloroquine-resistant strains of *P. falciparum* and other malariaspecies.

Lesson 19. General anesthetics, sleeping pills, ethanol

Task 3

a. 1A, 2C, 3D, 4B, 5E

b. 1A, 2B, 3E, 4D, 5C

Case tasks

1. Propofol is an intravenous anesthetic with an onset and duration of anesthesia similar to that of thiopental. It is the only anesthetic with antiemetic action, so it is the preferred drug in patients at high risk of nausea and vomiting, as in this case.
2. To maintain unconsciousness and muscle relaxation. Unconsciousness, which is usually achieved with thiopental, cannot be maintained with nitrous oxide alone (the drug has a minimum alveolar concentration higher than 100%), and therefore another potent anesthetic is needed. Moreover, nitrous oxide has negligible effects on skeletal muscle tone, so a halogenated anesthetic is given with it most of the time (all halogenated anesthetics cause relaxation of skeletal muscle and enhance the effects of neuromuscular blocking agents).
3. Sevoflurane is a potent coronary vasodilator, simultaneously producing increased coronary blood flow and decreased myocardial oxygen consumption. It is a particularly safe anesthetic to use for patients with ischemic heart disease, as in this case.
4. Correct answer is b. Z-hypnotics (zolpidem, zaleplon) bind selectively to the α1 subunit of the GABAA receptor−chloride channel complex. This selectivity may account for their relative lack of effect on sleep architecture and stages, as well as for the negligible anxiolytic, anticonvulsant, and muscle relaxant properties. The binding increases the GABA-mediated opening of Cl^--channels, leading to an increase in Cl^- conductance. The enhanced concentration of Cl^- inside the cell causes hyperpolarization of the cell membrane.
5. Benzodiazepine (BZDs) overdose. BZDs exert their effect via modulation of the gamma-aminobutyric acid A (GABA-A) receptor, which is the primary inhibitory neurotransmitter in the central nervous system. The classic presentation in patients with benzodiazepine overdose will include central nervous system (CNS) depression. The mainstay treatment for acute benzodiazepine toxicity is supportive care which may include endotracheal intubation to provide definitive airway management. A single-dose or multi-dose activated charcoal. Flumazenil is a nonspecific competitive antagonist at the benzodiazepine receptor that can reverse BZD induced sedation.
6. People who have been using high doses of benzodiazepines, such as alprazolam, for long periods can experience withdrawal symptoms on abrupt termination of

the administration. The withdrawal syndrome may include the following symptoms:

- Following moderate dose usage: anxiety, agitation, increased sensitivity to light and sound, paresthesias, myoclonic jerks, sleep disturbances, dizziness
- Following high-dose usage: delirium, seizure

The abrupt onset of the withdrawal syndrome, as well as its severity, is a function of the half-life of the drug. Benzodiazepines with shorter elimination half-lives (alprazolam, lorazepam, temazepam, and midazolam) produce a rapidly evolving and severe withdrawal syndrome (symptoms within 12 to 24 hours after the last dose), whereas those with longer half-lives usually have a built-in tapering-o action that makes the withdrawal syndrome less severe but longer in duration.

7. Correct answer is c. Ethanol withdrawal can occur when an alcoholic person is forced to stop drinking because of some external event, such as the hospital admission in this case. The signs and symptoms of the patient (agitation, tremulousness, and hallucinations) are consistent with the first phase of alcohol withdrawal that typically occurs 8 to 48 hours after the last ethanol intake.

