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# **PHARMACOLOGY**

## **PRACTICAL MANUAL**

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This practical manual covers both general and specific aspects of pharmacology, including medical prescriptions that are commonly used and included in standard treatment guidelines for primary healthcare. It also includes self-assessment materials, case studies, and exam questions.

"Pharmacology: Practical Manual" has been developed for the discipline of Pharmacology in accordance with the Federal State Educational Standard for higher professional education. It is intended for students enrolled in the General Medicine specialty (bilingual program).

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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: Gamma-Aminobutyric Acid
- 5-HT: 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: to study how to write prescriptions for solid dosage forms.*

### **KEY TOPICS FOR PREPARATION**

1. Organization of pharmacy services in Russia.
2. Rules for dispensing drugs and forms of prescriptions.
3. Technologies for producing solid dosage forms. Classification of drug forms (solid, liquid, soft [semi-solid]).
4. Differences between "medicinal raw materials," "medicinal products (pharmaceutical substances)," and "dosage forms."
5. Differences between expanded and short forms of prescriptions.
6. International non-proprietary names of drugs versus brand names.
7. Rules for prescribing medications.
8. Structure and components of a prescription.
9. Guidelines for writing a prescription.
10. Types of solid dosage forms (tablets, pills, capsules, powders, granules).

### **QUESTIONS AND TASKS IN CLASS**

**Task 1.** Theoretical material to prepare for the lesson.

*Powders* are a dosage form consisting of solid, dry particles and have the property of flowability. They can be classified by composition, dose division, and route of administration.

1. Classification of powders by composition:
  - A. Simple powders (pulveres simplices): Contain one medicinal substance;
  - B. Complex powders (pulveres compositi): Contain two or more medicinal substances.
2. Classification by dose division:
  - A. Separated: Divided into separate doses;
  - B. Undivided: The powder comes in one package, and the dosage is determined by the patient.

3. Classification by the route of administration:
  - A. Powders for topical administration (applied to the affected area of the skin);
  - B. Powders for preparing solutions and suspensions (must be dissolved or dispersed in a liquid medium, e.g., water or a 0.9% sodium chloride solution);
  - C. Powders for oral administration;
  - D. Powders for inhalation.

**Tablets** are solid dosage forms created by pressing powders and granules containing one or more drugs, with or without excipients.

1. Classification by composition:
  - A. Simple: One-component;
  - B. Complex: Multi-component.
2. Classification by the speed and nature of the release:
  - A. Enteric-coated tablets: Coated to protect the drug from gastric juice and allow release in the small intestine;
  - B. Modified-release tablets: Allow controlled release of the active ingredient over time through specific technologies. Drug release may occur through diffusion after swelling or by biodegradation of the membrane (matrix and membrane systems). In osmotic systems, the drug is released as a result of increased osmotic pressure in the reservoir that contains the drug.
  - C. Sustained-release tablets: Tablets containing special substances designed for extended release of the active ingredient.
3. Classification by the route of administration:
  - A. Chewable tablets: Require chewing before swallowing;
  - B. Soluble tablets: Must be dissolved in a solvent (typically water) before use;
  - C. Sublingual and buccal tablets: Placed under the tongue or against the cheek until dissolved.

**Capsules** are dosage forms that contain one or more active substances enclosed in a hard or soft shell (made of gelatin or starch).

1. Classification by the route of administration:
  - A. Oral administration;
  - B. Capsules with powder for inhalation;

2. Classification by release speed and nature:

A. Modified-release capsules;

B. Enteric-coated capsules.

**Granules** are solid dosage forms consisting of grains that can be round, cylindrical, or irregularly shaped, containing one or more medicinal substances.

**Dragees** are solid dosage forms created by applying multiple layers of medicinal and excipient substances onto sugar granules.

**Units used in pharmacology**

1.0 g (gram) = 1,000 mg (milligram) = 1,000 000 mcg (microgram)

1 teaspoon = 5 ml (milliliter)

1 dessert spoon = 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, Zinc oxide
Simple separated	0.1–1.0	–
Complex separated	0.1–1.0	Saccharum, Saccharum lactis, Glucosum

**Principles of Writing a Prescription Order**

A prescription is a written request from a doctor to a pharmacy to dispense a medication to a patient in a specific dosage form and amount, indicating the route of administration. Certain rules govern the writing of prescriptions:

1. The prescription must be written legibly as it is a medico-legal document.

2. There is a specific pattern to follow when writing prescriptions, whether for a single drug or a mixture of multiple drugs. Only one prescription should be written on each order blank.

The prescription consists of several parts:

- 1. Date:** The date on which the prescription is issued.
- 2. Patient Information:** This section must include the patient's name, address, and age. This information is essential for accurately processing the prescription and preventing confusion with other medications.
- 3. Prescription Symbol:** The letter "R" (not "Rx") is an abbreviation for the Latin word "Recipe," meaning "take."
- 4. Drug Information:** The body of a prescription must contain the name and strength of the prescribed drug. Most drugs can be prescribed using their official names, generic (nonproprietary) names, or brand names (proprietary names). If multiple drugs are included in the same prescription, each drug's name and quantity should be listed consecutively.
- 5. Directions to the Pharmacist:** These instructions specify how the pharmacist should dispense or prepare the medication. For single-drug prescriptions, this typically includes directives like "Dispense tablets," "Dispense 200 ml," or "Dispense the oral syringe." For multiple drugs, instructions may be as simple as "Prepare a solution" or "Mix and place into 10 capsules."
- 6. Directions to the Patient:** Instructions for the patient must be clear and understandable. Latin abbreviations should be avoided, as they provide no real benefit. This section should detail the amount of the drug to take, the time and frequency of doses, and any relevant information about dilution and the route of administration. Specific instructions are crucial for topical medications (begin with "Apply"), oral medications (begin with "Take"), suppositories (begin with "Insert"), and medications for the conjunctival sac, external auditory canal, or nostril (begin with "Place"). If a drug must be taken at specific times or intervals (for instance, every 8 hours), this should be emphasized and explained clearly to avoid confusion. Particular attention should be given to elderly, ill, or disabled patients, as well as those with language barriers. For these individuals, provide a separate instruction sheet with detailed explanations. Reminders about the

prescription's purpose should also be included, using phrases like "for pain relief," "for headache relief," or "for itching relief." However, any potentially confusing directions should be communicated privately rather than included on the prescription label.

**7. Signature:** The practitioner signs the prescription, including their professional degree.

**Example of a prescription**

1. Date	May 3, 2017
2. Patient's name, age, address	Dee Fleming, Age 6 817 Woodhaven Dr Cincinnati, OH 45229
3. R̄ (Recipe)	R̄ (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.** Study the following set of formulations: powders, capsules, tablets, dragees, granules, spansules, caramels, and pastilles.

**Task 3.** An example of a card for classwork.

**Prescribe drugs:**

1. 50 g powder containing 10% Zinc oxide, 80% Talcum, and Amylum.
2. 30 g powder containing 1% Clotrimazole, 6% Amylum, and Talcum 93%.
3. 20 powders of Acetylcysteine, 600 mg. Prescribe a therapeutic dose (TD 300 mg) two times a day, instructing the patient to dissolve the powder in 1 glass of boiled water before use.
4. 10 Theophyllum powders, 30 mg each. Prescribe 1 powder twice daily.
5. 30 Diclofenac powders, 50 mg. Prescribe 1 powder twice daily.
6. 20 coated tablets of Verapamil, 40 mg. Prescribe 1 tablet three times daily.
7. 20 Chlorpromazine dragees, 25 mg each. Prescribe 1 dragee twice daily.
8. 40 g Cefalexin granules. Dilute the contents of the bottle in boiled water to make a total volume of 100 ml (the resulting suspension shall contain 250 mg of cephalexin per 5 ml). Prescribe TD 25 mg/kg orally to a child weighing 20 kg twice daily.

**SELF-ASSESSMENT TASKS (HOMEWORK)**

**Prescribe drugs:**

1. 10 g Acidum boricum. Prescribe for mouth rinse, instructing the patient to dissolve 1 teaspoon of powder in a glass of boiled water before use.
2. Barii sulfas, 50 g. Dissolve the powder in ½ cup of water and drink the resulting suspension.
3. 5 g Sulfanilamidum powder. Apply onto the affected areas of the skin.

4. 100 g of powder containing 2% Acidum salicylicum, 10% Zinci oxydum, Amylum and Talcum 44% each.
5. 10 g powder containing Bacitracinum 2,500 IU, Neomycini sulfas 50,000 IU, Amylum 9 g.
6. 10 Nimesulide powders, 100 mg each. Prescribe 1 powder 2 times a day, instructing the patient to dissolve it in  $\frac{1}{2}$  cup of boiled water before use.
7. 10 Coffeinum powders, 50 mg each. Prescribe 1 powder to be taken orally in the morning.
8. 20 powders of the following composition: Phenylephrinum 10 mg; Pheniramine 20 mg; Paracetamol 325 mg. Prescribe 1 powder two times a day, instructing the patient to dissolve it in 1 glass of boiled water before use.
9. 3 bottles of Azithromycin powder, 800 mg each. Dilute the powder in 15 ml of boiled water (the resulting suspension shall contain 200 mg of azithromycin per 5 ml). Prescribe TD 10 mg/kg orally to a child weighing 20 kg once a day for 3 days.
10. 60 capsules and tablets of Pyracetam, 400 mg. Prescribe 1 capsule (tablet) 2 times a day.
11. 30 tablets and capsules of Isosorbide mononitrate, 50 mg. Prescribe 1 tablet (capsule) 1 time per day.
12. 6 tablets of Citramonum. Prescribe 1 tablet for headache.
13. 15 tablets containing Amoxicillin 500 mg and Acidum clavulanicum 125 mg ("Augmentin"). Prescribe 1 tablet 3 times a day. Write down in the expanded and short forms (using the commercial name of the drug).
14. 30 capsules of Acidum cromoglicicum, 100 mg. Prescribe TD 100 mg 4 times a day before meals.
15. 20 Indapamide 2.5 mg tablets. Prescribe 1 tablet 1 time per day.  
40 dragees of Ergocalciferolum 500 IU. Prescribe DD 2500 IU a day.
16. 60 sachets containing Mesalazine granules of 1.0 g. Prescribe a daily dose of 4 g in four divided doses. Instruct the patient to place the contents of the sachet under the tongue and allow it to dissolve without chewing. The patient should swallow it with a glass of water or orange juice.

17. 20 sachets containing Budesonide 9 mg granules. Instruct the patient to place the contents of the sachet under the tongue and allow it to dissolve without chewing. The patient should swallow it with a glass of water, once a day in the morning 30 minutes before meals.
18. 20.0 g Josamycin granules. Dilute the contents of the bottle in boiled water to make a total volume of 100 ml (5 ml of the resulting suspension shall contain 500 mg of Josamycin). Prescribe TD 25 mg/kg of body weight orally to a child weighing 40 kg 2 times a day.

## **Lesson 2**

### **Liquid Dosage Forms (Solutions, Drops). Aerosols, Sprays**

*The learning objective is to study how to write prescriptions for liquid dosage forms, aerosols, and sprays, and to calculate the concentration of solutions and therapeutic doses.*

#### **KEY TOPICS FOR PREPARATION**

1. Composition of solutions, volume, and composition of solvents.
2. Technologies for preparing solutions for external use, oral administration, eye drops, and injectable forms.
3. Routes of administration for solutions.
4. Therapeutic dose of solutions for oral administration, drops, or injectable forms.
5. Classification of solutions by route of administration: for external, internal use, and injection.
6. Characteristics of solvents: purified water (Aqua purificata), water for injections (Aqua pro injectionibus), ethanol 70%, 90%, 95% (Ethanolum), glycerin (Glycerinum), olive oil (Oleum olivarum), peach oil (Oleum persicorum).
7. Rules for prescribing solutions for external and internal use.
8. Drops as a type of solution. Dosing solutions in drops. Rules for prescribing drops for external and internal use.
9. Requirements for injectable solutions. Methods of sterilization for injectable solutions.
10. Dosage forms and rules for prescribing injectable solutions (vials, ampoules, prefilled syringes).
11. Rules for prescribing dry substances in ampoules and vials, liquid biotechnological preparations.
12. Aerosols, sprays: composition, dosage, prescribing rules.

#### **QUESTIONS AND TASKS IN CLASS**

**Task 1.** Theoretical material to prepare for the class.

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

1. Solutions for external and local use: Applied to the skin, mucous membranes, or injected into body cavities; also used for wound and bedsore treatment.
2. Solutions for internal use:
  - Dosed by drops.
  - Dosed by spoons.
3. Solutions for parenteral administration.

Methods of expressing concentration:

- Percentage: Grams of substance per 100 ml of solution (in the prescription it is indicated as follows: 5%);
- Mass-volume: Grams or milliliters of substance per specified volume (in the prescription it is indicated as follows: 10 mg / 1 ml);
- Ratio: Parts of solution corresponding to 1 part of dissolved substance (in the prescription it is indicated as follows: 1:5000). This method of expressing concentration may be used only when prescribing an antiseptic solution.

#### **A. Aqueous solutions:**

For subcutaneous administration: a volume of 1–2 ml. It is prohibited to inject irritating agents (e.g., calcium chloride) and strong vasoconstrictors (e.g., norepinephrine). When these solutions are administered under the skin, they can cause necrosis.

For intramuscular injections: the maximum volume is 10 ml. It is prohibited to inject irritating agents (e.g., calcium chloride) strong vasoconstrictors (e.g., norepinephrine) because of the reason stated above.

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

#### **B. Oily solutions:**

- For subcutaneous injections;
- For intramuscular injections.

Intravenous administration of oily solutions is prohibited (due to the risk of developing Fat Embolism Syndrome).

### **C. Ultraemulsions:**

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

The substance may be produced in the form of dry 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 Lidocaine solution are usually used as solvents.

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

*Spray* is an aerosol without a propellant. The contents are released via a mechanical sprayer or package compression.

**Task 2.** Study the set of solutions.

**Task 3.** An example of a card for classwork.

### **Prescribe drugs:**

1. 1% solution of Methylthioninium chloride for bladder irrigation, 300 ml.
2. Calcium chloride solution for internal use (TD 600 mg), 12 tablespoons (expanded and short forms). Prescribe 1 tablespoon twice daily.
3. Periciazine solution in 125 ml bottles containing 40 mg per ml. Prescribe TD 16 mg orally in drops three times daily (expanded and short forms).
4. Morphinum solution in ampoules of 1 ml, each containing 10 mg of Morphinum per 1 ml, 5 ampoules. Inject TD 5 mg subcutaneously.
5. Meropenem powder in 500 mg bottles, 20 bottles. Dissolve the contents of one bottle in isotonic sodium chloride solution to obtain a solution containing 1 mg per ml. Inject intravenously three times daily.
6. Flurbiprophen spray in 15 ml bottles with each dose delivering 8.75 mg. TD 8.75 mg is released with three presses of the dispenser.

Spray on the back of the throat in a daily dose of 43,75 mg.  
Calculate the number of doses per day.

### **SELF-ASSESSMENT TASKS (HOMEWORK)**

#### **Prescribe drugs:**

1. 0.02% solution of Nitrofurazone for irrigating wounds, 600 ml.
2. 3% alcohol solution of Boric acid, 10 ml in a dark glass bottle (short form). Instill 1–2 drops into the sore ear twice daily.
3. 10% Camphor oil solution, 30 ml (short form). Apply to the skin and rub gently.
4. Diphenhydramine solution for internal use (TD 50 mg), 20 doses (expanded and short forms). Prescribe 1 dessert spoon three times daily.
5. 30 ml (1 bottle) of Sodium Picosulfate solution containing 7.5 mg of active substance per 1 ml. Prescribe TD 7.5 mg (in drops) one time a day.
6. 1% Pilocarpine eye drops, 5 ml. Administer 1–2 drops in each eye.
7. Digoxin solution, 1 ml ampoules containing 0.25 mg per ml, 6 ampoules. Inject TD 125 mcg intravenously after diluting in 10 ml of 5% glucose solution.
8. Valproic acid solution in 5 ml ampoules containing 10 mg per ml, 5 ampoules. Administer 15 mg/kg TD intravenously as a bolus to a patient weighing 60 kg.
9. "Microlax" 5 ml, 4 micro-enemas. Administer the contents of 1 micro-enema rectally.
10. Oxytocin in 2 ml ampoules (1 ml – 5 IU), 10 ampoules. Administer intramuscularly (TD 2 IU).
11. 20 bottles of Fosfomicin, 2 g each. Dissolve the contents of one bottle sterilely in isotonic sodium chloride solution to obtain a concentration of 100 mg per ml. Administer intravenously every 8 hours at a daily dose of 300 mg/kg to a child weighing 20 kg.

12. Gentamycinum in 80 mg bottles, 10 bottles. Dissolve the contents of one bottle sterilely in 2 ml of water for injection. Inject TD 4 mg/kg into muscles of a patient weighing 60 kg twice daily.
13. Choriogonadotropin alpha solution containing 250 mcg of active substance per 0,5 ml, 1 pen syringe. Administer a single subcutaneous injection of 250 mcg.
14. Interleukin beta in 1 mcg ampoules, 10 ampoules. Dissolve the contents of one ampoule sterilely in 1 ml of isotonic sodium chloride solution. Inject TD 0.02 mcg/kg subcutaneously for a patient weighing 80 kg once a day for 5 days.
15. Benzylpenicillinum-natrium in vials, 500,000 IU per vial. Dissolve the contents of one vial in 2 ml of 0.5% Lidocaine solution, administer intramuscularly at a DD (daily dose) 50,000 IU/kg of body weight to a child weighing 30 kg every 4 hours.
16. Salbutamol aerosol, 100 mcg per dose, 1 bottle. Instruct to inhale 1 dose as prescribed.