Lesson 20. Antiepileptic drugs. Opioid analgesics

Task 3

a. 1E, 2C, 3D, 4B, 5A

b. 1A, 2D, 3C, 4B, 5E

Case tasks

1. The therapeutic effect of morphine in pulmonary edema likely involves
   - Reduced perception of shortness of breath
   - Reduced fear and apprehension (pain anticipatory anxiety is reduced).
   - Reduced preload due to peripheral venous dilation and afterload due to arteriolar vasodilation, likely due both to histamine release and decreased sympathomimetic activity secondary to decreased anxiety
2. Correct answer is d. Morphine depresses all phases of respiratory activity (respiratory rate, minute volume, and tidal exchanges) mainly because the drug reduces the responsiveness of the brainstem respiratory centers to partial pressure of arterial carbon dioxide ($PaCO_2$).
3. The triad of coma, miosis, and respiratory depression indicates that opioid analgesic was most likely the drug the woman had self-injected. The respiratory rate can be very low, or the patient may even be apneic, and cyanosis is often present. The pupils are symmetrical and pinpoint in size, although if hypoxia is severe, they may be dilated. Blood pressure can be near normal at first but falls progressively.

4. Carbamazepine is a potent enzyme inducer and can induce its own metabolism; this appears to be mediated via its effects on the hepatic CYP3A4 isoenzyme. Onset of enzyme induction is at about 3 days, with maximum effect at about 30 days.
5. The signs of the patient are classical adverse effects of phenytoin. Hirsutism and gingival hyperplasia occur to some degree in most patients. Blurred vision, diplopia, and broadening of the lips and nose are associated in some patients with long-term use of the drug.
6. The patient was most likely suffering from myoclonic seizures, a type of epilepsy that occurs mainly during childhood. Valproic acid is a first-line agent for myoclonic seizures and can control the symptoms in most cases.

Lesson 21. Drugs for neurodegenerative diseases. Drugs for the treatment of migraine

Task 3

a. 1A, 2C, 3D, 4E, 5B

b. 1A, 2D, 3C, 4B

Case tasks

1. Levodopa. The adverse effects reported by the patient and the timing of the effects suggest that they are levodopa-induced dyskinesias, which occur in up to 80% of patients receiving the drug for long periods. The development of dyskinesias is dose-related, and dyskinesias are usually associated with peak striatal dopamine levels or when the level of the drug is rising or falling. The exact mechanism of these dyskinesias is not known, but simplistically it can be thought of as too much movement caused by too much striatal dopamine receptor stimulation.
2. Rivastigmine. The man was most likely in the early stages of Alzheimer disease (AD). He displayed several symptoms associated with dementia, including impaired reasoning (recognition deficits), loss of memory, confusion, and disorientation. A major approach to the treatment of AD has involved the attempt to augment the cholinergic function in the brain, because a loss of cholinergic neurons is a prominent feature of the disease. Rivastigmine, and galantamine are cholinesterase inhibitors approved for treatment of AD.
3. Correct answer is c. A variety of cardiac arrhythmias have been described in patients receiving levodopa. Like all levodopa-induced effects, they are due to dopamine that can activate cardiac β_1 and β_2-adrenoceptors. Concomitant administration of carbidopa reduces the likelihood of these effects, but arrhythmias are sometimes reported in patients receiving levodopa/carbidopa, as in this case.
4. The patient is most likely suffering from the on-off phenomenon, in which off periods of marked akinesia alternate over the course of a few hours with on periods of improved mobility and marked dyskinesia. These response fluctuations

can be decreased by adjunctive drugs, including dopamine agonists such as pramipexole, catechol-*O*-methyltransferase (COMT) inhibitors such as entacapone, and, in some cases, selegiline.

5. Correct answer is d. Triptans (e.g., sumatriptan and zolmitriptan) are specific 5-$HT_{1B/1D}$ agonists that are equally as or more effective than ergot alkaloids in the acute treatment of migraine attack.

   There are two major proposed mechanisms for effectiveness of triptans in acute migraine headache:

   - Vasoconstriction of cerebral vessels via the activation of vascular 5-HT_{1B} receptors
   - Inhibition of release of neuropeptides with inflammatory properties via the activation of presynaptic 5-HT_{1D} receptors

   Triptans are not intended for use in the prophylaxis of migraine.