### **Lesson 3**

## **Liquid Dosage Forms (Mixtures, Suspensions). Soft (Semi-Solid) Dosage Forms (TTS, Ointments, Gels, Pastes, Creams, Suppositories).**

*The learning objective is to study how to write prescriptions for liquid and soft (semi-solid) dosage forms.*

### **KEY TOPICS FOR PREPARATION**

1. Mixtures: composition, rules for prescription.
2. Mucilage and syrups as components of mixtures.
3. Syrups: composition, rules for prescription.
4. Suspensions: composition, rules for prescription.
5. Emulsions: composition, rules for prescription.
6. Aerosols and sprays: composition, dosage, rules for prescription.
7. 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.
8. Ointments, pastes, creams, gels: composition, rules for prescription, uses.
9. Eye ointments: rules for prescription, features.
10. Liniments: varieties, composition, rules for prescription.
11. Suppositories: varieties; substances used as a base, rules for prescription.
12. Transdermal therapeutic systems (TTS): design, rules for prescription, uses.

### **QUESTIONS AND TASKS IN CLASS**

**Task 1.** Theoretical material to prepare for the class.

**Suppositories** are soft (semi-solid) dosage forms that is solid at room temperature and melts at body temperature. They are designed for insertion into body cavities. Cocoa butter and gelatin-glycerol mixtures are used as bases.

Suppositories are classified into:

1. Vaginal (spherical or ovoid, with approximate weight of 1.5–4 g);
2. Rectal (cone-shaped or cylindrical with a pointed end, with approximate weight of 1.1–3 g).

**Ointment** is a soft (semi-solid) dosage form consisting of oil and medicinal substances evenly distributed in it. They are used for topical application to the skin, wounds, and mucous membranes.

The bases that are used for the production of ointments are classified into:

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

Categories of ointments:

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

Most ointments are now available in ready-made forms.

**Cream** is a soft (semi-solid) dosage form, an emulsion of the water/oil or oil/water type.

**Pastes** are dense ointments with powdery substances must not exceed 65% and cannot be less than 25%.

**Gels** are ointments that using gelling agents of natural or synthetic origin. They are elastic and maintain their shape.

**Transdermal therapeutic systems (TTS)** are soft (semi-solid) dosage forms for external use, typically patches or membranes that release the drug.

Types of TTS:

1. Membrane-controlled systems (consisting of a reservoir with the drug substance and a polymer membrane regulating release rate);
2. Adhesive systems (the drug substance is distributed within an adhesive polymer).

**Emulsion** is a liquid dosage form composed of two or more mutually insoluble/immiscible liquids, with active substance particles suspended as fine droplets.

**Oil emulsions** are prepared from liquid oils (e.g., castor or almond oil) with emulsifiers added.

**Infusions and decoctions** are liquid dosage forms representing aqueous extracts of medicinal plant materials, used both internally and externally and administered by spoonfuls.

**Tincture** is a liquid dosage form, an alcohol or water-alcohol extract of medicinal plant materials, dosed in drops.

**Extracts** are available in liquid (*fluidum*), dense (*spissum*), and dry (*siccum*) forms. For the extraction of active substances not only alcohol is used, but also chloroformate (chloroformic acid ester) at high temperature and pressure. Liquid extracts are administered as drops; dense extracts can be encapsulated or coated; dry extracts are administered as tablets or powders.

**Mixture** is a liquid dosage form obtained by mixing several solids and/or liquids, prescribed for internal use and administered by spoonfuls. Sugar syrup may be added to a mixture to improve its taste (sugar syrup can add up to 10–20% of the total volume of a mixture) or mucilage/starch (10–30% of total volume) may be added to improve taste or reduce irritation.

**Suspensions** are a liquid dosage form, with insoluble powders as active ingredients, evenly distributed in a liquid. The active substance particles are suspended as fine droplets. Suspensions can be used for:

- Internal use;
- Subcutaneous injections;
- Intramuscular injections;
- Insertion into body cavities.

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

**Task 2.** Study the set of liquid, soft (semi-solid) dosage forms, and phytopharmaceuticals.

**Task 3.** An example of the card for classwork.

**Prescribe drugs:**

1. Mixture of Diphenhydraminum (TD 20 mg) and sugar syrup, for 10 doses measured in dessert spoons (10 ml each). Prescribe one dessert spoonful at night.
2. Suspension of Posaconazolum, 40 mg/ml in a 105 ml bottle. Prescribe to take orally with meals, 200 mg 3 three times daily.
3. Aerosol – Salbutamolum, 10 ml. Prescribe 1 inhalation dose.
4. Tincture of Absinthium, 25 ml. Prescribe 15 drops three times a day.
5. Liquid extract of Eleutherococcus, 50 ml. Prescribe 20 drops three times daily.
6. 3% Aciclovir eye ointment, 2.0 g.
7. Rectal and vaginal suppositories with Hyaluronidase (TD 3000 IU) for 10 administrations.
8. 7 Nicotine TTS patches, 15 mg each. Apply 1 patch to the skin once daily in the morning and remove before bed.
9. 5 Fentanyl TTS patches with a release rate of 50 mcg per hour (each patch). Apply 1 patch every three days.

**SELF-ASSESSMENT TASKS (HOMEWROK)**

**Prescribe drugs:**

1. Mixture of Kalii bromidum (TD 0.1), Natrii bromidum (TD 0.2), starch mucilage and sugar syrup, for 12 dessert spoonfuls. Prescribe 1 dessert spoonful three times a day.
2. Phenoxymethylpenicillin syrup, 60 ml (1 ml – 150,000 IU). Prescribe TD 750,000 IU orally four times a day.

3. Ethosuximide syrup (Aethosuximidum) in a 250 ml bottle containing 50 mg of the active substance per ml. Take TD 250 mg orally once a day.
4. Suspension of Betamethasone (Betamethasonum) in 1 ml ampoules, containing 7 mg of the active substance per ml, 5 ampoules. Inject 2 ml intra-articularly once every 4 weeks.
5. Mesalazine suspension in 30 ml micro-enemas, containing 4 g of the active substance per 30 ml, 7 micro-enemas. Prescribe rectally TD 30 ml one time a day before bedtime.
6. Tincture of Crataegus, 25 ml. Prescribe 20 drops three times a day.
7. Liquid extract of Rhodiola, 25 ml. Prescribe 20 drops in the morning.
8. 50 g of ointment containing 1% Acidum salicylicum and 5% Bismuthi subgallas.
9. 50 g of paste containing 1% Diclofenac and 10% Bismuthi subgallas.
10. 10 g of Erythromycinum ophthalmic ointment, containing 10,000 units per gram. Apply behind the the lower eyelid four times a day.
11. 10% Indomethacin gel, 40 g. Rub into the skin.
12. Rectal and vaginal suppositories with Benzocainum (TD 200 mg) for 10 administrations.
13. "Relief" rectal suppositories for 10 administrations. One suppository rectally at night.
14. Three transdermal patches "Evra," each containing Norelgestromin 203 mcg/h and Ethinylestradiol 33.9 mcg/h. Apply one patch once a week (Please prescribe using both international non-proprietary and commercial names).

## **Lesson 4**

### **Final Lesson on General Prescription**

*The learning objective is to assess students' skills in writing prescriptions for all medicinal forms that have been studied.*

#### **KEY TOPICS FOR PREPARATION**

1. Revise the theory regarding general prescription.
2. Repeat the rules for prescribing solid, soft (semi-solid), and liquid dosage forms and phytopharmaceuticals.

#### **EXAMPLES OF INDIVIDUAL TASKS**

##### **Card No.1**

##### **Prescribe:**

1. 10 tablets of Acidum ascorbinicum, 50 mg. Prescribe 1 tablet three times a day.
2. 20 coated tablets of Nicergoline, 5 mg. Prescribe 1 tablet three times a day.
3. 0.05% solution of Kalii permanganas for gastric lavage, 250 ml in a dark bottle (both in the expanded and short forms).
4. 2.5% solution of Phenylephrinum, 5 ml. Prescribe 1 drop in each eye.
5. Metoprolol solution in 5 ml ampoules, containing 1 mg per ml, 10 ampoules. Inject TD 5 mg intravenously in 20 ml of 5% glucose solution.
6. Cisplatin solution in 50 ml bottles, containing 50 mg per 50 ml; 6 bottles. Inject TD 50 mg intravenously every 4 weeks.
7. Fenoterol aerosol containing 100 mcg per dose, 2 bottles. Prescribe 1 dose by inhalation.
8. Ginseng tincture, 25 ml. Prescribe 20 drops twice a day.
9. 2% paste of Acidum fusidicum, 15 g (in the expanded form).
10. Rectal suppositories with Indomethacin, TD 50 mg, for 10 administrations.

## Card No. 2

### Prescribe:

1. 50 g of powder containing 20% Bismuthi subgallas and 80% Zinci oxydum.
2. 20 Chlorpromazine dragees, 25 mg. Prescribe TD 50 mg three times daily after meals.
3. 1% alcohol solution of Viride nitens, 10 ml. Apply to the affected skin areas (in the short form).
4. 0.5% solution of Tropicamide, 5 ml. Prescribe TD 1 drop in each eye.
5. Trimeperidine solution in 1 ml ampoules, containing 10 mg per ml, 10 ampoules. Inject TD 5 mg subcutaneously.
6. Amikacin solution in 2 ml ampoules, containing 250 mg per ml, 5 ampoules. Inject TD 5 mg/kg into the muscle 2 times a day to a patient weighing 50 kg.
7. Liquid extract of Leuzeae, 25 ml. Prescribe 20 drops three times a day.
8. 1% ophthalmic ointment – Tetracyclinum, 5 g.
9. Rectal suppositories "Cefeconum" for 10 administrations.
- 10.5 Fentanyl TTS patches with a release rate of 100 mcg/h. Apply 1 patch to the skin once every 3 days.

## **Lesson 5**

### **General Pharmacology. Pharmacokinetics**

*The learning objective is to study the general patterns of drug absorption, distribution, biotransformation, and elimination, as well as the individual characteristics of pharmacokinetics.*

#### **KEY TOPICS FOR PREPARATION**

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 (etiologic, pathogenetic, replacement, symptomatic).
3. Penetration of drugs through biological membranes, types of transport (passive diffusion, active transport, pinocytosis).
4. Routes of drug administration: effects on pharmacokinetics, pharmacological effects, disadvantages, rational dosage forms:
  - enteral — sublingual, buccal, oral, rectal;
  - parenteral — under the skin (subcutaneous), in the muscle (intramuscular), in the vein (intravenous), in the artery (intra-arterial), subarachnoid, 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 to medicinal products — capillary walls, blood-brain barrier (BBB), placental barrier.
7. Distribution of drugs in 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 (gene polymorphism of biotransformation enzymes).
10. Induction and inhibition of biotransformation and their medical significance.
11. Pharmacogenetics, pharmacogenomics as the foundation for personalized, predictive therapy.
12. Elimination of drugs from the body (with urine, bile, exhaled air, secretory 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, elimination constant. Bioequivalence of drugs.

### **SELF-ASSESSMENT TASKS**

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

1. Define the terms "placebo," "nocebo," "multicenter controlled trial," "double-blind method," "randomization," "compliance," "pleiotropic effect."
2. Indicate the ratio of neutral molecules and ions in a weak acid with  $pK_a = 4.4$  in gastric juice (pH 1.4) and blood (pH 7.4); similarly, determine the ratio for a weak base with the same  $pK_a$ . List medicines with the properties of weak acids and weak bases.
3. What medicinal products – endobiotics or xenobiotics — penetrate membranes by filtration and active transport? Explain why.
4. Can the bioavailability of a drug administered orally be 5% if it is completely absorbed in the intestine?
5. The binding of a 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 displaced by another drug?

6. What is targeted drug delivery? How is it achieved?
7. What can be assumed about the pharmacokinetic properties of a synthetic chemotherapeutic agent if its volume of distribution is 128 liters?
8. What toxic products are formed during the oxidation of drugs by cytochrome P-450, and how are they neutralized? What are the "suicide substrates" of cytochrome P-450?
9. Which genes of cytochrome P-450 isoenzymes are most susceptible to polymorphism?
10. Why does warfarin at a dose of 5 mg/day cause increased bleeding in patients with the CYP2C9\*3 genotype compared to those with CYP2C9\*1 and CYP2C9\*2?
11. The antituberculosis drug isoniazid is inactivated via acetylation. Why do some patients experience mild adverse effects during tuberculosis treatment with isoniazid, while others report headache, dizziness, nausea, vomiting, chest pain, irritability, insomnia, tachycardia, and polyneuritis?
12. How does the effect of warfarin – an indirect anticoagulant – change in case of combined administration with rifampicin (chloramphenicol)? Why?
13. What is the purpose of intravenous sodium bicarbonate administration in case of acetylsalicylic acid poisoning?
14. Which antibiotic – benzylpenicillin (a weak acid) or erythromycin (a weak base) – achieves a high concentration in breast milk (pH 6.5–7.0) during lactation? Explain why.

## Task 2.

- a. Match each parameter (A–E) with the appropriate description (1–5).

A. $T_{1/2}$ (elimination half-life)	1. The fraction of the administered drug that reaches systemic circulation unchanged
B. $T_C$ max	2. The volume of plasma cleared of drug per unit time
C. F (bioavailability)	3. The 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 required to reach the maximum concentration of an administered drug in the blood

b. Combine the pharmacokinetic parameter (A–E) and its corresponding clinical value (1–5).

A. T <sub>1/2</sub> (elimination half-life)	1. This parameter allows you to calculate the time for the next dose of medication
B. Equilibrium concentration	2. This parameter allows you to assess the ability of a drug to penetrate histohematic barriers
C. F (bioavailability)	3. This parameter must be known to calculate the maintenance dose and assess drug elimination
D. Vd (volume of distribution)	4. This parameter corresponds to the amount of drug in the blood achieved over time, reflecting balanced transport, biotransformation, and excretion systems, leading to the manifestation of the full clinical effect
E. Cl (clearance)	5. This parameter is necessary for selecting the dose of a drug for oral administration

c. Match each route of administration (A–E) with the appropriate description (1–5).

A. Enteral	1. The route where bioavailability is 100%
B. Sublingual	2. The route where the volume of the injected drug cannot exceed 2 ml
C. Intravenous	3. The route ensuring rapid drug delivery across the large surface area of the mucous membranes in the respiratory tract and pulmonary epithelium

D. Subcutaneous	4. The route available for lipophilic drugs that avoids first-pass metabolism
E. Inhalation	5. The route where 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, and randomized methods in clinical trials.
3. Ethical issues in clinical trials.

### QUESTIONS AND TASKS IN CLASS

**Task 1.** Analyze the tasks illustrating the relationship between pharmacokinetics and the physicochemical properties of drugs (the set of graphic tasks).

**Task 2.** Analyze case tasks.

1. An 85-year-old man 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,  $pK_a = 9.5$ )
  - b. Diazepam (base,  $pK_a = 3.0$ )
  - c. Amiodarone (base,  $pK_a = 7.4$ )
  - d. Theophylline (acid,  $pK_a = 8.8$ )
  - e. Ibuprofen (acid,  $pK_a = 4.8$ )

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 drug will remain 6 hours after its administration?

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

**Task 3.** Answer the test questions (in the ICT classroom).

## **Lesson 6**

### **General Pharmacology. Pharmacodynamics**

*The learning objective is to study the general patterns of drug action, the effects of repeated and combined drug use, and the dependence of pharmacodynamics on individual characteristics of the body.*

#### **KEY TOPICS FOR PREPARATION**

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

- synergism (additive (summarized), potentiation);
- antagonism (physical, chemical, physiological indirect, direct competitive and non-competitive).

12. Adverse effects, adverse events, adverse reactions, complications of pharmacotherapy.

### SELF-ASSESSMENT TASKS

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

1.  $\beta_1$ -adrenoreceptors activate adenylate cyclase and increase the synthesis of cyclic adenosine monophosphate (cAMP);  $m_2$  cholinergic receptors reduce the enzyme's activity and the synthesis of cAMP. How will heart rate change after these receptors are activated?
2. Histamine receptors function through various effector systems. Smooth muscle  $H_1$  receptors, activating phospholipase C, increase the production of inositol triphosphate and diacylglycerol.  $H_2$  receptors in gastric glands activate cAMP synthesis. What are the effects of activating these cytoceptors?
3. Caffeine is used to increase blood pressure in arterial hypotension and to improve mental performance in healthy people. What functional changes does caffeine induce in each case?
4. What liver enzyme deficiency in newborns causes unconjugated hyperbilirubinemia? What drugs activate bilirubin conjugation?
5. What medications are contraindicated for people with glucose-6-phosphate dehydrogenase deficiency? Why?
6. What quantitative indicators characterize the degree of drug safety?
7. Determine the type of antagonism in the following scenarios:
  - a. sodium thiosulfate in iodine poisoning;
  - b. gastric lavage was performed with a suspension of activated carbon in morphine poisoning;
  - c. caffeine in acute ethanol poisoning;

- d. naloxone (the opioid receptor antagonist) in acute morphine poisoning.
8. Calculate the maintenance dose of the drug if the loading (initial) dose is 2 mg and the elimination coefficient is 20%.
9. Are there differences between the biochemical processes that underlying tolerance and dependence?

**Task 2.**

- a. Match each type of receptor (A–E) with the appropriate description (1–5).

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. Cytokine receptors	5. Erythropoietin receptors

- b. Match the drugs (A–D) with their targets (1–4), using the Internet and the following link <https://go.drugbank.com>.

A. Propranolol	1. Specific receptor
B. Captopril	2. Ion channels
C. Amlodipine	3. Enzymes
D. Furosemide	4. Transport system

- c. Match each type of drug interaction (A–E) with the appropriate description (1–5).

A. Potentiation	1. Competition between an antagonist and an agonist for the same receptor binding site
B. Competitive antagonism	2. Antagonist acts at a different receptor, producing opposite effects to the agonist

C. Non-competitive antagonism	3. Formation of a complex between an effector drug and another compound
D. Chemical antagonism	4. Combined effect of substances A and B is equal to the sum of their individual effects
E. Additive (summarized) type of interaction	5. Combined effect of substances A and B is greater than the sum of individual effects

**Task 3.** Topics for reports.

1. Pharmacological "target" — a receptor, ion channel, transport protein, cytokine, enzyme. Principles and methods of action of targeted therapies.
2. Definition of teratogenic drugs. FDA pregnancy categories for drugs.
3. Regulation of intracellular calcium: calcium entry mechanism, calcium release mechanism.
4. Sodium and potassium channel functioning.
5. Biotransformation and drug effects in enzymopathy.

**QUESTIONS AND TASKS IN CLASS**

**Task 1.** Analyze the tasks related to pharmacodynamics (the set of graphic tasks).

**Task 2.** Analyze case tasks.

1. A 45-year-old woman, recently diagnosed with a urinary tract infection (UTI), began treatment with a trimethoprim-sulfamethoxazole combination. While both trimethoprim and sulfamethoxazole are bacteriostatic when taken alone, they produce a bactericidal effect when used together. Identify the type of drug interaction in this case.
2. A 2-year-old girl was rushed to the emergency department after ingesting several tablets of a medication containing iron. Emergency treatment included intravenous administration of

deferoxamine, a drug that binds to iron in the plasma to form an inactive complex, thereby antagonizing the effects of iron. Which term best defines this type of antagonism?

3. A 46-year-old woman complained to her physician that the sedative effect of the drug she had been taking had increased substantially. The woman, who was suffering from generalized anxiety disorder, was 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 describes this cimetidine–diazepam interaction?
4. A 57-year-old man recently hospitalized after surgery complained of severe abdominal pain. The physician considered starting him on an analgesic treatment with either morphine (10 mg IM) or buprenorphine (0.3 mg IM). Morphine is a full agonist at mu ( $\mu$ ) opioid receptors, whereas buprenorphine is a partial agonist at the same receptors. The abovementioned 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. Suffering from continuous pain, a 64-year-old man with terminal cancer was started on 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 had most likely 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 the effects of the following drugs:

- a. Prednisone is a synthetic glucocorticoid drug primarily used to suppress the immune system after abrupt discontinuation. Patients report weakness, fatigue, decreased appetite, weight loss, nausea, vomiting, and 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 decrease gastric acidity. Discontinuation of sodium bicarbonate after long-term treatment makes the stomach produce even more acid after the consumption of foods and drinks.

**Task 3.** Answer the test questions (in the ICT classroom).

## **Lesson 7**

### **Vitamins and Drugs for Bone Disorders**

*Learning objectives are to study the classification, mechanisms of action, pharmacokinetics, and indications for the use of vitamins; adverse effects of vitamin therapy and 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.*

#### **KEY TOPICS FOR PREPARATION**

1. Vitamins: the history of discovery, sources of production, significance for the organism, participation in metabolic reactions, classification based on 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, adverse effects, contraindications to fat-soluble vitamins and their synthetic analogs:
  - vitamin A – retinol, beta-carotene;
  - retinoids
    - first generation (non-aromatic) – isotretinoin, tretinoin;
    - second generation (monoaromatic) – acitretin;
    - third generation (polyaromatic) – adapalene;
    - fourth generation – trifarotene;
  - vitamin D<sub>2</sub> – ergocalciferol;
  - vitamin D<sub>3</sub> and its analogs – 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, adverse effects, contraindications to water-soluble vitamins and their synthetic analogs:
  - vitamin B<sub>1</sub> – thiamine;
  - vitamin B<sub>2</sub> – riboflavin;
  - vitamin B<sub>5</sub> – sodium dimercaptopropanesulfonate + calcium pantothenate, dexpanthenol;

- vitamin B<sub>6</sub> – pyridoxine, pyridoxal phosphate;
  - vitamin B<sub>9</sub> – folic acid;
  - vitamin B<sub>12</sub> – cyanocobalamin;
  - vitamin PP – nicotinic acid, nicotinamide;
  - vitamin C – ascorbic acid;
  - vitamin P – rutoside (rutin), dihydroquercetin.
5. Hypervitaminosis A and D: causes, pathogenesis, symptoms, prevention, treatment.
6. Mechanisms, features of action, use, adverse effects, contraindications to drugs used in osteoporosis treatment:
- 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

**Isotretinoin** – 10 mg capsules; 0.025% solution in 10 and 20 ml bottles for external use; 0.05% ointment in 10 g tubes. TD: orally, 10 mg twice daily with meals; apply to affected skin areas twice daily.

**Colecalciferolum** – oil solution in 10 ml bottles containing 15,000 IU per ml (1 drop contains 500 IU). TD: orally during meals once a day. For the prevention of rickets – 500–1,000 IU, for the treatment of rickets – 1,000–5,000 IU; for the prevention and treatment of osteoporosis – 1,000 IU.

**Calcipotriolum** – 0.005% ointment in 30 g tubes. Apply to the affected area of skin once or twice a day.

**Thiaminum** – solution available in 1 ml ampoules containing 50 mg per ml. TD: 25–50 mg intramuscularly once a day.

**Pyridoxinum** – tablets, 50 mg; solution in 1 ml ampoules containing 10 mg per ml. TD: orally, 50–100 mg 3 times a day; intravenously, 10 mg diluted in 10 ml of a 5% glucose solution.

**Acidum nicotinicum** – tablets, 50 mg; solution in 1 ml ampoules containing 10 mg per ml. TD: orally, 50–100 mg 3 times a day; intravenously, 10 mg diluted in 10 ml of a 5% glucose solution.

**Acidum ascorbinicum** – tablets and dragees, 50 mg; solution in 2 ml ampoules containing 50 mg per ml. TD: orally, 50–100 mg 3 times a day after meals; intramuscularly, 50–100 mg once a day; intravenously, 100 mg diluted in 10 ml of a 5% glucose solution.

### **SELF-ASSESSMENT TASKS**

**Task 1.** Questions on pharmacotherapy. Write prescriptions, justifying the choice of each drug.

1. Drug for acne with resorptive action.
2. Drug for rickets prevention.
3. Drug for the treatment of rickets.
4. Drug for the treatment of osteoporosis.
5. Drug for the treatment of psoriasis.
6. Drug for the treatment of neuropathic pain.
7. Drug for metabolic acidosis.
8. Drug for correcting the adverse effects of the anti-tuberculosis drug isoniazid.
9. Drug for the treatment of peripheral vascular spasm.
10. Drug for impaired cerebral circulation.
11. Drug for the treatment of hemorrhagic diathesis.
12. Drug for immunodeficiency.
13. Drug for bleeding gums.
14. Immune stimulant for influenza.
15. Drug for the treatment of anemia.
16. Drug for the treatment of liver diseases.
17. Drug for the treatment of allergic diseases.
18. Drug for malnutrition in children.

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

1. Which fat-soluble vitamin functions as a hormone in the body? What type of metabolism does it regulate and how?
2. Which fat-soluble vitamin can prevent aging in the body? What is the mechanism of this effect?
3. Which vitamin supplements improve epithelization of the skin? Which diseases is this effect used for?
4. Which vitamin preparations are used in ophthalmology? Consider their mechanisms of action in eye diseases.
5. Which vitamins are involved in carbohydrate and energy metabolism in the nervous tissue? Which diseases of the nervous system are these drugs used for?
6. Which vitamin preparations are used to treat liver diseases? Consider the mechanisms of their hepatoprotective action.
7. Which vitamin preparations have a therapeutic effect on anemia? What are the mechanisms of their stimulating effect on hematopoiesis?
8. Which vitamin supplements stimulate the immune system? Which diseases is this effect used for?
9. What groups of drugs are used to treat osteoporosis? Indicate the differences in the mechanisms of action of various drugs used to treat this disease.

### Task 3.

- a. Match each drug (A–E) for bone disorders with the appropriate description (1–6).

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 $\kappa$ B ligand)
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 drug of vitamin (A–F) with the appropriate description (1–6).

A. Thiamine	1. Essential for normal vision
B. Menadione sodium bisulfite	2. Maintains normal blood levels of calcium and phosphorus
C. Cholecalciferol	3. Essential in the synthesis of several proteins that mediate both coagulation and anticoagulation
D. Retinol	4. Coenzyme of this vitamin plays a role in activating transketolase, an enzyme involved in the direct oxidative pathway for glucose
E. Riboflavin	5. This vitamin is required by the body to use oxygen and metabolize amino acids, fatty acids, and carbohydrates
F. Ascorbic acid	6. This vitamin is required for the synthesis of collagen in connective tissues

**Task 4.** Topics for reports.

1. Vitamin supplements during pregnancy: pros and cons.
2. Multivitamin complexes: pros and cons of combination therapy.
3. Retinoid receptors: structure, localization, and functioning.
4. Evidence-based effectiveness of osteoporosis drugs.
5. Effects of drugs on the RANKL/RANK and Wnt signaling pathways in bone tissue.

## QUESTIONS AND TASKS IN CLASS

**Task 1.** Analyze tasks illustrating drug mechanisms, key characteristics, indications for their clinical use, and adverse effects (the set of graphic tasks).

**Task 2.** Analyze case tasks.

1. A 55-year-old patient reports difficulty driving at night and sudden visual impairment in low light conditions, although daytime vision

remains normal. The patient has an irregular diet and a history of pancreatitis. What could be causing the symptoms described?

2. During a consultation with a dermatologist, a 22-year-old woman complains of dry skin, poorly healing wounds (ulcers) on the skin and mucous membranes, dry mouth, and blurred vision. She has a history of anorexia (previously observed by a psychiatrist). The examination revealed hyperkeratosis, a papular rash, atrophy of sweat glands, and xerophthalmia. Can you explain the mechanism behind these symptoms?
3. A 7-year-old boy was admitted to the emergency department after falling while playing in the yard. The physical examination revealed only minor skin scratches, but an X-ray showed two rib fractures, a demineralized bone, and metaphyseal widening and cupping with abnormally increased concavity and irregular calcification. The serum values on admission were calcium 8.3 mg/dL (the reference value is 8.5–10.5 mg/dL), phosphate 2.2 mg/dL (the reference value is 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 persistent gastric pain that occurred every time she took a prescribed medication. She was recently diagnosed with severe osteoporosis and had started therapy with oral alendronate one week earlier. The physician discontinued 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. can you explain why the drug shows such a prolonged efficacy?

**Task 3.** Answer the test questions (in the ICT classroom).

## **Lesson 8**

### **Hormones and Antihormonal Agents (Part 1)**

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

#### **KEY TOPICS FOR PREPARATION**

1. Characteristics of hormones: classification, biosynthesis, secretion, principles of action, receptors. Hormonal regulation of body functions. History of hormonal drug discovery.
2. Mechanisms of action, receptors, pharmacokinetics, use, adverse effects, and contraindications of hormonal and antihormonal agents.
3. Drugs affecting pituitary hormone production:
  - somatostatin drugs – octreotide, lanreotide, pasireotide;
  - drugs that inhibit the secretion of gonadotropic hormones – goserelin, danazol, cetrorelix;
  - inhibitors of prolactin and growth hormone secretion – D-receptor agonists (bromocriptine), selective agonists of D<sub>2</sub>- receptors (cabergoline).
4. Anterior pituitary hormones:
  - somatotropin;
  - gonadotropins with luteinizing activity – lutropin alfa, choriogonadotropin alfa;
  - gonadotropins with follicle-stimulating activity – urofollitropin, follitropin alfa, menotropin.
5. Posterior pituitary hormones:
  - vasopressin and its analogs – desmopressin;
  - oxytocin.
6. Thyroid hormones and antithyroid drugs:
  - agents for replacement therapy in hypothyroidism – potassium iodide, levothyroxine sodium;
  - antithyroid drugs – thiamazole;
  - agents that reduce blood calcium levels – calcitonin.

7. Parathyroid hormone drugs – teriparatide.
8. 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
    - sulfonylurea derivatives – glibenclamide, gliclazide, glimepiride;
    - meglitinides (prandial regulators) – nateglinide, repaglinide;
    - incretin mimetics (glucagon-like peptide-1 receptor agonists) – exenatide, liraglutide, lixisenatide, dulaglutide, albiglutide;
    - inhibitors of dipeptidylpeptidase-4 (gliptins) – vildagliptin, saxagliptin, sitagliptin;
  - b) drugs that increase glucose uptake in 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, canagliflozin, empagliflozin;
  - e) inhibitors of glucagon secretion:
    - amylin analogs – pramlintide.
10. Diabetic and hypoglycemic coma: causes, mechanisms of development, symptoms, treatment. Clinical use of glucagon.

## PRESCRIPTIONS

**Kalii iodidum** – tablets, 100 and 200 mcg. TD: orally 1 time a day in the morning after meals – prophylactic doses of 100–200 mcg; therapeutic doses – 200–500 mcg.

**Levothyroxin natrium** – tablets, 50 and 100 mcg. TD: orally 50–200 mcg once a day in the morning before meals.

**Thiamazole** – 5 mg tablets. TD: orally 5–10 mg three times a day after meals.

**Human insulin** – 10 ml bottles (1 ml – 100 IU). TD: subcutaneous injection, 0.3 IU/kg body weight three times a day 30 minutes before meals; for diabetic coma –in the form of an intravenous bolus, 10 IU in 100 ml of isotonic sodium chloride solution every hour while controlling the plasma glucose level.

**Dextrose** – solution in 20 ml ampoules containing 400 mg per ml. TD: intravenous bolus, 8,000–10,000 mg.

**Gliclazide** – 80 mg tablets. TD: 80 mg orally two times a day with meals.

**Metformin** – 1,000 mg tablets. TD: orally 1,000 mg two times a day with meals.

**Sitagliptin** – 100 mg tablets. TD: orally 100 mg once a day.

**Empagliflozin** – tablets, 10 and 25 mg. TD: orally, 10–25 mg once a day.

## SELF-ASSESSMENT TASKS

**Task 1.** Questions on pharmacotherapy. 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. Hormonal therapy for hypothyroidism.
4. Replacement therapy after the thyroid gland removal.
5. Drug for thyrotoxicosis.
6. Drug used in preparation for the thyroid gland removal.
7. Drug for type 1 diabetes mellitus.
8. Sulfonylurea derivative for the treatment of type 2 diabetes mellitus.
9. Dipeptidyl peptidase-4 inhibitor for the treatment of type 2 diabetes mellitus.
10. Emergency treatment for diabetic coma.
11. Emergency treatment for hypoglycemic coma.

12. Drug that stimulates insulin secretion for the treatment of diabetes mellitus.
13. Drug for overcoming insulin resistance in diabetes mellitus.
14. Drug for the prevention of type 2 diabetes mellitus in patients with prediabetes.
15. Drug for metabolic syndrome.
16. Drug for obesity.
17. Drug for type 2 diabetes mellitus in patients with cardiovascular diseases.
18. Drug for chronic heart failure.

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

1. Explain the mechanisms of action of levothyroxine sodium on the central nervous system, cardiovascular system, cellular oxygen demand, and lipid metabolism.
2. Do patients with thyrotoxicosis who are scheduled for thyroid gland resection need to be prescribed potassium iodide after a course of treatment with thiamazole?
3. How does the insulin receptor function? How does its function change in different types of diabetes?
4. Which genetically engineered human insulin preparations are recommended for long-term therapy of diabetes mellitus, and which ones are used for managing diabetic coma? What is the significance of the pharmacokinetics of insulin preparations?
5. Which drugs used in the treatment of type 2 diabetes mellitus have hypolipidemic, anorexigenic and angioprotective effects? What is the significance of these effects in diabetes mellitus? Why?
6. Why is the effect of metformin compared to the metabolic effects of exercise?
7. Is it advisable to prescribe antihyperglycemic drugs to individuals with normal plasma glucose levels? Why?

**Task 3.**

- a. Match each drug (A–D) with the appropriate description (1–4).

A. Levothyroxine	1. Blocks peroxidase and disrupts the synthesis of thyroid hormones
B. Potassium iodide	2. Causes thyroid cell necrosis
C. Radioactive iodine	3. Acts mainly by inhibiting hormone release from the thyroid gland
D. Thiamazole	4. Targets thyroid deiodinase

b. Match each drug (A–E) with the appropriate description (1–5).

A. Liraglutide	1. Activates PPAR $\gamma$ receptors, which are expressed primarily in adipose tissue with lesser expression in cardiac, skeletal, and smooth muscle cells
B. Metformin	2. Inhibits the dipeptidyl peptidase-4 and increases incretin levels
C. Empagliflozin	3. Suppresses hepatic gluconeogenesis, inhibits glucose absorption, stimulates peripheral uptake of glucose in tissues, stimulates glycolysis in the tissues
D. Vildagliptin	4. Inhibits Na <sup>+</sup> -Glucose Transporter 2 and reduces reabsorption of glucose and sodium
E. Pioglitazone	5. Activates GLP-1 receptor and stimulates glucose-dependent insulin secretion

**Task 4.** Topics for reports.

1. The history of insulin invention.
2. Combination therapy with oral hypoglycemic agents in patients with type 2 diabetes mellitus.
3. Insulin: an anabolic hormone.

## QUESTIONS AND TASKS IN CLASS

**Task 1.** Analyze the tasks that illustrate the relationship between pharmacokinetics and the physicochemical properties of drugs (the set of graphic tasks).

**Task 2.** Analyze the following case tasks.

1. A 52-year-old man with a history of alcoholism was brought to the emergency department in an unconscious state. Upon admission, he was sweating, had a body temperature of 34.7°C (94.5°F), and a cardiac pulse of 135 beats per minute. Shortly after his arrival, he experienced a tonic-clonic seizure. His wife informed the medical staff that he was also a diabetic undergoing insulin therapy. What disorder most likely caused the patient's symptoms? Please 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 only responded to pain stimuli. The medical history obtained from her mother was unremarkable. A physical examination revealed contusions on her face and arms, but no signs of cranial trauma. Vital signs of the patient: temperature – 36.1°C (97°F), blood pressure – 105/70 mm Hg, pulse – 112 bpm, respiratory rate – 22/min. The serum values were bicarbonate 6 mEq/L (the reference value is 22–28 mEq/L), glucose 847 mg/dL (the reference value is 70–110 mg/dL), creatinine 1.1 mg/dL (the reference value is 0.6–1.2 mg/dL). Urinalysis showed the following: specific gravity 1.036, glucose 4+, ketones 4+. What diagnosis can be made, and what emergency treatment should be administered?
3. Finally, a 29-year-old woman presented to her physician with complaints of fatigue, constipation, and irregular menstrual cycles over the past two months. A physical examination revealed delayed deep tendon reflexes, mild bradycardia, and a nontender, nodular thyroid goiter. Blood tests showed thyroid peroxidase antibodies at 120 IU/L (reference value: < 0.8 IU/L). What is the diagnosis, what mechanism explains her symptoms, and what treatment should be prescribed?