6. Correct answer is c. Ergot alkaloids such as ergotamine are contraindicated in patients with coronary artery disease and peripheral vascular disease because of the vasoconstricting properties of these drugs. It is even recommended that ergotamine not be given to patients in whom unrecognized coronary artery disease can be predicted by the presence of risk factors (hypertension, hypercholesterolemia, smoking, obesity, etc.), as in this case.

Lesson 22: Antipsychotic, anxiolytic, and sedatives

Task 3

a. 1D, 2A, 3C, 4B

b. 1C, 2A, 3B, 4E, 5D

Case tasks

1. The patient's assaultive behavior and persecutory delusions suggest that he was most likely suffering from a schizophrenic disorder, for which he received a neuroleptic drug. The neurologic signs of the patient indicated that he suffered from acute dystonia, an extrapyramidal symptom that usually occurs after few days of high-dose neuroleptic therapy. Acute dystonias present with a sudden onset of brief abnormal postures, such as tongue protrusion, oculogyric crisis, torticollis, and unusual positions of the trunk and limbs. The extrapyramidal adverse effects of neuroleptics occur more often with high-potency drugs, such as haloperidol and fluphenazine.
2. Clozapine. The poor response to several neuroleptic drugs and the prevalence of negative symptoms of schizophrenia indicate that the patient is a candidate for clozapine therapy. Clozapine is the only neuroleptic approved by the Food and Drug Administration for the treatment of resistant schizophrenia.
3. The amenorrhea and galactorrhea are adverse effects of neuroleptics that are related to their blockade of D_2 receptors in the anterior pituitary gland. Dopamine

acts as a prolactin-inhibiting factor by activating these receptors in the pituitary. When D_2 receptors are blocked, prolactin secretion increases. High plasma levels of prolactin can result in amenorrhea, galactorrhea, and anovulation in women, and azoospermia, impotence, and gynecomastia can develop in men. All typical neuroleptics can cause the above-mentioned symptoms, whereas atypical neuroleptics are minimally associated with hyperprolactinemia.

4. Haloperidol which caused NMS. The clinical picture is typical of neuroleptic malignant syndrome (NMS), a rare but potentially lethal complication that may present in a sudden, unpredictable fashion. The etiology of NMS is unknown, but a proposed mechanism suggests that a neuroleptic-induced, excessively rapid blockade of dopaminergic receptors in the diencephalon may play a role.
5. Clozapine. The low white blood cell count and the low neutrophil percentage indicate that the man was most likely suffering from drug-induced agranulocytosis. Agranulocytosis is the most fatal adverse drug reaction, accounting for 26% of all drug-related deaths. Clozapine can cause agranulocytosis in about 0,8% of patients (a rate lower than the original estimate of 1 to 2%). The onset of the disorder is variable, as it can occur a few days after starting the treatment or even several years after a daily chronic treatment. However, the first 6 months of clozapine therapy is the period of greatest risk. Discontinuation of the drug usually results in correction of neutrophil count within 30 days.
6. Diazepam. The time-honored principle of treating an abstinence syndrome with an agent to which the abused drug induces cross-tolerance holds for ethanol as well. A long-acting benzodiazepine, such as diazepam, is the drug most commonly used in alcohol withdrawal, but a short-acting agent such as oxazepam can be administered every 4 to 6 hours according to the stage and severity of withdrawal.

Lesson 23. Antidepressants, psychostimulants, nootropic drugs, analeptics

Task 3

a. 1A, 2C, 3B, 4D,5E
b. 1B, 2A, 3C

Case tasks

1. Correct answer is e. The patient was most likely suffering from a social anxiety disorder (SAD). Several trials have provided evidence of the efficacy of pharmacotherapy with selective serotonin reuptake inhibitors (SSRIs) or serotonin−norepinephrine reuptake inhibitors (SNRIs) in SADs. Approximately one fifth of patients with SAD also suffer from an alcohol use disorder, as in this case. Paroxetine significantly reduces social anxiety and decreases the frequency of alcohol use in patients with both disorders.
2. Tricyclic antidepressant poisoning may produce any of three major toxic syndromes:

- Anticholinergic syndrome: sedation, delirium, tachycardia, mydriasis, dry mucous membranes, hyperthermia, constipation, and urinary retention
- Cardiovascular syndrome: hypotension, sinus tachycardia with prolongation of QT-intervals, torsade de pointes (rare). Bradyarrhythmias (various degrees of atrioventricular block) can occur in severe poisoning and carry a poor prognosis. They are due to the quinidine-like activity common to all tricyclic antidepressants, which can severely impair cardiac conduction.
- Convulsing syndrome: seizures may be recurrent or persistent. Depending on the dose, patients may experience some or all of these toxic effects. The patient's coma indicates that the poisoning was severe and most likely included all three toxic syndromes.

3. The history, signs, and symptoms of the patient indicate that she was most likely suffering from serotonin syndrome. This disorder is a rare but potentially fatal interaction that can be caused by several drugs either alone or in combination, when given in high doses. These include antidepressants, opioids, psychostimulants, triptans, psychedelics, and herbs (e.g., St. Johns wort, ginseng, and nutmeg). The combination of two drugs that enhance serotonin transmission (i.e., SSRIs/SNRIs with monoamine oxidase inhibitors or with tricyclic antidepressants) can be particularly dangerous. The syndrome involves mental, autonomic, and neurologic disorders of sudden onset less than 24 hours after the beginning of treatment or of an overdose. For mild cases, discontinuation of the offending drug is the only needed treatment. For more serious cases, therapy includes benzodiazepines for agitation and somatic effects, atypical neuroleptics with serotonin-blocking activity (e.g., olanzapine), β-blockers for tachycardia and autonomic instability, and dantrolene for hyperthermia.
4. Phenelzine is a nonselective monoamine oxidase inhibitor (MAOI). These drugs are rarely prescribed today because of frequent adverse effects and the risk of serious drug−drug and drug−food interactions. However, for the treatment of atypical depression, MAOIs are among the most effective agents available and are still prescribed for patients with this depressive subtype, usually after failure of a selective serotonin reuptake inhibitor (SSRI) therapy, as in this case.
5. The history and symptoms of the patient indicate that she was most likely suffering from the depressive phase of a bipolar disorder. The depression is often difficult to control and puts patients at significant risk of suicide. Lithium (alone or in combination) remains the first-line agent for maintenance therapy of bipolar disorder.

Lesson 25. Cardiotonic and antiarrhythmic drugs

Task 3

a. 1B, 2C, 3A, 4E, 5D

b. 1D, 2C, 3A, 4B

Case task

1. The patient's signs and symptoms indicate a pulmonary disorder. Microbial infect ion is unlikely, and diffuse bilateral lung infiltrates are consistent with pulmonary fibrosis. Amiodarone-induced pulmonary fibrosis is the most serious adverse effect of the drug. Its incidence is variable (1 to 7% of the population), and mortality is also quite variable (0,1 to 10,0% of those affected).
2. Prolongation of QT-interval indicates prolongation of action potential duration, which is related to a decreased outward potassium current during phase 3 of the action potential. Long QT-interval is present prior to the onset of tachycardia and is due to hereditary or acquired potassium channel defects. Drugs include class Ia and III antiarrhythmic drugs, tricyclic antidepressants, neuroleptics, some antihistamines, macrolide antibiotics, and quinolones. All of these drugs are able to increase action potential duration by blocking or modifying potassium channels. High doses of these drugs can trigger polymorphic ventricular tachycardia in patients at risk. Sotalol is the only β-blocker that can block potassium channels (a property not related to β-receptor blockade), and it can cause polymorphic ventricular tachycardia. Moreover, the patient was taking a quinolone and so was already at risk of developing the disorder.
3. Correct answer is e. The patient's history and symptoms indicated that the patient attempted suicide by ingesting several digoxin tablets. The best way to treat digoxin poisoning is to administer digoxin antibodies (digoxin immune Fab) that bind digoxin with very high affinity, thus removing the drug from its tissue-binding sites. This approach is extremely effective in reversing digoxin intoxication.
4. The patient's symptoms (nausea and vomiting), as well as the arrhythmia shown by the electrocardiogram, are classic signs of digoxin toxicity. Furosemide treatment most likely caused hypokalemia, which is a well-recognized predisposing factor to digoxin toxicity. In fact, in patients with serum K^+ of 3 m Eq/L, the dose of digoxin needed to produce toxicity is about one half of that needed in patients with serum K^+ of 5 mEq/L. Moreover, the patient had reduced renal function (see the creatinine serum level), which most likely decreased the renal excretion of digoxin. Potassium supplementation, discontinuation of digoxin and providing of digoxin antibodies are the rational therapy for this case.