**Task 3.** Answer the test questions (in the ICT classroom).

## **Lesson 9**

### **Hormones and Antihormonal Agents (Part 2)**

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

#### **KEY TOPICS FOR PREPARATION**

1. Characteristics of steroid hormones: classification, biosynthesis, secretion, cytoceptors.
2. Pharmacological effects, pharmacokinetics, use, adverse effects and contraindications of steroid hormones and their antagonists.
3. Hormones of the adrenal cortex:
  - a) synthetic mineralocorticoids – fludrocortisone;
  - b) natural glucocorticoids – hydrocortisone;
  - c) synthetic glucocorticoids:
    - with resorptive action – prednisolone, methylprednisolone, dexamethasone, triamcinolone, betamethasone, budesonide;
    - inhaled forms – beclomethasone, budesonide, fluticasone;
    - for local action on the nasal mucosa – mometasone;
    - for local action on the skin – flumetasone, fluocinolone acetonide.
4. Sex hormones:
  - estrogen drug – estradiol, ethinyl estradiol, estriol, estradiol valerate;
  - progestogen drugs – progesterone, gestoden, medroxyprogesterone, levonorgestrel, desogestrel;
  - androgen drugs – testosterone.
5. Anabolic steroids – nandrolone.
6. Oral contraceptives:
  - a) combination of an estrogen and a progestogen:
    - monophasic – ethinyl estradiol and norgestrel (Ovral G); ethinyl estradiol and levonorgestrel (Ovral L; Mala D); ethinyl estradiol and desogestrel (femilon);

biphasic – ethinyl estradiol and norethindrone and ethinyl estradiol and desogestrel;

triphasic – ethinyl estradiol and levonorgestrel (triquilar).

b) Progestogen only:

(mini-pill) – norethisterone, levonorgestrel, ethynodiol;

parenteral – levonorgestrel (intrauterine system).

7. Anticlimacteric drugs (menopausal hormone therapy, hormone replacement therapy) – dydrogesterone and estradiol (Femoston\*), drospirenone and estradiol (Angeliq\*), estradiol valerate (Progynova\*).

8. Antagonists of sex hormones:

- antiestrogen drugs – fulvestrant, clomiphene, tamoxifen;
- antigestagen agents – mifepristone;
- antiandrogen drugs – cyproterone, flutamide, finasteride.

## PRESCRIPTIONS

**Hydrocortisone** – 10 mg tablets; 0.5% eye ointment in 5 g tubes; 0.1% emulsion in 30 ml bottles. TD: orally, 20–200 mg once a day; place behind the lower eyelid 2–3 times a day; apply to skin twice daily.

**Betamethasone** – suspension in 1 ml ampoules containing 7 mg per ml. TD: intra-articular injections (in the joint cavity), 7–14 mg.

**Prednisolone** – 5 mg tablets; 3% solution in 1 ml ampoules containing 3 mg per ml; 0.5% ointment in 10 g tubes. TD: orally, 5–20 mg once a day in the morning with meals; intravenously, 0.075–0.15 in 500 ml of 5% glucose solution.

**Beclometasone** – aerosol containing 50 and 100 mcg per dose; spray containing 50 mcg per dose. TD: inhalation, 100–300 mcg twice daily; 100–400 mcg in each nostril twice daily.

**Dexamethasone** – 0.5 and 4 mg tablets; solution in 1 and 2 ml ampoules containing 4 mg per ml; 0.1% solution in 10 ml bottles (eye drops). TD: orally, 2–8 mg once a day in the morning with meals; intravenously, 4–12 mg in 500 ml of 5% glucose solution 2 times a day; 1–2 drops in each eye 1–2 times a day.

**Mometasone** is a nasal spray containing 50 mcg per dose. TD: 100 mcg in each nostril once a day.

**Desogestrel** – 75 mcg tablets. TD: orally, 75 mcg once a day for 28 days, starting from the first day of the menstrual cycle.

**Nandrolone** – an oil solution in 1 ml ampoules containing 50 mg perml. TD: intramuscularly, 25–50 mg once every 3–4 weeks.

### **SELF-ASSESSMENT TASKS**

**Task 1.** Questions on pharmacotherapy. Write prescriptions and justify the choice of each drug for the following conditions:

1. Drug for the treatment of primary and secondary adrenal insufficiency.
2. Drug for the treatment of rheumatoid arthritis.
3. Drug for the treatment of acute bursitis of the elbow joint.
4. Drug for the treatment of glomerulonephritis.
5. Emergency medicine for anaphylactic shock.
6. Medicine for pulmonary edema.
7. Medicine for allergic dermatitis.
8. Drug for the treatment of psoriasis.
9. Drug for the treatment of bronchial asthma.
10. Medicine for acute allergic reaction to insect bites.
11. Drug for the treatment of keratoconjunctivitis.
12. Medicine for superficial injuries of the cornea.
13. Medicine for the treatment of allergic rhinitis.
14. Drug for the treatment of rhinosinusitis.
15. Contraceptive during breastfeeding.
16. Drug for the treatment of osteoporosis.
17. Medicine for the adverse effects of radiation therapy.
18. Medicine for progressive muscular dystrophy.

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

1. How do mineralocorticoid and glucocorticoid receptors function? Discuss the mechanisms of interaction between these receptors and hormones, as well as their functions.

2. Aldosterone and hydrocortisone are known to interact with the same corticosteroid receptor, but the plasma concentration of hydrocortisone is 400–1600 times greater than that of aldosterone. Explain the mechanisms of aldosterone's pharmacological effects in tissues sensitive to it.
3. What is the difference in the effects of glucocorticoids at physiological versus pharmacological concentrations? What is meant by the permissive action of glucocorticoids?
4. Describe the impact of glucocorticoids on the metabolism of carbohydrates, proteins, and lipids during resorptive action. How do glucocorticoids affect liver enzymes activity?
5. Why are glucocorticoid drugs prescribed for shock, regardless of its etiology? Discuss the mechanisms of the anti-shock action of glucocorticoid drugs.
6. Explain the mechanisms behind the anti-inflammatory action of glucocorticoids. For which diseases are the anti-inflammatory effect of these hormonal drugs utilized?
7. How should glucocorticoid drugs be prescribed, taking into account the daily biorhythms of the adrenal cortex and the sensitivity of cytochrome P-450? Indicate the advantages of such prescriptions.
8. What adverse effects of glucocorticoids can patients experience even with topical application? Explain the advisability of combined use of topical glucocorticoids and antimicrobial and antifungal agents for topical use.
9. What sex hormone medications are prescribed for both men and women? List the indications for the use of these drugs.
10. Consider the phases of the menstrual cycle. Which contraceptives best mimic the secretion of natural ovarian hormones during the normal menstrual cycle?
11. What contraceptives are used to prevent pregnancy during breastfeeding?

12. How do hormonal agents influence processes in bone tissue? Which hormonal agents increase bone formation, and which increase bone resorption?

13. Why are anabolic steroids indicated after severe infectious diseases, burns, and radiation sickness?

**Task 3.**

a. Match each drug (A–D) with the appropriate description (1–4).

A. Fludrocortisone	1. It is an inhaled corticosteroid used as maintenance treatment in the prophylaxis of asthma attacks.
B. Prednisolone	2. It is a fluorinated corticosteroid used to treat endocrine, rheumatic, collagen, dermatologic, allergic, ophthalmic, gastrointestinal, respiratory, hematologic, neoplastic, edematous and other conditions
C. Dexamethasone	3. It is a glucocorticoid similar to cortisol. It is used for its anti-inflammatory, immunosuppressive, anti-neoplastic, and vasoconstrictive effects
D. Beclomethasone	4. It is functionally similar to aldosterone and is structurally analogous to cortisol, indicated in Addison's disease

b. Match each drug (A–D) with the appropriate description (1–4).

A. Finasteride	1. A progestational and glucocorticoid hormone antagonist
B. Mifepristone	2. An antiandrogenic compound prescribed for the treatment of symptomatic benign prostatic hyperplasia (BPH) and male-pattern hair loss in adult males by inhibiting type II 5-alpha reductase.

C. Tamoxifen	3. An anabolic steroid indicated to increase bone density and muscle mass in patients with osteoporosis
D. Nandrolone	4. A selective estrogen receptor modulator used to treat estrogen receptor-positive breast cancer

**Task 4.** Topics for reports.

1. History of the invention of glucocorticoids.
2. Advantages of modern topical glucocorticoid preparations.
3. Localization, structure, and functions of estrogen receptors.
4. Anabolic steroids and bodybuilding.
5. Modern methods of emergency contraception.
6. Contraceptives and menopausal hormone therapy (MHT).

### QUESTIONS AND TASKS IN CLASS

**Task 1.** Analyze the tasks that illustrate the mechanisms of action and key characteristics of drugs, their clinical uses, and potential adverse effects (the set of graphic tasks).

**Task 2.** Analyze the following case tasks.

1. A 40-year-old woman was admitted to the hospital complaining of nausea and vomiting, weight loss, fatigue, and weakness. She also reported persistent dizziness when standing and decreased tolerance to cold. Physical examination showed moderate distress, increased pigmentation around the nipples, absence of axillary and pubic hair, and diffuse tanning of exposed areas of her body. Serum levels on admission were  $\text{Na}^+$  – 125 mEq/L (the reference rate is 136–145 mEq/L),  $\text{K}^+$  – 6.2 mEq/L (the reference rate is 3.5–5.0 mEq/L), fasting blood glucose – 42 mg/dL (the reference rate is 70–110 mg/dL). The patient’s signs and symptoms indicate that she was suffering from Addison’s disease. Explain the mechanism behind the symptoms and prescribe appropriate treatment for this patient.
2. A 55-year-old woman was admitted to the hospital with increasing muscle weakness, anxiety, and loss of emotional control. The patient was diagnosed with polymyositis 5 months ago and has

been receiving appropriate therapy since then. Physical examination showed face and truncal obesity, thin and easily bruised skin. Vital signs: blood pressure – 168/98 mm Hg, pulse – 84 bpm, respiratory rate – 18/min. A bone X-ray revealed diffuse osteoporosis. What drug is most likely responsible for the patient's signs and symptoms?

3. A 45-year-old man complained to his physician of severe shoulder pain. Further examination resulted in the diagnosis of acute bursitis, and intra-articular injections of dexamethasone were prescribed. Which of the following actions most likely contributed to the therapeutic efficacy of the drug in the patient's case?
  - A. Inhibition of adrenocorticotrophic hormone (ACTH) release
  - B. Increased catabolism of prostaglandins
  - C. Increased postcapillary permeability
  - D. Increased release of interleukin-1
  - E. Induction of lipocortin synthesis
4. A 26-year-old woman consulted her family physician regarding a hormonal contraceptive. She refused other methods of contraception. Her medical history indicated disseminated intravascular coagulation following an abortion due to placental abruption. Which of the following hormonal contraceptives would be the most appropriate for her?
  - A. Diethylstilbestrol
  - B. Ethinyl estradiol and norethindrone
  - C. Mestranol and norethindrone
  - D. Mifepristone
  - E. Ethinyl estradiol and levonorgestrel
  - F. Levonorgestrel

**Task 3.** Answer the test questions (in the ICT classroom).

## **Lesson 10**

### **Drugs Affecting Adrenergic Synapses**

*Learning objectives are to classify adrenergic drugs, understand their mechanisms, pharmacokinetics, and clinical applications, and practice prescription writing.*

#### **KEY TOPICS FOR PREPARATION**

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 ( $\alpha$ ,  $\beta$ , presynaptic, postsynaptic, extrasynaptic), localization, significance.
6. Adrenomimetics: mechanism of action and classification
  - a. direct adrenomimetics
    - $\alpha$ ,  $\beta$ -adrenomimetics – epinephrine;
    - $\alpha$ -adrenomimetics – norepinephrine, phenylephrine, naphazoline, xylometazoline, oxymetazoline;
    - $\beta$ -adrenomimetics – dobutamine;
    - selective  $\beta_2$ -adrenomimetics:
      - short-acting – salbutamol, fenoterol, terbutaline;
      - long-acting – salmeterol, formoterol, vilanterol, indacaterol, olodaterol;
      - selective  $\beta_3$ -adrenomimetics – mirabegron.
  - b. adrenomimetics 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 for use.
10. Dopamine: dependence of pharmacological effects on dose, use, adverse effects and contraindications for use.
11.  $\alpha$ -Adrenoblockers: mechanisms of action and classification
  - $\alpha_1$ ,  $\alpha_2$ -adrenoblockers – phentolamine, nicergoline, propoxane;
  - selective  $\alpha_1$ -adrenoblockers – prazosin, alfuzosin, doxazosin, tamsulosin, terazosin.
12. Effect of  $\alpha$ -adrenoblockers on the cardiovascular system and organs with smooth muscles. Pharmacokinetics. Indications, adverse effects, contraindications for use.
13.  $\beta$ -Adrenoblockers: mechanisms of action and classification.
  - nonselective  $\beta$ -adrenoblockers – propranolol, timolol;
  - cardioselective  $\beta_1$ -adrenoblockers – atenolol, bisoprolol, metoprolol, esmolol;
  - $\beta_1$ -adrenoblockers with vasodilator action – nebivolol.
14.  $\alpha$ ,  $\beta$ -adrenoblockers – carvedilol.
15. Effect of  $\beta$ -adrenoblockers and  $\alpha$ ,  $\beta$ -adrenoblockers on the central nervous system, cardiovascular system and metabolic processes.
16. Features of cardioselective  $\beta_1$ -adrenoblockers,  $\beta$ -adrenoblockers with vasodilator action,  $\alpha$ ,  $\beta$ -adrenoblockers.
17. Pharmacokinetics, use, adverse effects, contraindications of  $\beta$ -adrenoblockers.
18. Reserpine: mechanism of action, pharmacokinetics, use, adverse effects, contraindications.

## PRESCRIPTIONS

**Epinephrine** – solution in 1 ml ampoules containing 1 mg per ml.  
 TD: intravenously, 0.25–1 mg in 10 ml of isotonic sodium chloride solution.

**Phenylephrine** – solution in 1 ml ampoules containing 10 mg per ml; 2.5% solution in 5 ml bottles (eye drops); 0.125% solution in 10 ml bottles (nasal drops); nasal spray in 15 ml bottles containing 0.125 mg per dose; rectal suppositories 5 mg. TD: intravenously, shall be administered slowly, 1–5 mg in 20 ml of 5% glucose solution; subcutaneously, intramuscularly, 3–5 mg; 1–2 drops in each eye 2–3 times a day; 2 drops in each nostril 2 times a day; 0.125–0.375 mg in each nostril; rectally, 5 mg in the morning and before bedtime.

**Fenoterol** – aerosol containing 100 mcg per dose. TD: inhalation, 100–200 mcg.

**Salmeterol + Fluticasone** – aerosol containing 25 mcg of salmeterol and 125 mcg of fluticasone per dose. TD: inhalation, 1 dose 2 times a day.

**Tamsulosin** – tablets and capsules, 0.4 mg. TD: orally, 0.4 mg once a day.

**Metoprolol** – tablets, 50 and 100 mg; solution in 5 ml ampoules containing 1 mg per ml. TD: orally, 50–100 mg 2 times a day (in the morning and in the evening); intravenously, shall be administered slowly, 5 mg in 10–20 ml of 5% glucose solution.

**Nebivolol** – tablets, 5 and 10 mg. TD: orally, 5–10 mg once a day.

## SELF-ASSESSMENT TASKS

**Task 1.** Questions on pharmacotherapy. Write the prescriptions, justifying the choice of drug.

1. Drug for cardiac arrest treatment (asystole).
2. Drug for anaphylactic shock.
3. Drug for the treatment of vascular collapse in trauma.
4. Drug for vascular collapse during anesthesia.
5. Drug for the treatment of conjunctivitis.
6. Drug for examining the eye fundus.
7. Decongestant for the treatment of rhinitis.
8. Drug for the treatment of hemorrhoids.
9. Drug for the relief of bronchospasm in bronchial asthma.
10. Drug for the relief of bronchospasm in chronic obstructive pulmonary disease.
11. Drug for the preventive treatment of bronchial asthma.

12. Drug for the treatment of sinus tachycardia.
13. Drug for the treatment of ventricular extrasystole.
14. Adrenergic blocker for the treatment of arterial hypertension.
15. Adrenergic blocker for the treatment of thyrotoxicosis.
16. Drug for the treatment of angina pectoris.
17. Drug for the treatment of myocardial infarction.
18. Drug for benign prostatic hyperplasia.

**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 subcutaneously? What medications should be used urgently to prevent this adverse effect?
3. Why are adrenomimetics used to stop cardiovascular collapse during anesthesia?
4. Why is dobutamine not used for the long-term treatment of heart failure, despite its pronounced heart-stimulating (cardiotonic) effect'?
5. What is the difference between salbutamol and salmeterol?
6. Which  $\beta$ -adrenergic blocker should be chosen for treating arrhythmia in a patient with liver cirrhosis – lipophilic propranolol or hydrophilic atenolol?
7. Why did a patient with angina, who had been taking propranolol for a long time, experience chest pain again after discontinuing propranolol rapidly?
8. Which pharmacological effects of nebivolol result from the blockade of  $\beta$ -adrenoreceptors, and which of them are pleiotropic?
9. What is the difference between influence of  $\alpha_1$ -adrenergic blockers and  $\beta$ -adrenergic blockers on lipid metabolism?
10. Which  $\alpha$ -blockers facilitate urination in benign prostatic hypertrophy without reducing blood pressure? How does this relate to their mechanism of action?