Lesson 26. Antianginal drugs. Lipid-lowering drugs

Task 3

a. 1A, 2D, 3C, 4B, 5E

b. 1A, 2D, 3B, 4C, 5E

Case tasks

1. Tolerance to nitrates does occur. Because it appears rapidly (24 hours) and disappears rapidly (6 to 10 hours), brief periods of no therapy (overnight) can be sufficient to permit recovery, but this patient was continuously receiving the drug.
2. The dose of nitroglycerin given to this patient was likely too high, as the symptoms the patient is referring to are classic for nitrate toxicity.
3. Correct answer is d**.** Nifedipine is a dihydropyridine calcium channel blocker that causes vasodilation by blocking L-type calcium channels in smooth muscle membranes. The antianginal effect of both calcium channel blockers and nitrates in variant angina is mainly due to coronary vasodilation, which in turn increases oxygen supply to the heart. Today, calcium channel blockers are considered the drug of choice to prevent attacks of variant angina that are characterized by coronary spasms. Dihydropyridines, verapamil and diltiazem, are considered equally efficacious in this disease
4. The patient was most likely affected by myopathy, a rare but serious adverse effect of statins. The disorder occurs in less than 0,1% of patient s when statins are given alone, but it can occur more often when they are given together with niacin or fibrates (up to 5% when given with gemfibrozil). Myopathy can cause rhabdomyolysis with myoglobinuria, as in this case.
5. Statins are often prescribed after a myocardial infarction to prevent reinfarction. Statins cause an increase in liver enzymes in about 2% of patients. Abnormal enzyme values usually resolve with cessation of treatment, but the drug should be discontinued when the aminotransferase activity is persistently elevated to more than 3 times the normal limits because of the risk of hepatotoxicity.

Lesson 27. Diuretics

Task 3

a. 1A, 2F, 3E, 4D, 5B, 6C

b. 1C, 2D, 3E, 4A, 5B

Case tasks

1. The patient exhibits the classic symptoms of pulmonary edema. Furosemide is the diuretic of first choice for this condition because it is able to quickly reduce preload (and therefore the left ventricular filling pressure) through the following actions:
   - Rapid increase in venous capacitance, likely mediated by prostaglandin release (the initial beneficial effect may result more from this action than from diuresis)
   - Brisk and abundant natriuresis
2. The history and symptoms of the patient suggest that he has been suffering from liver cirrhosis. Moreover, the low K^+ and high bicarbonate levels suggest that high levels of aldosterone are present. Secondary hyperaldosteronism is common in advanced liver cirrhosis for the following reasons:

- Ascites-induced hypovolemia activates the renin−angiotensin−aldosterone system.
- Liver metabolism of aldosterone is reduced because of liver impairment.
- Hypoalbuminemia is a known consequence of liver cirrhosis.
- Because aldosterone is highly bound to albumin, cirrhotic patients have a higher free, active concentration of aldosterone. Spironolactone is an aldosterone receptor antagonist and therefore is a rational diuretic choice.