### Task 3.

a. Match each drug (A–E) with the appropriate description (1–5).

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

b. Match each drug (A–E) with the appropriate description (1–5).

A. Atenolol	1. This drug is non-selective beta-adrenergic blocker used in the treatment of elevated intraocular pressure
B. Esmolol	2. This drug is a selective $\beta_1$ antagonist frequently used for the chronic treatment of atrial fibrillation
C. Timolol	3. This drug is a $\beta$ -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 and 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 illustrate the mechanisms of action and key characteristics of adrenergic drugs (the set of graphic tasks).

**Task 2.** Analyze the following 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, showing no sensation or reflex activity below the thorax. Vital signs were blood pressure 80/40 mm Hg, heart rate 42 bpm, respiratory rate 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 receiving fluid therapy, she remained hypotensive (80/50 mm Hg) and tachycardic (125 bpm). An intravenous infusion of norepinephrine was initiated, and a few minutes later, her blood pressure rose to 120/85 mm Hg, while her heart rate decreased to 85 bpm. Which action best explains the drug-induced decrease in heart rate for this patient?
3. A 47-year-old man with a 10-year history of diabetes was admitted to the hospital following a myocardial infarction. He was discharged 10 days later with a post-discharge treatment plan that included atenolol. The patient was instructed to monitor his blood glucose levels closely for both hyperglycemia and hypoglycemia after starting the medication. What is the reason for monitoring glucose levels during atenolol treatment?
4. A  $\beta$ -blocker, propranolol, was prescribed for hypertension in a female asthma patient. After about a week of treatment, her asthma attacks worsened, and the patient was advised to stop taking the  $\beta$ -blocker. Which  $\beta$ -blocker (that is less likely to worsen the patient's asthma) would you offer as an alternative and why?

**Task 3.** Answer the test questions (in the ICT classroom).

## **Lesson 11**

### **Drugs Affecting Functions of Cholinergic Synapses**

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

#### **KEY TOPICS FOR PREPARATION**

1. Cholinergic synapses: localization and structure.
2. Acetylcholine: chemical structure, synthesis, secretion, and inactivation.
3. Cholinergic receptors: types (muscarinic, nicotinic), localization, functional significance.
4. N-cholinomimetics (ganglionic stimulants): origin, effects, medical significance, and use. Drugs used as aids in smoking cessation – cytisine, nicotine, varenicline.
  - M, N-cholinomimetics – acetylcholine, carbachol;
  - M-cholinomimetics – pilocarpine, bethanechol.
5. Cholinesterase inhibitors: origin, mechanisms of action, classification:
  - reversible inhibitors:
    - tertiary amines – physostigmine, galantamine, ipidacrine;
    - quaternary amines – neostigmine, pyridostigmine;
  - selective reversible inhibitor of acetylcholinesterase in the brain – rivastigmine;
  - irreversible inhibitors (organophosphate toxic agents) – ecothiophate.
6. Effects of cholinomimetics and cholinesterase inhibitors on the eye: mechanisms of action and importance in 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, adverse 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, umeclidinium bromide, pirenzepine, oxybutynin, solifenacin.
9. Mechanisms of action of anticholinergic agents on the eye. Features of the action of atropine, platyphyllin and tropicamide. Indications and contraindications of anticholinergic agents in ophthalmology.
10. Resorptive effect of anticholinergic agents: action on the central nervous system, cardiovascular system, smooth muscle organs, glands. Pharmacokinetics. Use, adverse effects, contraindications.
11. Organophosphate and atropine poisoning: causes of intoxication, stages, pathogenesis, symptoms and treatment.
12. Cholinesterase reactivators: mechanisms and features of the action of pralidoxime.

### **PRESCRIPTIONS**

**Pilocarpine** – 1% solution in 5 ml vials. TD: 1–2 drops in each eye 2–4 times a day; in acute glaucoma attack – 1–2 drops in the first hour every 15 minutes, in the second hour – 2 times.

**Neostigmine methylsulfate** – tablets, 15 mg; solution in 1 ml ampoules containing 0.5 mg per ml. TD: 15 mg orally 30 minutes before meals; subcutaneously, 0.5 mg 1–2 times a day.

**Ipidacrine** – tablets, 20 mg; solution in ampoules 1 ml containing 15 mg per 1 ml. TD: orally 20 mg 1–3 times a day; subcutaneously, into muscles 15 mg 1–2 times a day.

**Atropine** – solution in 1 ml ampoules containing 1 mg per ml; 1% solution in 5 ml vials. TD: subcutaneously, intramuscularly – 0.25–0.5 mg 1–2 times a day; 1–2 drops in each eye 1–2 times a day; in organophosphate poisoning – intravenously, 1 mg every 15 min.

**Tropicamide** – 1% solution in 10 ml vials. TD: 1–2 drops in each eye.

**Platyphylline** – solution in 1 ml ampoules containing 2 mg per ml. TD: 2–4 mg subcutaneously 1–2 times a day.

**Tiotropium bromide** – powder for inhalation in capsules, 18 mcg. TD: inhalation, 18 mcg once a day.

**Solifenacin** – tablets, 5–10 mg. TD: orally 5–10 mg once a day.

**Oxybutynin** – 5 mg tablets. TD: 5 mg orally 2–3 times a day.

### **SELF-ASSESSMENT TASKS**

**Task 1.** Questions on pharmacotherapy. Write the prescriptions, justifying the choice of drugs.

1. Drug for the long-term treatment of glaucoma.
2. Drug for relieving an attack of acute angle-closure glaucoma.
3. Drug to reduce the effects of polio.
4. Drug for autoimmune myasthenia gravis.
5. Drug for intestinal atony.
6. Drug for bladder atony.
7. Drug that causes paralysis of accommodation for the selection of glasses.
8. Drug for the treatment of iritis.
9. Drug for examining the eye fundus.
10. Drug that prevents cardiac arrest during anesthesia.
11. Drug that reduces salivation during anesthesia.
12. Drug for renal colic.
13. Drug for the treatment of chronic obstructive bronchitis.
14. Drug for urinary incontinence in children.
15. Drug for neurogenic bladder dysfunction.
16. Antagonist for Amanita poisoning.
17. Physiological antagonist for organophosphate poisoning.
18. Antagonist for atropine poisoning.

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

1.  $M_3$ -cholinoceptors are found in the smooth muscles of arteries and various organs. Why do cholinomimetics that activate  $M_3$ -cholinergic receptors cause dilation of arteries but increase the tone of smooth muscle organs?
2. Name the toxic substances commonly found in mushrooms. What are the differences in their toxicokinetics and effects on the body?

3. What are the non-anticholinesterase mechanisms of action of cholinesterase inhibitors?
4. Which agents are used to treat myasthenia gravis? In which forms of myasthenia are they effective? Why is atropine administered simultaneously with these drugs?
5. Which M-cholinoblockers are used in ophthalmology for diagnostic purposes, and which one or treatment?
6. Identify M-cholinoblockers with selective action that are used to treat peptic ulcer disease, chronic obstructive pulmonary disease (COPD), and urinary incontinence? What mechanisms underpin the selective action of these drugs?

**Task 3.**

- a. Match each drug (A–G) with the appropriate description (1–7).

A. Galantamine	1. An antagonist at Nn-acetylcholine receptors in autonomic ganglia
B. Neostigmine	2. The muscarinic agonist used to treat postoperative and postpartum nonobstructive functional urinary retention and neurogenic atony of the bladder with retention
C. Carbachol	3. The CNS selective cholinesterase inhibitor for the treatment of mild to moderate dementia associated with Parkinson's disease or of Alzheimer's type
D. Bethanechol	4. The muscarinic agonist administered ophthalmically to decrease intraocular pressure after cataract surgery, and to induce miosis during surgery
E. Rivastigmine	5. The cholinesterase inhibitor used in the treatment of myasthenia gravis and to reverse the effects of muscle relaxants such as gallamine and tubocurarine; it does not cross the blood-brain barrier
F. Pilocarpine	6. The drug of choice to rapidly decrease intraocular pressure in emergencies in both open-angle and angle-closure glaucoma
G. Nicotine	7. The tertiary alkaloid and reversible, competitive inhibitor of the acetylcholinesterase enzyme

b. Match each drug (A–E) with the appropriate description (1–5).

A. Ipratropium	1. The drug used as an antispasmodic agent to relax the GI tract
B. Atropine	2. One of the most effective anti-motion sickness drugs available
C. Scopolamine	3. The drug used in the management of acute bronchospasm in asthma
D. Oxybutynin	4. The drug is an antimuscarinic agent that reduces detrusor muscle activity, relaxing the bladder and preventing the urge to void

**Task 4.** Topics for reports.

1. History of research on nicotinic and muscarinic cholinergic receptors.
2. Edrophonium: the drug used as a test for myasthenia gravis.
3. Bethanechol: mechanism of action, use.
4. Organophosphates as insecticides and pesticides.
5. Glaucoma: types, causes, and symptoms.
6. Myasthenia gravis: causes, symptoms, diagnosis.
7. Calabar beans: Prehistoric lie detectors.

### QUESTIONS AND TASKS IN CLASS

**Task 1.** Analyze the tasks that illustrate the mechanisms of action and key characteristics of cholinergic agents (the set of graphic tasks).

**Task 2.** Analyze the following case tasks.

1. A 71-year-old man suffering from myasthenia gravis was admitted to the hospital for evaluation. His therapy included neostigmine, taken three tablets a day. 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 preventive measures should be taken in this case?
2. A 49-year-old farmer presented to the emergency department complaining of blurred vision, nausea, and painful muscle contractions in his legs. He said the symptoms began soon after

returning from his soybean field. Which class of drugs is most likely responsible for the patient's symptoms? What medication should be administered to relieve 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 excessive 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, heart rate – 46 bpm. Which agent most likely caused 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 reported that he had eaten several blackberries from a wild plant while playing with friends in the woods. A physical examination revealed mydriasis; dry, hot, and scarlet (red) skin; and a distended abdomen with no bowel sounds. Vital signs were temperature 104.5°F (40.3°C), heart rate 145 bpm, and blood pressure 105/60 mm Hg. Which agent most likely caused this patient's poisoning? Prescribe treatment for 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 began when she was in her garden spraying flowers with an insecticide. Which agent is most likely responsible for this patient's poisoning? Which drug should be used to treat this condition?
6. Atropine was administered intramuscularly to several dogs during a laboratory 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 ICT classroom).

## **Lesson 12**

### **Drugs Affecting Function of Cholinergic Synapses (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, pharmacokinetics, indications for use, and contraindications, adverse 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.*

#### **KEY TOPICS FOR PREPARATION**

1. Cholinergic synapses: localization, structure. Localization and functions of N-cholinergic receptors.
2. Ganglion-blocking agents: mechanisms and site of action, effects on sympathetic and parasympathetic ganglia.
3. Hexamethonium: features of action, use, adverse effects, and contraindications.
4. Neuromuscular-blocking agents: mechanisms and site of action, classification (non-depolarizing, depolarizing).
5. Non-depolarizing neuromuscular blockers (curare-like drugs, pachimurare): mechanisms and features of action, synergists and antagonists, classification:
  - long-acting – tubocurarine, pancuronium, pipecuronium;
  - intermediate-acting – atracurium, cisatracurium, vecuronium;
  - short-acting – mivacurium.
6. Depolarizing neuromuscular blockers (leptokurare): mechanisms and features of action, synergists – suxamethonium.
7. Pharmacokinetics of neuromuscular blockers. Uses.
8. Adverse effects of neuromuscular blockers, contraindications. Treatment for overdose of non-depolarizing neuromuscular blockers – neostigmine methylsulfate, galantamine, sugammadex.

9. Botulinum neurotoxin type A: mechanisms and features of action.
10. Local anesthetics: history of use, requirements for local anesthetics, classification:
  - esters – procaine, benzocaine, tetracaine;
  - substituted amides – lidocaine, articaine, bupivacaine, mepivacaine, ropivacaine, trimecaine;
  - substituted amides used only in dentistry – articaine, mepivacaine;
  - drug combinations – articaine + epinephrine, bupivacaine + epinephrine.
11. Local anesthetics: mechanism of action and pharmacokinetics.
12. Types of local anesthesia. Drugs of choice for different types of local anesthesia.
13. Resorptive action of local anesthetics on the central nervous system and cardiovascular system. Adverse effects of local anesthetics.
14. Acute cocaine poisoning: pathogenesis, stages, symptoms, treatment.
15. Chronic cocaine poisoning (cocainism): mechanism of addiction, prevention measures against drug addiction.
16. Astringents: mechanisms and features of action, indications for use:
  - metal salts – bismuth chelate, sucralfate, calcium chloride and gluconate, copper sulfate, zinc sulfate.
17. Absorbents: mechanism of action; uses of activated charcoal and talcum powder.
18. Irritating agents: mechanisms of action, indications for use. Vanilloid receptors (TRPV).
19. Features of action and uses of irritating agents:
  - a) drugs of plant origin:
    - levomenthol-based – levomenthol + benzocaine + procaine;
    - racementhol-based – eucalyptus oil + racementhol;
    - mustard plasters;

- chili pepper extract (pepper plasters);
- b) synthetic products – ammonia (hartshorn — aqueous ammonia solution).

## PRESCRIPTIONS

**Atracurium besilate** – solution in 5 ml ampoules containing 10 mg per ml. TD: intravenously, 0.3–0.6 mg/kg body weight.

**Lidocaine** – 2% solution in 5 ml vials (eye drops); solution in 5 ml ampoules containing 10 and 20 mg per ml; a transdermal patch, 700 mg; a spray delivering 4.6 mg per dose; 2% gel in 10 g tubes.

- for terminal anesthesia – instill 1–2 drops per eye; apply 1 patch on the skin once a day for 12 hours; spray 4.6–13.8 mg and apply gel to the oral mucosa;
- for conduction anesthesia – administer 100–200 mg;
- for epidural anesthesia – administer 200–300 mg;
- for infiltration anesthesia – administer 100–200 mg.

**Ropivacaine** – solution in 10 ml ampoules containing 10 mg per ml. For conduction, epidural and infiltration anesthesia, 100–200 mg.

**Calcium chloride** – solution in 5 and 10 ml ampoules containing 100 mg per ml. TD: intravenously, administer 75–150 mg slowly.

**Neostigmine methylsulfate** – tablets, 15 mg; solution in 1 ml ampoules containing 0.5 mg per ml. TD: 15 mg orally 30 minutes before meals; subcutaneously, 0.5 mg 1–2 times a day.

**Atropine** – solution in 1 ml ampoules containing 1 mg per ml; 1% solution in 5 ml vials. TD: subcutaneously, intramuscularly, 0.25–0.5 mg 1–2 times a day; 1–2 drops in each eye 1–2 times a day; in organophosphate poisoning – 1 mg intravenously every 15 min.

## SELF-ASSESSMENT TASKS

**Task 1.** Questions on pharmacotherapy. Write the prescriptions and justify the choice of drugs.

1. Drug for potentiated anesthesia.
2. Drug that facilitates intubation in inhalation anesthesia.

3. Antagonist in case of an overdose of non-depolarizing muscle relaxants.
4. Drug for recurarization.
5. Drug that eliminates the muscarinic-like effect of cholinesterase inhibitors during recurarization.
6. Drug that prevents cardiac arrest during anesthesia.
7. Drug for corneal anesthesia in keratitis.
8. Local anesthetic for ophthalmological operations.
9. Local anesthetic for postherpetic ganglioneuropathy.
10. Local anesthetic for osteochondrosis.
11. Local anesthetic for stomatitis.
12. Local anesthetic for oral burns.
13. Drug for conduction anesthesia.
14. Drug for infiltration anesthesia.
15. Drug for spinal anesthesia.
16. Drug for epidural anesthesia.
17. Drug for the treatment of allergic diseases.
18. Drug to stop bleeding.

**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)? Which synaptotropic drugs can cause orthostatic hypotension? What guidelines should be followed when administering synaptotropic drugs that cause orthostatic hypotension?
3. Under what circumstances is the effect of local anesthetics enhanced and prolonged? In which types of surgeries are adrenomimetics not combined with local anesthetics?
4. Why are substituted amides (local anesthetics) preferred in modern anesthesiology?
5. How do cocaine, procaine, tetracaine, and lidocaine affect the central nervous system (CNS)?
6. Why is bupivacaine contraindicated in patients with cardiovascular disease?

7. What are the features of astringents' action? In what diseases are astringents used?
8. Discuss the mechanisms of desensitizing and hemostatic effects of calcium chloride. Why is this drug contraindicated for subcutaneous and intramuscular administration?

**Task 3.**

- a. Match each drug (A–D) with the appropriate description (1–4).

A. Tubocurarine	1. An agonist at Nm-acetylcholine receptors
B. Succinylcholine	2. The drug which depolarizes autonomic ganglia, resulting first in stimulation and then in paralysis of all ganglia
C. Vecuronium	3. An amino steroid
D. Botulinum toxin	4. The protein produced by the anaerobic bacterium <i>Clostridium botulinum</i>

- b. Match each local anaesthetic (A–D) with the appropriate description (1–4).

A. Lidocaine	1. A local anesthetic with very low solubility. It is used as a dry powder to treat painful skin ulcers or as throat lozenges
B. Cocaine	2. A local anesthetic known to induce euphoria
C. Benzocaine	3. A local anesthetic with particularly long duration of action
D. Bupivacaine	4. A local anesthetic suitable for topical 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: used in the cosmetic industry and neurology.

4. The history of cocaine in medicine and its role in the discovery of the different forms of anesthesia.
5. Other drugs that affect sodium channels: tetrodotoxin and saxitoxin.