3. Correct answer is c. Hypokalemia is a common adverse effect of the thiazides and causes fatigue and lethargy in the patient. Supplementation with potassium chloride or foods high in K^+ corrects the problem. Alternatively, a potassium-sparing diuretic, such as spironolactone, may be added. Calcium, uric acid, and glucose are usually elevated by thiazide diuretics. Sodium loss would not weaken the patient.
4. Correct answer is d. The effects described are typical of loop diuretics, which inhibit the Na^+-K^+-$2Cl^-$ cotransporter in the thick ascending limb. This action prevents the reabsorption of Ca^{2+} from the paracellular pathway and provides for the use of these drugs in hypercalcemia. The increased load of Na^+ in the collecting tubules leads to increased excretion of both K^+ and H^+, so hypokalemia and alkalosis may occur.

Lesson 28. Drugs affecting the blood pressure

Task 3

a. 1E, 2C, 3B, 4D, 5A

b. 1B, 2C, 3D, 4A

Case tasks

1. The patient's symptoms are most likely due to sudden clonidine withdrawal. Rebound hypertension can occur (to levels above those present prior to treatment), but the syndrome can appear in the absence of an overshoot in blood pressure. The signs and symptoms of the syndrome are associated with increased sympathetic discharge (plasma levels of catecholamines are increased). The rebound hypertension seems to be due to an upregulation of α_1 receptors.
2. A dry, disturbing cough is a typical adverse effect of ACE inhibitors that occurs in up to 20% of patients and is most likely due to the increased plasma levels of bradykinin. The loss of taste (dysgeusia) reported by the patient is another typical effect of ACE inhibitors (the reason is unknown).
3. Correct answer is d. Because the systolic blood pressure is more than 20 mm Hg above goal (10 mm Hg above goal diastolic), treatment with two different medications is preferred. Because the patient is diabetic, he also has a compelling indication for an ACE inhibitor or ARB.

4. Correct answer is c. The therapy of cardiogenic shock requires a rapid-acting inotropic drug to increase myocardial contractility and cardiac output. Dobutamine and dopamine are the two drugs most frequently used. In both cases, the therapeutic efficacy is mediated mainly by the direct (dobutamine) or indirect and direct (dopamine) activation of β_1-receptors, which in turn increase the synthesis of cAMP.
5. Norepinephrine. The shock due to the spinal cord injury is vasodilatory (also called neurogenic or distributive shock), which occurs because the injured sympathetic nervous system fails to maintain the arteriolar tone. Drugs with α_1-adrenergic activity such as norepinephrine, phenylephrine, and dopamine are used to restore the arteriolar tone, thus counteracting the decreased blood pressure.

Lesson 29. Drugs affecting the blood system

Task 3

a. 1A, 2D, 3C, 4B, 5E

b. 1B, 2C, 3A, 4D

Case tasks

1. The primary approach to prevent valvular thrombosis and systemic thromboembolism associated with mechanical prosthetic valve replacement is long-term anticoagulation with warfarin. Most likely, the dose of warfarin was too high, so bleeding occurred, as pointed out by the signs and symptoms of the patient.
2. The sudden dyspnea, hypotension, and pleuritic chest pain, particularly in a high-risk setting (gastric cancer), would suggest the diagnosis of massive pulmonary embolism, which is confirmed by the computed tomography scan. Heparin is a drug of choice to prevent further thrombus formation and embolization.
3. The patient's signs and symptoms are classic for pernicious anemia. The disease occurs equally in both genders, with an average onset of age 60. The anemia is caused by vitamin B_{12} malabsorption due to severe atrophy of the gastric glands with loss of parietal cells and inability to secrete intrinsic factor. The cause of the disease is unknown, but several findings point to an immunologic or inherited basis of the disease. Approximately 90% of patients have antibodies to parietal cells, and 2 to 10% of relatives of these patients exhibit similar antibodies. Parenteral cyanocobalamin should be given daily to replenish tissue stores, and a monthly maintenance dose should be given for life.
4. The large hematemesis and the pregnancy of the mother suggest the possible ingestion of iron tablets. The signs and symptoms of the patient are indicative of first-stage acute iron poisoning. As few as 10 to 12 prenatal multivitamin with iron tablets can cause serious illness in a young child. Deferoxamine is an iron-chelating compound that can bind iron that has already been absorbed. The iron−deferoxamine complex is not toxic and is excreted by the kidney.

Lesson 31. Immunotropic, antiallergic agents. Nonsteroidal anti-inflammatory drugs and medications for the treatment of gout.

Task 3

a. 1C, 2A, 3B

b. 1E, 2B, 3A, 4C, 5D

c. 1C, 2B, 3A

d. 1C, 2D, 3B, 4A

Case tasks

1. Celecoxib is a selective inhibitor of cyclooxygenase-2. Drugs of this class (sometimes called coxibs) have analgesic, antipyretic, and anti-inflammatory actions. However, they lack action on platelet aggregation and have lower adverse effects on the gastric mucosa than nonselective inhibitors of cyclooxygenases. These drugs are therefore preferred in patients at risk of peptic ulcer disease, as in this case.
2. Unlike first-generation H_1 antagonists, second-generation H_1 antagonists are devoid of blocking activity on muscarinic receptors. Therefore, they do not have effects on pupil size and accommodation when applied into the conjunctiva. This explains why only second-generation is used for this disorder.
3. Correct answer is d. The profound leukopenia and thrombocytopenia exhibited by the patient suggest bone marrow suppression. Transplant patients always receive immunosuppressive therapy to prevent organ allograft rejection. Cyclosporine, azathioprine, and a glucocorticoid are the drugs most frequently used for this purpose. Azathioprine is a prodrug that is converted in the body to mercaptopurine, an antimetabolite anticancer drug. It is therefore a cytotoxic agent that can cause significant myelosuppression.
4. Correct answer is c. Patients who receive an initial immunosuppressant therapy with cyclosporine are sometimes converted to tacrolimus, either because of persistent drug reactions or of a poor response, as in this case. Tacrolimus has a mechanism of action very close to that of cyclosporine. Nevertheless, patient survival rates exceeding 80% have been reported in liver transplant patients who were converted from cyclosporine to tacrolimus because of failure of cyclosporine therapy. a, b, d these drugs are not immunosuppressants.
5. Methotrexate is currently a first-line treatment for most patients with rheumatoid arthritis because of its high rate of response, relatively rapid onset of action (1 to 2 months), and long sustained efficacy. Moreover, it has been shown that the drug can enhance the action of some other disease-modifying antirheumatic drugs (DMARDs), including hydroxychloroquine, so it would be an appropriate drug to add to the ongoing therapy in this case.

Lesson 33. Combination drug therapy. Drug incompatibility

Case tasks

1. The patient has developed a side effect of antipsychotics — drug-induced parkinsonism, caused by the blockade of dopamine D_2 receptors in the striatum. It is possible to prescribe antiparkinsonian drugs of central M-cholinoblockers (trihexyphenidyl). This is an absolute pharmacodynamic incompatibility, based on the enhancement of side effects.
2. Pseudomembranous colitis caused lincomycin or clindamycin, which are used in periodontitis. Loperamide decreased intestinal motility and retained an antibiotic in the intestine. This is an absolute pharmacodynamic incompatibility.
3. Physiological non-competitive antagonism. The patient was prescribed an angiotensin-converting enzyme inhibitor as an antihypertensive agent. Nonsteroidal anti-inflammatory drugs, nonselective cyclooxygenase inhibitor (including diclofenac), inhibiting the synthesis of substances with vasodilator and diuretic effect — prostacyclin and prostaglandin E_2, prevents the decrease in blood pressure, which occurs during treatment with angiotensin-converting enzyme inhibitors, and promotes hyperkalemia and nephrotoxicity.

Educational edition

PHARMACOLOGY

PRACTICAL MANUAL

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