## QUESTIONS AND TASKS IN CLASS

**Task 1.** Analyze the tasks that illustrate the mechanisms of action and key characteristics of cholinergic agents (the set of graphic tasks).

**Task 2.** Analyze the following 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 remained insufficient, so another dose of lidocaine was administered. What adverse effect is most likely to occur after this administration?
2. A 55-year-old diabetic man was admitted to the emergency department with a fever of 38.6°C (101.5°F) and abdominal pain. Physical examination revealed a superficial abscess on the right side of the abdomen. A local anesthetic was injected around the abscess when preparing the patient for surgery. Which of the following tissue properties most likely accounts for the slower onset of local anesthetic action in the infected tissues?
  - a. High levels of drug-metabolizing enzymes
  - b. Low vessel density
  - c. Higher extracellular K<sup>+</sup>
  - d. High levels of para-aminobenzoic acid
  - e. Lower extracellular 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 primarily inactivated by spontaneous breakdown. Which drug was most likely administered?
4. A 48-year-old woman underwent heart surgery for artificial valve implantation. Anesthesia was induced with thiopental, and a muscle

relaxant was then administered intravenously to facilitate intubation. Soon after the administration of the drug, the patient exhibited transient muscle fasciculations that progressed to generalized paralysis within one minute. Which muscle relaxant was most likely administered?

5. A 64-year-old woman complained to her physician of involuntary blinking and eye closure. She noticed that eyelid spasms worsened due to fatigue and anxiety. Further examinations led to the diagnosis of benign essential blepharospasm. Treatment with local injections of botulinum toxin was prescribed. What adverse effect was the patient most likely to experience?
6. A 28-year-old man was brought to the psychiatric clinic by the police after attempting to assault a woman in the street. The man showed elevated mood, rapid speech, muscle twitching, and dilated pupils. He repeatedly scratched himself, claiming that bugs were crawling under his skin. His vital signs were blood pressure 170/105 mm Hg, heart rate 120 bpm, respiratory rate 20/min. Shortly afterward, stereotyped behavior and paranoid delusions developed, but the man remained cognizant and alert. Which drug most likely caused the patient's syndrome?

**Task 3.** Answer the test questions (in the ICT classroom).

## **Lesson 13**

### **Final Lesson About Drugs Affecting the Autonomic Nervous System**

*Learning objectives are to assess prescription writing skills; to evaluate and reinforce knowledge of the mechanisms of action, classifications, pharmacokinetics, use, adverse effects of agents, and drug poisoning within the topics which have been studied.*

#### **TOPICS TO PREPARE FOR THE FINAL LESSON**

1. Types of peripheral nerves. Types of neurotransmitters in the peripheral nervous system.
2. Localization, structure, and function of adrenergic synapses. Classification of drugs affecting the function of adrenergic synapses.
3. Adrenoreceptors: types, localization, functions.
4. Adrenomimetics: mechanisms of action, classification.
5. Epinephrine: mechanisms and features of action, use, adverse effects, contraindications.
6.  $\alpha$ -Adrenomimetics: mechanisms of action, use, adverse effects, contraindications.
7.  $\beta$ -Adrenomimetics: classification, mechanisms of action, use, adverse effects, contraindications.
8. Ephedrine: mechanisms of action, use, adverse effects, contraindications.
9.  $\alpha$ -Adrenergic blockers: classification, mechanisms of action, use, adverse effects, contraindications.
10.  $\beta$ -Adrenergic blockers: classification, mechanisms of action and use, antianginal and antiarrhythmic effects.
11.  $\beta$ -Adrenergic blockers: mechanism of action and use, hypotensive action, adverse effects, contraindications.
12. Mechanisms of action and use of cardioselective  $\beta_1$ -blockers,  $\beta$ -blockers with vasodilator action,  $\alpha,\beta$ -blockers.

13. Localization, structure and function of cholinergic synapses. Classification of drugs that affect the function of cholinergic synapses.
14. Cholinergic receptors: types, localization, functions.
15. Cholinomimetics: classification, mechanisms and features of action, use, adverse effects, contraindications.
16. Cholinesterase inhibitors: classification, mechanisms of action.
17. Indications, adverse effects and contraindications of cholinesterase inhibitors.
18. Muscarinic antagonists: classification; mechanisms of action on the eye, use in ophthalmology.
19. Muscarinic antagonists: resorptive effect, use, adverse effects, contraindications.
20. Non-depolarizing muscle relaxants: classification, mechanisms and features of action, synergists and antagonists, indications, adverse effects.
21. Depolarizing muscle relaxants: mechanisms of action, synergists, indications, adverse effects.
22. Local anesthetics: classification, mechanisms of action.
23. Types of local anesthesia: characteristics, medical importance, choice of local anesthetics, resorptive action, adverse effects, and contraindications.
24. Astringents and adsorbents: mechanisms of action, drugs, and their 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, Phenylephrine, Fenoterol, Salmeterol + Fluticasone, Tamsulosin, Metoprolol, Nebivolol, Pilocarpine, Neostigmine Methylsulfate, Ipidacrine, Atropine, Tropicamide, Platyphylline, Tiotropium Bromide, Oxybutynin, Solifenacin, Atracurium Besylate, Lidocaine, Ropivacaine, Calcium Chloride.

## **QUESTIONS ON PHARMACOTHERAPY**

1. Drug for the treatment of anaphylactic shock.
2. Drug for the treatment of vascular collapse.
3. Drug for the treatment of bronchial asthma.
4. Drug for the treatment of benign prostatic hyperplasia.
5. Drug for the treatment of sinus tachycardia.
6. Drug for the treatment of angina pectoris.
7. Drug for the treatment of arterial hypertension.
8. Drug for the treatment of glaucoma.
9. Drug for the treatment of intestinal atony.
10. Drug for the treatment of autoimmune myasthenia gravis.
11. Drug for the treatment of iritis.
12. Drug for the treatment of renal colic.
13. Drug for the treatment of intestinal spasms.
14. Drug for the treatment of urinary incontinence.
15. Drug for the treatment of corneal anesthesia.
16. Drug for the treatment of conduction anesthesia.
17. Drug for the treatment of infiltration anesthesia.
18. Drug to stop bleeding.

## **CONTROL TASK**

Answer the questions regarding the mechanisms of action and key characteristics of drugs that affect the autonomic nervous system (a computer-based test).



- for systemic use (triazoles) – fluconazole, itraconazole, voriconazole, posaconazole;
  - for topical use (imidazoles) – isoconazole, clotrimazole;
  - for both systemic and topical use (triazoles) – ketoconazole;
- c) allylamines:
- for topical use – naftifine;
  - for systemic use and topical use – terbinafine;
- d) drugs of different groups:
- for systemic use – caspofungin, micafungin, flucytosine; griseofulvin.
5. Classification of antifungal agents by their nature and spectrum of action:
- a) classification by the nature of 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:
- broad-spectrum antifungal drugs – amphotericin B, azoles and triazoles, caspofungin;
  - drugs that are effective against candidiasis – nystatin, natamycin;
  - drugs that are effective against dermatomycosis – allylamines, griseofulvin.
6. Selection and methods of application of antifungal agents for superficial and invasive fungal infections.
7. Drugs for the treatment of giardiasis, amebiasis and trichomoniasis – furazolidone, metronidazole, tinidazole, diloxanide.
8. Drugs for the treatment of trypanosomiasis – suramin, pentamidine.
9. Drugs for the treatment of leishmaniasis – miltefosine, sodium stibogluconate.

10. Anthelmintic drugs: classification, spectrum of anthelmintic action, mechanism of action, routes of administration, adverse effects, contraindications:

- broad-spectrum anthelmintic drugs– albendazole, mebendazole, praziquantel, ivermectin;
- drugs for the treatment of nematodes – levamisole, piperazine, niclosamide.

### PRESCRIPTIONS

**Potassium permanganate** – 0.05% solution, 500 ml for gastric lavage in poisoning; 0.1–0.5% solution, 100–250 ml for wound irrigation; 2–5% solution, 5–10 ml for application to ulcers and burns.

**Nitrofurantoin** – 0.02% solution, 500 ml; tablets, 0.02 g for the preparation of aqueous solutions.

**Ethanol** –70%, 90% and 95% concentrations, 50–100 ml.

**Fluconazole** – 150 mg capsules; solution in 50 and 100 ml bottles containing 2 mg per ml. TD: orally, in candidiasis – 150–300 mg once, in dermatomycosis – 150 mg once a week for 4–6 weeks; 400 mg delivered by an intravenous drip on the first day, 200 mg – on the subsequent days.

**Voriconazole** – 200 mg tablets; 200 mg powder in bottles. TD: orally, 200 mg; 3–6 mg/kg by an intravenous drip after dissolving the contents of the bottle sterilely in 200 ml of isotonic sodium chloride solution, every 12 hours.

**Caspofungin** – 50 and 70 mg powder in bottles. TD: 70 mg in 250 ml of isotonic sodium chloride solution by an intravenous drip on the first day, 50 mg in 100 ml on the subsequent days, 1 time a day.

**Metronidazole** – tablets, 250 and 500 mg; vaginal suppositories, 500 mg; solution in 100 ml bottles containing 5 mg per ml. TD: orally, 250 mg 2 times a day after a meal; intravaginally – 500 mg before bedtime; intravenously – 500 mg.

**Mebendazole** – 100 mg tablets. TD: orally, in enterobiosis – 100 mg once, for other nematodes – 200 mg in the morning and in the evening for 3 days.

**Praziquantel** – tablets, 300 mg and 600 mg. TD: orally, in opisthorchiasis – 25 mg/kg 3 times with a 4-hour interval between doses; in cestodiasis – 25 mg/kg once.

### **SELF-ASSESSMENT TASKS**

**Task 1.** Questions on pharmacotherapy. Write the prescriptions, justifying the choice of drugs.

1. Antiseptic used for burn treatment.
2. Drug with a dehydrating effect for burn treatment.
3. Drug with a deodorizing effect for injury treatment.
4. Nitrofurantoin antiseptic for the treatment of pyogenic wounds.
5. Drug used to sterilize the surgical site.
6. Drug for sterilizing surgical instruments.
7. Chemical antagonist for morphine poisoning.
8. Drug for treating gastrointestinal candidiasis.
9. Drug for the treatment of mucosal candidiasis.
10. Drug for the treatment of dermatomycosis.
11. Drug for the treatment of aspergillosis.
12. Drug for the treatment of severe infections caused by anaerobic microorganisms.
13. Drug for the eradication of *Helicobacter pylori* in peptic ulcers.
14. Drug for the treatment of trichomoniasis.
15. Drug for the treatment of enterobiasis.
16. Drug for the treatment of ascariasis.
17. Drug for the treatment of opisthorchiasis.
18. Drug for the treatment of cestodiasis.

**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. At what concentrations does ethanol exhibit maximum bactericidal effects in aqueous and protein environments? What are the indications for using ethanol at different concentrations?
3. Describe the chemical reactions between iodine and proteins, as well as iodine and sodium thiosulfate.

4. Why do polyene antibiotics affect fungi and do not affect bacteria?
5. It is known that voriconazole reduces the activity of the enzyme chitin synthase in fungi and inhibits 14-alpha-demethylase. What assumptions can be made about its mechanism of action, and how does its activity compare to that of other triazoles?
6. Terbinafine, azoles, and amphotericin B damage the cytoplasmic membrane of fungi. What drug exerts a fungicidal effect by inhibiting the fungal cell wall?
7. Metronidazole is a prodrug transformed by ferredoxin oxidoreductase in protozoa into a cytotoxic compound. Levamisole selectively inhibits succinate dehydrogenase and fumarate dehydrogenase in nematodes. As an agonist of GABA receptors, Piperazine disrupts neuromuscular transmission in nematodes. What can be inferred about the mechanisms of selective toxicity of these antiparasitic agents?
8. What microorganisms are susceptible to the action of metronidazole, and what common characteristics do they share?
9. Which anthelmintic drugs cause muscle paralysis in helminths, and which cause muscle spasms?
10. Piperazine was prescribed to enhance the effect of pyrantel in the treatment of ascariasis. However, the treatment was unsuccessful. What is the reason for the treatment failure?

**Task 3.**

- a. Match each antifungal drug (A–D) with the appropriate description (1–4).

A. Amphotericin B	1. This drug has the broadest antifungal spectrum but is used only in severe mycoses because of its toxicity
B. Caspofungin	2. The mechanism of action of this drug involves inhibiting the synthesis of $\beta$ -glucan, an essential component of the fungal cell wall

C. Flucytosine	3. The drug is based on the imidazole nucleus
D. Ketoconazole	4. The drug is transformed into the antimetabolite 5-fluorouracil in fungi

b. Match each anthelmintic drug (A–D) with the appropriate description (1–4).

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

c. Match each antiseptic (A–F) with the appropriate description (1–6).

A. Formaldehyde	1. An agent which induces progressive leakage of intracellular components, 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 potential. It targets the bacterial cytoplasmic or inner membrane or the yeast plasma membrane
E. Hydrogen peroxide	5. It is a strong oxidizing agent that dissolves in water to produce intensely pink or purple solutions
F. Potassium permanganate	6. It can rapidly degrade into the harmless products of water and oxygen. Its action is due to the formation of hydroxyl radicals (OH) that oxidize thiol groups in enzymes and proteins

**Task 4.** Topics for reports.

1. A history of early antiseptics. The first antiseptics used in medical practice.
2. Antiseptics in the treatment of 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 illustrate the mechanisms of action and key characteristics of antiseptics, disinfectants, antifungal, antiparasitic drugs (the set of graphic tasks).

**Task 2.** Analyze the following case tasks.

1. A 55-year-old female has been admitted to the hospital with shortness of breath, fever, and malaise. She has a history of breast cancer, which was diagnosed 3 months ago. The patient has been undergoing chemotherapy. A chest X-ray suggests pneumonia, and respiratory cultures confirm the presence of *Aspergillus fumigatus*. What is the most appropriate treatment?
2. A 48-year-old immigrant from Mexico presents with seizures and other neurological symptoms. Examination of a stool specimen reveals eggs of *T. solium*. A brain MRI shows multiple cysts, some of which are calcified. What drug would be beneficial for this patient?
3. A 40-year-old woman with AIDS was admitted to the hospital with a fever of 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. A chest X-ray showed scattered pulmonary lesions consistent with a granulomatous process. A blood culture identified typical yeasts with chlamydospores. Which of the following options correctly pairs the most likely 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 visited 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 mount of her vaginal discharge showed budding yeast cells and pseudohyphae. A diagnosis was made, and local therapy was prescribed. Which of the following options pairs the most likely 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, he had been diagnosed with a \**Taenia solium*\* infection and had started appropriate treatment. The physician explained to the patient that these symptoms are common adverse effects of the drug and should resolve within one or two days. Which drug most likely caused the patient's symptoms?
6. A 5-year-old boy, while his mother was distracted by a video, opened a cupboard, removed the cap from a container of dishwasher detergent, and swallowed the powder. After some time, the mother heard his cry and rushed to the kitchen to find him vomiting blood. An ambulance took the boy to the hospital. He exhibited excessive salivation, hoarseness, and dysphagia. The child appeared restless and was crying loudly. Examination revealed redness and ulceration of the oral mucosa, along with swelling in the mouth and epigastric tenderness on palpation. Make a diagnosis, explain the pathogenesis and symptoms of poisoning, and prescribe treatment.
7. A 10-year-old girl was admitted to the hospital within two hours after accidentally ingesting an unknown liquid. She was irritable

and had excessive salivation. Her lips and tongue were brown, and she experienced difficulty breathing due to laryngeal swelling. Vital signs were as follows: body temperature of 37.6°C, heart rate of 90 bpm, and blood pressure of 80/50 mm Hg. One hour after hospitalization, she began vomiting blue masses mixed with blood. Make a diagnosis, explain the pathogenesis and symptoms of poisoning, and prescribe treatment.

**Task 3.** Answer the test questions (in the ICT classroom).

## **Lesson 15**

### **Antibiotics and Antitumor Agents**

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

#### **KEY TOPICS FOR PREPARATION**

1. Antibiotics: requirements for antibiotics; history of antibiotics.
2. Classification of antibiotics:
  - by mode of action – bactericidal, bacteriostatic;
  - by 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 proteins;
  - by antimicrobial spectrum – narrow-, broad-, extended-spectrum;
  - by chemical structure –  $\beta$ -lactam antibiotics, glycopeptides, lipopeptides, aminoglycosides, tetracyclines, chloramphenicol, macrolides, lincosamides.
3. Antimicrobial spectrum, mechanism of action, pharmacokinetics, indications for use, routes of administration, adverse effects, contraindications of antibiotics:
  - a) antibiotics that disrupt the synthesis of the cell wall of microorganisms (bactericidal)
    - natural penicillins with narrow spectrum, unstable to  $\beta$ -lactamases – benzylpenicillin (penicillin G), benzylpenicillin sodium salt, benzathine benzylpenicillin, phenoxymethylpenicillin (penicillin V);
    - semi-synthetic penicillins with narrow spectrum, resistant to  $\beta$ -lactamases – oxacillin, nafcillin;
    - semi-synthetic penicillins with extended-spectrum, not resistant to  $\beta$ -lactamases – ampicillin, amoxicillin, piperacillin, ticarcillin;
    - drug combinations of broad-spectrum penicillins (that are

unstable against  $\beta$ -lactamases) with  $\beta$ -lactamase inhibitors (inhibitor-protected penicillins) – ampicillin + oxacillin, ampicillin + sulbactam, amoxicillin + clavulanic acid, amoxicillin + sulbactam, piperacillin + tazobactam;

- cephalosporins

1<sup>st</sup> generation – cefazolin, cephalexin;

2<sup>nd</sup> generation – cefamandole, cefuroxime, cefoxitin, cefaclor;

3<sup>rd</sup> generation – cefoperazone, cefoperazone + sulbactam, cefotaxime, ceftazidime, ceftriaxone, ceftibuten, cefditoren pivoxil;

4<sup>th</sup> generation – cefepime;

5<sup>th</sup> 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)

- polymyxin B;

- gramicidin D;

- lipopeptides – daptomycin;

- glyco-lipopeptides – telavancin;

- antifungal polyenes – amphotericin B, nystatin, natamycin;

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

- rifampicin (bactericidal);

- aminoglycosides (bactericidal)

1<sup>st</sup> generation – neomycin, streptomycin, kanamycin;

2<sup>nd</sup> generation – gentamicin, tobramycin, amikacin;

3<sup>rd</sup> generation – netilmicin;

- tetracyclines (bacteriostatic) – tetracycline, doxycycline;

- tigecycline (bacteriostatic);

- amphenicols – chloramphenicol (bacteriostatic);

- lincosamides (bacteriostatic) – lincomycin, clindamycin;

- macrolides (bacteriostatic / bactericidal) –

14-membered ring agents – erythromycin, clarithromycin,

roxithromycin;

15-membered ring agents – azithromycin;

16-membered ring agents – josamycin, midecamycin, spiramycin.

4. Principles of rational antimicrobial therapy: selection of appropriate antimicrobial agents, routes of administration, doses, regimens and duration of administration, combined use of antibiotics.
5. Mechanisms of resistance of microorganisms to antibiotics, methods for prevention and overcoming resistance.
6. Antitumor agents: classification, antitumor spectrum, mechanisms of action, use:
  - a) cytotoxic agents:
    - alkylating agents – dacarbazine, ifosfamide, carboplatin, carmustine, lomustine, oxaliplatin, temozolomide, cyclophosphamide, cisplatin;
    - antitumor antibiotics – bleomycin, dactinomycin, daunorubicin, doxorubicin, idarubicin, mitoxantrone, mitomycin, epirubicin;
    - antimetabolites – gemcitabine, hydroxycarbamide, decitabine, capecitabine, mercaptopurine, methotrexate, pemetrexed, raltitrexed, fludarabine, fluorouracil, cytarabine;
    - alkaloids and other herbal products and their semi-synthetic analogs – 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 targeting antigens of tumor cells – alemtuzumab, bevacizumab, panitumumab, rituximab, cetuximab;
  - d) enzyme – asparaginase.
7. Adverse effects of antitumour agents. Contraindications.

## PRESCRIPTIONS

**Benzathine Benzylpenicillin** – powder in vials, 1,200,000 IU and 2,400,000 IU. TD: intramuscularly, 1,200,000–2,400,000 IU in 5 ml of 0,5% lidocaine solution, once in 4 weeks.

**Amoxicillin + Acidum clavulanicum (Clavulanic acid)** – film-coated tablets, 625 mg (500 mg Amoxicillin and 125 mg Acidum clavulanicum) and 1,000 mg (875 mg Amoxicillin and 125 mg Acidum clavulanicum); powder in 1.2 g vials (1,000 mg Amoxicillin and 200 mg Acidum clavulanicum). TD: orally, 625–1,000 mg three times a day 1 hour before a meal; by an intravenous drip, 1,200–2,400 mg in 500 ml of isotonic sodium chloride solution 2–3 times a day.

**Ceftriaxone** – powder in 0.5 and 1.0 g vials. TD: intramuscularly, 0.5–1.0 g in 2–3 ml of 1% lidocaine solution; intravenously, 0.5–1.0 g in 5–10 ml of water for injection one time a day.

**Ceftazidime** – powder in 0.5 g and 1.0 g vials. TD: Intramuscularly, 0.5–1.0 g in 2–3 ml of water for injection; intravenously, 0.5–1.0 g in 10–20 ml of 5% glucose solution 2–3 times a day.

**Meropenem** – powder in 0.5 g and 1.0 g vials. TD: by an intravenous drip, 0.5 g and 1.0 g in 250 ml of 5% glucose solution every 8 hours.

**Rifampicin** – capsules, 150 and 300 mg. TD: orally, 450–600 mg once a day 1 hour before a meal.

**Doxycyclinum** – 100 mg capsules. TD: orally, 100 mg twice daily after a meal.

**Azithromycin** – 500 mg tablets. TD: orally, 500 mg once a day one hour before a meal for 3 days.

**Clarithromycin** – 250 and 500 mg tablets; powder in vials, 500 mg. TD: orally, 250–500 mg 2 times a day; by an intravenous drip, 500 mg in 250 ml of 5% glucose solution twice daily.

## SELF-ASSESSMENT TASKS

**Task 1.** Questions on pharmacotherapy. 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 infections.
6. Antibiotic for the treatment of gas gangrene.
7. Antibiotic for the treatment of osteomyelitis.
8. Antibiotic for the treatment of diphtheria.
9. Antibiotic for the 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 the treatment of pyelonephritis.
15. Antibiotic for Lyme disease.
16. Antibiotic for the treatment of rickettsial infections.
17. Antibiotic for the treatment of infections caused by chlamydia.
18. Antibiotic for the prevention of relapse in rheumatism.

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

1. What are the minimum inhibitory concentration (MIC), post-antibiotic effect (PAE), decontamination, and biofilm?
2. Explain the mechanisms of selective toxicity of antibiotics that inhibit bacterial cell wall synthesis. Why are these antibiotics more effective against rapidly dividing bacteria?
3. What is the reason for the high toxicity of antibiotic-detergents (antibacterial cleaning agents)? What is their primary route of administration?
4. Which stages of protein synthesis in microorganisms do antibiotics disrupt? Explain the mechanisms of selective toxicity of antibiotics that inhibit protein synthesis.

5. Why do aminoglycosides, which inhibit the protein synthesis of microorganisms, still have a bactericidal effect?
6. Name the pleiotropic effects of macrolides.
7. Why is it recommended to combine bacteriostatic antibiotics 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 effective against <i>Klebsiella</i> species
B. Streptomycin	2. A third-generation cephalosporin effective against <i>Pseudomonas aeruginosa</i>
C. Azithromycin	3. A glycyclcycline antibiotic effective against vancomycin-resistant <i>Staphylococci</i>
D. Ceftazidime	4. An aminoglycoside antibiotic effective 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 adverse 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. The use of antibiotics during pregnancy and breastfeeding: guidelines for selection.
4. Antitumor vaccination.

## QUESTIONS AND TASKS IN CLASS

**Task 1.** Analyze the tasks that illustrate the mechanisms of action and key characteristics of antibiotics and antitumor agents (the set of graphic tasks).

**Task 2.** Analyze the following case tasks.

1. A 54-year-old man was admitted to the hospital with a fever of 38.1°C (100.6°F), night sweats, arthralgia, and an unintentional weight loss of 6.8 kg (15 lb). His past medical history included rheumatic fever at the age of 9 and a dental surgery 1 month ago. The symptoms began approximately 2 weeks after the dental procedure. Physical examination revealed mitral regurgitation, subungual splinter hemorrhages, and hemorrhagic plaques on the soles of both feet. Three blood cultures were ordered, and an empiric therapy was initiated. Which of the following is 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 was brought to his pediatrician with a fever of 38.5°C (101.3°F) and sharp pain in his left ear. Physical examination revealed that the left tympanic membrane was red, opaque (cloudy), and bulging. Amoxicillin was prescribed; however, the symptoms did not improve after 3 days. The pediatrician decided to modify the therapy and prescribed amoxicillin—potassium clavulanate combination. Explain the advantage of adding potassium clavulanate to amoxicillin.
3. A 53-year-old woman hospitalized for resection of a breast carcinoma, developed a fever of 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 X-ray showed dense infiltrates in the right upper lung field, leading to a diagnosis of nosocomial pneumonia. 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 was started on a treatment that included tetracycline. The physician instructed the patient to avoid milk or dairy products for at least 2 hours before and after taking the medication. Explain the interaction between tetracycline and dairy products and how this can affect drug efficacy.
5. A 7-year-old child presented with pharyngitis and a fever that had lasted for two days. Microbiology revealed small, translucent, beta-hemolytic colonies that are sensitive *in vitro* to bacitracin. The child's medical history includes a severe allergic reaction to amoxicillin when it was previously used for an ear infection. The physician aimed to treat this infection without using a drug that requires parenteral administration. Which of the following agents is most likely to be appropriate in terms of both effectiveness and safety? Explain your choice.
  - a. Azithromycin
  - b. Cefaclor
  - c. Doxycycline
  - d. Penicillin G
  - e. Vancomycin

**Task 3.** Answer the test questions (in the ICT classroom).

## **Lesson 16**

### **Sulfonamides, Quinolones, Antituberculosis, Antiviral, Antimalarial Drugs**

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

#### **KEY TOPICS FOR PREPARATION**

1. Sulfonamide drugs: the history of development, relationship between chemical structure and antimicrobial effect, classification:
  - a) drugs with resorptive action
    - short-acting – sulfadimidine;
    - long-acting – sulfadimethoxine;
  - b) drugs acting in the intestinal lumen – phthalylsulfathiazole, sulphaguanidine;
  - c) locally-acting drugs – sulfadiazine;
  - d) salicylic acid derivatives – sulfasalazine;
  - e) combination drug – co-trimoxazole (sulfamethoxazole + trimethoprim).
2. Sulfonamides: spectrum of antimicrobial action, mechanism of action, pharmacokinetics, use, adverse effects, contraindications.
3. Quinolones: spectrum of antimicrobial action, mechanism of action, pharmacokinetics, use, adverse effects, contraindications:
  - a) non-fluorinated quinolones (NFQs) – nalidixic acid;
  - b) fluoroquinolones:
    - first-generation – ofloxacin, norfloxacin, pefloxacin, ciprofloxacin,
    - second-generation – levofloxacin, lomefloxacin, sparfloxacin;
    - third-generation – gemifloxacin, moxifloxacin.
4. Spectrum of antimicrobial action, mechanism of action, pharmacokinetics, use, adverse effects, contraindications of linezolid and tedizolid.
5. 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.
6. Antituberculosis drugs: mechanism of action, pharmacokinetics, adverse effects, contraindications.
  7. Mechanisms of drug resistance in *Mycobacterium tuberculosis*, methods of its prevention and strategies for overcoming resistance.
  8. 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.
  9. Antiviral agents: requirements for antiviral agents; classification, spectrum of antiviral action, mechanism of action, pharmacokinetics, use, adverse effects, contraindications.
    - 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<sub>2</sub> – 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;
      - agents that inhibit HIV fusion with host cells – enfuvirtide;
      - integrase inhibitors – raltegravir
    - e) antiviral drugs for the treatment of hepatitis B

- nucleoside analogs:  
thymidine nucleoside analog – telbivudine;  
guanosine nucleoside analog – entecavir;  
cytidine nucleoside analog – lamivudine;
- analogs 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 interferons – interferon alpha, interferon alfa-2a, interferon alfa-2b;
- pegylated recombinant interferons – peginterferon alfa-2a (Pegasys), peginterferon alfa-2b (Intron A).

10. Antimalarial drugs: classification, mechanism of action, adverse effects, contraindications:

- hematoschizontropic drugs (drugs suppressing erythrocytic forms) – quinine, chloroquine, mefloquine, pyrimethamine;
- histoschizontropic agents:  
suppressing pre-erythrocytic forms of plasmodium – pyrimethamine;  
suppressing para-erythrocytic forms of plasmodium – primaquine;
- gamontotropes – transmission-blocking agents:  
gamontostatic (sporontocidal) drugs – pyrimethamine;  
gamontocidal (gametocytocidal) drugs – chloroquine, primaquine.

11. Drugs for individual and community-based chemoprophylaxis, treatment of malaria.

## PRESCRIPTIONS

**Ciprofloxacin** – film-coated tablets, 250 and 500 mg; 0.3% solution in 5 ml vials (eye drops); solution in 100 ml bottles containing 2 mg per ml. TD: orally, 250–500 mg 2 times a day; 1–2 drops in each eye 2 times a day; 200–400 mg by an intravenous drip.

**Levofloxacin** – tablets, 250 and 500 mg; solution in 100 ml bottles containing 5 mg per ml. TD: orally, 250–500 mg once a day; by an intravenous drip, 500 mg 1–2 times a day.

**Nifuratel** – film-coated tablets, 200 mg. TD: orally 200 mg 3 times a day.

**Isoniazid** – tablets, 200 and 300 mg; 10% solution in 5 ml ampoules. TD: orally, 200–300 mg 3 times a day after meals; intramuscularly or intravenously, 5–10 mg/kg once a day.

**Aciclovir** – 200 mg tablets; powder in 250 mg vials; 3% eye ointment and 5% cream in 2.0 g tubes. TD: orally, 200 mg 4 times a day; intravenously, 250–500 mg in 10 ml of isotonic sodium chloride solution.

**Ganciclovir** – powder in 500 mg vials. TD: intravenously, 5 mg/kg in 500 ml of isotonic sodium chloride solution 2 times a day.

**Oseltamivir** – 75 mg capsules. TD: orally, for the treatment of influenza – 75 mg every 12 hours; for the prevention of influenza – 75 mg once a day for 4–6 weeks.

**Rifampicin** – capsules, 150 and 300 mg. TD: orally, 450–600 mg once a day 1 hour before a meal.

## SELF-ASSESSMENT TASKS

**Task 1.** Questions on pharmacotherapy. 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 the treatment of 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 have no effect on dormant forms of microorganisms as well as on those that synthesize para-aminobenzoic acid? Is it rational to combine sulfonamide drugs with local anesthetics? How should sulfonamides be prescribed for the treatment of purulent wounds?
2. Why do sulfonamide drugs not interfere with folic acid metabolism in humans?
3. What additional properties does sulfamethoxazole gain when combined with trimethoprim? What about the azo compounds of sulfanilamide with salicylic acid? In which diseases are such drug combinations used?
4. Why are sulfonamide drugs used less frequently for bacterial infections?
5. Modern fluoroquinolones have low toxicity, but some believe that second and third-generation fluoroquinolones should be reserved for specific cases. What are the potential dangers of widely using fluoroquinolones in clinical practice?
6. How does isoniazid affect pyridoxine metabolism in *Mycobacterium tuberculosis* and in humans?
7. Why does isoniazid dosage depend on the genetic profile of the patient?
8. Why do aciclovir and other nucleoside analogs affect only cells infected by herpes virus, without impacting healthy human cells?

### Task 3.

a. Match antiviral drug (A–E) with the appropriate description (1–5).

A. Enfuvirtide	1. Integrase inhibitor
B. Efavirenz	2. HIV fusion inhibitor
C. Abacavir	3. Non-nucleoside reverse transcriptase inhibitor
D. Aciclovir	4. Nucleoside reverse transcriptase inhibitor
E. Raltegravir	5. DNA polymerase inhibitors

b. Match antibacterial drug (A–D) with the appropriate clinical use (1–4).

A. Sulfasalazine	1. Toxoplasmosis
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 caused by H1N1 (swine flu) and H5N1 (avian flu) viruses.
3. Antiretroviral therapy (ART): mechanism of action.
4. HIV vaccine: Truvada for PrEP (pre-exposure prophylaxis).

## QUESTIONS AND TASKS IN CLASS

**Task 1.** Analyze the tasks that illustrate the mechanisms of action and key characteristics of sulfonamides, quinolones, antituberculosis, antiviral, antimalarial drugs (the set of graphic tasks).

**Task 2.** Analyze the following case tasks.

1. A 75-year-old man with chronic obstructive pulmonary disease is diagnosed with influenza based on his complaints of flu-like symptoms that began 24 hours ago. Which drug should be administered for treatment?
2. A 43-year-old woman with AIDS started a highly active antiretroviral therapy (HAART) with zidovudine, lamivudine, and

raltegravir. What is the primary rationale for triple-drug therapy in AIDS patients?

- a. To destroy both the replicating and nonreplicating viral genome
  - b. To increase the half-life of any of the agents
  - c. To delay the development of drug resistance
  - d. To inhibit drug metabolism
  - e. To increase the antimicrobial efficacy against opportunistic infections
3. A 44-year-old woman complained of blurred vision and difficulty distinguishing green objects from red ones. The woman was recently diagnosed with cavitary pulmonary tuberculosis. She had been on a three-drug regimen for 2 months. An eye examination revealed visual field constriction. Which drug is most likely responsible for 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 (the reference value is 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. Her medical history included glucose-6-phosphate dehydrogenase deficiency and a recurrent urinary tract infection. Five days earlier, the patient had complained of burning sensation upon urination and had started the prescribed antimicrobial therapy. Urinalysis revealed bilirubin and urobilinogen. Which drug could have caused the patient's signs and symptoms?
6. A 34-year-old man residing in the United States was planning to visit his seriously ill father who lived 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 single drug 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 ICT classroom).

## **Lesson 17**

### **Final Class on Antimicrobial, Antiviral and Antiparasitic Agents**

*Learning objectives are to assess prescription writing skills; to review and reinforce knowledge about the mechanisms of action, classification, pharmacokinetics, uses, adverse effects of agents, and drug poisoning related to the topics studied.*

#### **TOPICS TO PREPARE 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, uses.
3. Nitrofurantoin antiseptics: mechanisms of action, uses, and adverse effects.
4. Acute poisoning with alkalis, strong acids and iodine: pathogenesis, symptoms, and treatment.
5. Antibiotics: requirements for antibiotics; classification based on the nature of action and antimicrobial spectrum.
6. Classification of antibiotics based on the mechanism of action. Mechanisms of selective toxicity.
7. The origin, classification, mechanisms of action, antimicrobial spectrum, use, adverse effects, and contraindications of:
  - penicillins;
  - cephalosporins and carbapenems;
  - aminoglycosides and rifampicin;
  - tetracyclines, chloramphenicol, lincosamides;
  - macrolides.
8. Antibiotic resistance mechanisms in bacteria, strategies for prevention and overcoming resistance.
9. Principles of rational antibiotic therapy.
10. Sulfanilamide drugs: mechanism of action, antimicrobial spectrum, principles of administration, classification.

11. Selection of sulfonamides for infectious diseases, adverse effects, and contraindications.
12. Quinolones: antimicrobial spectrum, mechanisms of action, classification, uses, adverse effects, and contraindications.
13. Antituberculosis drugs: classification, mechanisms of action, uses, and adverse effects.
14. Antifungal agents: classification, antifungal spectrum, mechanisms of action, uses, and adverse effects.
15. Antiviral drugs for the treatment of herpes virus: antiviral spectrum, mechanisms of action, uses, adverse effects, and contraindications.
16. Antiviral drugs for influenza prevention and treatment: mechanisms of action, uses, adverse effects, and contraindications.
17. Interferon drugs and its inducers: origin, mechanisms of action, uses, adverse effects, and contraindications.
18. Antimalarial drugs: classification, mechanisms of action, uses, adverse effects, and contraindications.
19. Anthelmintic drugs: classification, spectrum of anthelmintic action, mechanisms of action, uses, adverse effects, and contraindications.

### **PRESCRIPTIONS**

Prescribe: Potassium Permanganate, Ethanol, Nitrofurazone, Fluconazole, Voriconazole, Caspofungin, Metronidazole, Mebendazole, Praziquantel, Benzathine Benzylpenicillin, Amoxicillin + [Clavulanic Acid], Ceftriaxone, Ceftazidime, Meropenem, Rifampicin, Doxycycline, Azithromycin, Clarithromycin, Ciprofloxacin, Levofloxacin, Nifuratel, Isoniazid, Acyclovir, Ganciclovir, Oseltamivir.

### **QUESTIONS ON PHARMACOTHERAPY**

1. Drug used to disinfect an operating field.
2. Drug for the treatment of pyogenic infection.

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. Drug for the eradication of *Helicobacter pylori* in peptic ulcers.
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 the treatment of trichomoniasis.
16. Drug for the treatment of cestodiasis.
17. Drug for the treatment of nematodes.
18. Drug for the treatment of opisthorchiasis.

### **FINAL ASSESSMENT**

Answer the questions regarding the mechanisms of action and characteristics of antimicrobial, antiviral, and antiparasitic agents (computer-based test).

## **Lesson 18**

### **General Anesthetics, Sleeping Pills, Ethanol**

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

#### **KEY TOPICS FOR PREPARATION**

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. Volatile (gas-forming) agents for inhalation anesthesia: physical properties, anesthetic characteristics, pharmacokinetics – halothane, isoflurane, sevoflurane.
5. Anesthetic gases: anesthetic characteristics, pharmacokinetics – dinitrogen oxide, xenon.
6. Effects of inhalation anesthetics on the respiratory system, cardiovascular system, kidneys, liver and metabolism.
7. Advantages and disadvantages of inhalation anesthetics.
8. Intravenous anesthetics: mechanism of action, pharmacokinetics, use, adverse effects, contraindications: short-acting – propofol;
  - intermediate-acting – 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, gastrointestinal 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 drugs) – zopiclone, zolpidem, zaleplon;
  - antagonists of central H<sub>1</sub>-receptors – doxylamine;
  - synthetic analogs of the pineal hormone – melatonin, ramelteon, tasimelteon.
14. Mechanisms of action, pharmacokinetics, adverse effects and contraindications of sleeping pills.
15. Principles of selecting 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 dependence.

### **PRESCRIPTIONS**

**Propofol** – emulsion in 20 ml ampoules containing 10 mg per ml. TD: intravenously, 1.5–2.5 mg/kg.

**Nitrazepam** – tablets, 5 mg. TD: orally, 5–10 mg 30 minutes before bedtime.

**Zolpidem** – tablets, 10 mg. TD: orally, 5–10 mg before bedtime.

**Doxylamine** – tablets, 15 mg. TD: orally, 15 mg 30 minutes before bedtime.

**Flumazenil** – solution in 5 ml ampoules containing 0.5 mg per 5 ml. TD: intravenously, 0.5 mg; if necessary, injections are repeated up to a DD of 2 mg.

**Atropine** – solution in 1 ml ampoules containing 1 mg per ml; TD: subcutaneously, intramuscularly, 0.25–0.5 mg 1–2 times a day.

**Ethanol** – 70%, 90% and 95% solutions, 50–100 ml.

**Neostigmine methylsulfate** – tablets, 15 mg; solution in 1 ml ampoules containing 0.5 mg per ml. TD: orally, 15 mg 30 minutes before meals; subcutaneously, 0.5 mg 1–2 times a day.

**Phenylephrine** – solution in 1 ml ampoules containing 10 mg per ml. TD: intravenously, 1–5 mg in 20 ml of 5% glucose solution slowly; subcutaneously, intramuscularly, 3–5 mg.

**Metoprolol** – tablets, 50 and 100 mg; solution in 5 ml ampoules containing 1 mg per ml. TD: orally, 50–100 mg 2 times a day (in the morning and evening); intravenously, 5 mg in 10–20 ml of 5% glucose solution slowly.

### **SELF-ASSESSMENT TASKS**

**Task 1.** Questions on pharmacotherapy. Write the prescriptions, justifying the choice of drugs.

1. Drug for the induction of anesthesia.
2. Drug for potentiated anesthesia.
3. Drug for the prevention of acute pain associated with diagnostic procedures.
4. Drug that prevents cardiac arrest during anesthesia.
5. Drug that reduces salivation and bronchorrhea during anesthesia.
6. Drug for postoperative intestinal atony.
7. Drug for sterilization of an operating field.
8. Drug for disinfection of surgical instruments.
9. Drug to prevent burn blisters.
10. Drug for the treatment of sleep-onset insomnia.
11. Drug for the treatment of late insomnia.
12. Drug for the treatment of insomnia preserving the physiological structure of sleep.
13. Drug with the anxiolytic effect for the treatment of insomnia.
14. Long-acting drug for the treatment of insomnia.
15. Short-acting drug for the treatment of insomnia.
16. Fast-acting drug for the treatment of insomnia.
17. Antidote for poisoning with hypnotic drugs.
18. Competitive antagonist for poisoning with benzodiazepine receptor agonists.

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

1. Which receptors are affected by halothane and what are the clinical consequences of their activation?
2. It is known that nitrous oxide does not inhibit the respiratory and vasomotor centers. Can it be considered an absolutely safe drug?
3. What is dissociative anesthesia and which anesthetic induces it?
4. Which anesthetic agents have neuroprotective effects, and what mechanisms underlie these effects?
5. Describe the structure and function of glutamic acid receptors. What is the anti-excitotoxic effect?
6. Describe the structure and function of GABA receptors. Which anesthetic and hypnotic drugs affect GABA<sub>A</sub> receptors?
7. Formulate the requirements for an ideal hypnotic drug.

**Task 3.**

a. Match each drug (A–E) with the appropriate description (1–5).

A. Sevoflurane	1. A halogenated anesthetic with fast onset and recovery time
B. Nitrous oxide	2. A drug that can trigger an acute porphyria attack in susceptible patients
C. Thiopental	3. A drug associated with the risk of "coronary steal syndrome"
D. Isoflurane	4. An inhalation anesthetic that substantially reduces the required concentration of co-administered inhalation anesthetics
E. Ketamine	5. A drug that can induce a cataleptic state known as dissociative anesthesia

b. Match each drug (A–E) with the appropriate description (1–5).

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

**Task 4.** Topics for report.

1. History of general anesthesia.
2. W. Morton and surgical anesthesia.
3. Minimum alveolar concentration of volatile anesthetics.
4. Structure and localization of benzodiazepine receptors.
5. New clinical guidelines for the pharmacologic treatment of chronic insomnia in adults.

## QUESTIONS AND TASKS IN CLASS

**Task 1.** Analyze the set of graphic tasks that illustrate the mechanisms of action and key characteristics of general anesthetics and sleeping pills.

**Task 2.** Analyze the following 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 stimulation of the vomiting center during surgical manipulation of the extraocular muscles. Which anesthetic would be most appropriate for this patient?
2. A 52-year-old woman underwent a hysterectomy to remove endometrial carcinoma. Anesthesia was induced with thiopental and maintained with a combination of nitrous oxide and halothane. Why was halothane added to nitrous oxide?

3. A 60-year-old man was set to undergo surgery to remove prostate cancer. He had been suffering from ischemic heart disease for two years. The anesthesiologist decided to use nitrous oxide along with another general anesthetic that significantly increases coronary blood flow while simultaneously reducing myocardial oxygen consumption and having a negligible effect on cardiac output. Which anesthetic was most likely administered with nitrous oxide for maintenance?
4. A 57-year-old man complained to his physician about difficulty falling asleep. As a schoolteacher, he 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 in central nervous system neurons did the prescribed drug most likely induce?
  - a. Decreased  $\text{Na}^+$  conductance
  - b. Increased  $\text{Cl}^-$  conductance
  - c. Decreased  $\text{K}^+$  conductance
  - d. Decreased  $\text{Ca}^{2+}$  conductance
  - e. Increased  $\text{K}^+$  conductance
5. A 30-year-old woman was admitted to the hospital. The physical examination revealed slurred speech, ataxia, altered mental status, uncoordinated muscle movements, pale skin, cyanotic lips, and constricted pupils. Vital signs indicated a body temperature of  $37.6^\circ\text{C}$ , difficulty breathing, a pulse of 90 bpm, and blood pressure of 80/50 mm Hg. Further investigation revealed that one-month prior, the patient had been prescribed diazepam to treat insomnia. Make a diagnosis, explain the pathogenesis and symptoms of poisoning, and prescribe treatment.
6. A 53-year-old woman suffered a generalized seizure and was taken to the emergency department. Upon admission, she was extremely anxious and agitated. She reported no past medical history of epilepsy. Further questioning revealed a long history of drug abuse, but the day before, she decided to quit and abruptly stopped taking the abused drug. Withdrawal from which drug most likely caused the patient's seizure?

7. A 48-year-old woman became agitated and visibly tremulous, exhibiting hallucinatory behavior one 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 most likely explains the cause of the patient's behavior?
- a. Benzodiazepine medication administered before the surgery
  - b. A depressive episode triggered by the surgery
  - c. Ethanol withdrawal
  - d. Opioid medication administered before the surgery
  - e. Halothane anesthesia used during the surgery

**Task 3.** Answer the test questions (in the ICT classroom).

## **Lesson 19**

### **Antiepileptic Drugs. Opioid Analgesics**

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

#### **KEY TOPICS FOR PREPARATION**

1. Antiepileptic drugs: mechanism of action, classification:
  - drugs effective for partial and tonic-clonic seizures – phenytoin, phenobarbital, benzobarbital, carbamazepine, oxcarbazepine, topiramate, perampanel;
  - drugs effective for partial seizures – eslicarbazepine, gabapentin, pregabalin, lacosamide, zonisamide, brivaracetam;
  - drugs effective for absence seizures – ethosuximide;
  - drugs with broad-spectrum antiepileptic action — valproic acid, clonazepam, lamotrigine, levetiracetam.
2. Mechanisms of action, pharmacokinetics, drugs for different forms of generalized and partial epilepsy, neuropathic pain, adverse effects, contraindications of antiepileptic drugs.
3. Principles of epilepsy treatment.
4. Drugs for the treatment of symptomatic seizures: mechanisms of action and use – sodium oxybutyrate, magnesium sulfate, droperidol, diazepam.
5. Mechanism of nociceptive sensitivity. The antinociceptive system (opioid, cannabinoid, serotonin, GABA).
6. Opioid receptors ( $\mu$ ,  $\kappa$ ,  $\delta$ ): ligands, localization, functional significance.
7. Opium: origin and composition.
8. Opioid analgesics: neurophysiological and psychophysiological mechanism of analgesic action.
9. Classification of opioid analgesics based on the effect on opioid receptors and chemical structure:

a) full agonists:

- phenanthrene derivatives– morphine, codeine, oxycodone;
- piperidine derivatives – fentanyl;
- cyclohexanol derivatives – tramadol;
- other structurally distinct analgesics – tapentadol;
- mixed action agonists: phenanthrene derivatives – buprenorphine, butorphanol.

10. Effects of opioid analgesics on mental functions, sleep, autonomic and endocrine functions of the hypothalamus, midbrain, medulla oblongata, spinal cord reflexes, cardiovascular system and smooth muscle organs.

11. Pharmacokinetics of opioid analgesics.

12. The use of opioid analgesics: analgesics for different pain syndromes, neuroleptanalgesia, ataralgesia. Adverse effects and contraindications.

13. Acute morphine poisoning: pathogenesis, symptoms, antagonists. Mechanism of action and use of naloxone and naltrexone.

14. Chronic poisoning with opioid analgesics: mechanisms of dependence, preventive measures.

15. Non-opioid analgesics – paracetamol, metamizole sodium, ketorolac, dexmedetomidine, nefopam.

## PRESCRIPTIONS

**Benzobarbitalum** – 100 mg tablets. TD: orally, 100 mg 3 times a day after a meal.

**Carbamazepine** – 200 mg tablets. TD: orally, 200–400 mg 2–3 times a day with meals.

**Pregabalin** – capsules, 75, 150 and 300 mg. TD: orally, 75–300 mg once a day.

**Acidum valproicum** – tablets, 300 and 500 mg; solution in 50 ml bottles containing 300 mg per ml (drops for oral administration); solution in 5 ml ampoules containing 100 mg per ml. TD: orally, 600–1000 mg 1 time a day with meals (tablets); 5–10 mg/kg 2 times a day

(drops for oral administration for children); an intravenous bolus of 15 mg/kg.

**Ethosuximide** – capsules, 250 mg. TD: 15 mg/kg twice daily.

**Morphinum** – tablets, 10 mg; solution in 10 ml bottles containing 20 mg per ml (drops for oral administration); solution in 1 ml ampoules containing 10 mg per ml. TD: orally, subcutaneously, intramuscularly, 10 mg.

**Oxycodone + Naloxone** – tablets containing 10 mg oxycodone and 5 mg naloxone. TD: orally, 1 tablet every 12 hours.

**Fentanylum** – solution in 1 ml ampoules containing 50 mcg per ml; nasal spray in 5 ml bottles containing 50, 100 and 200 mcg per dose; TTS patches with fentanyl release rates of 25 and 100 mcg/h. TD: intramuscularly, 25–100 mcg; intravenously, 25–100 mcg in 10 ml of isotonic sodium chloride solution; 50–200 mcg in each nostril; apply 1 patch on the skin once every 3 days.

**Tramadolum** – capsules and tablets, 50 and 100 mg; solution in 1 and 2 ml ampoules containing 50 mg per ml. TD: orally, intramuscularly, subcutaneously, 50–100 mg; intravenously, 50–100 mg in 10 ml of isotonic sodium chloride solution.

**Buprenorphine** – solution in 1 ml ampoules containing 0.3 mg per ml. TD: intramuscularly, 0.3–0.6 mg; intravenously, 0.3–0.6 mg in 10 ml of isotonic sodium chloride solution, every 8 hours.

#### **Morphine antagonists:**

**Naloxone** — solution in 1 ml ampoules containing 0.4 mg per ml. TD: intramuscularly, 0.4–0.8 mg; intravenously, 0.4–0.8 mg in 10 ml of isotonic sodium chloride solution.

- **Atropinum** – solution in 1 ml ampoules containing 1 mg per ml. TD: subcutaneously, 0.5 mg.
- **Kalii permanganas (potassium permanganate)** — 0.05% solution, 500 ml for gastric lavage.

**Paracetamololum** – 500 mg tablets; rectal suppositories, 250 mg; solution in 100 ml bottles containing 10 mg per ml. TD: orally, 500

mg 2–3 times a day, 1–2 hours after meals; rectally, 250 mg 2–3 times a day; intravenously, 1000 mg slowly.

**Acetylcysteine** – solution in 3 ml ampoules, containing 100 mg per ml. TD: in case of paracetamol poisoning, administer intravenously as 150 mg/kg body weight in 100 ml of 5% glucose solution.

### **SELF-ASSESSMENT TASKS**

**Task 1.** Questions on pharmacotherapy. 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 to terminate status epilepticus.
6. Drug for diabetic neuropathy.
7. Drug for trigeminal neuralgia.
8. Drug for fever.
9. Drug for the prevention of pain-induced shock in trauma.
10. Analgesic for myocardial infarction.
11. Analgesic for postoperative pain relief.
12. Analgesic for cancer pain relief.
13. Analgesic for renal colic.
14. Drug for paracetamol poisoning.
15. Competitive antagonist for morphine poisoning.
16. Physiological non-competitive antagonist for morphine poisoning.
17. Chemical antagonist for morphine poisoning.
18. Drug for the treatment of headache.

**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 neuronal sodium and calcium channels, metabolism and functions of brain mediators? Compare the mechanisms of action of the antiepileptic drugs with their clinical use.

3. Which antiepileptic drugs have psychotropic effects? What is the significance of these psychotropic effects in epilepsy management?
4. What is aggravation of epileptic seizures? Which antiepileptic drugs can cause it?
5. What drugs are used to treat neuropathic pain?
6. Discuss the potential mechanisms underlying centralized pain and emerging therapeutic interventions.
7. Can opioid analgesics be prescribed for severe chronic pain? Which drugs are used for chronic pain management?
8. Why is gastric lavage necessary in case of poisoning with morphine which was administered intravenously?
9. What are euphoria and dysphoria?
10. What are the mechanisms of opioid addiction?
11. What are the mechanisms of analgesic and antipyretic action of paracetamol?
12. What are the adverse effects and contraindications of paracetamol? What metabolites are formed during the biotransformation of paracetamol? Why is it important not to exceed the dose recommended by the doctor?

**Task 3.**

- a. Match each drug (A–E) with the appropriate description (1–5).

A. Carbamazepine	1. This drug is effective in all forms of epilepsy across all age groups
B. Lamotrigine	2. This drug selectively binds to the synaptic vesicle protein (SV2A protein), altering the synaptic release of glutamate and gamma-aminobutyric acid (GABA)
C. Levetiracetam	3. This drug is a highly lipid-soluble analog of gamma-aminobutyric acid (GABA) and inhibits the release of excitatory neurotransmitters

D. Gabapentin	4. This drug inhibits glutamate release
E. Valproic acid	5. This drug affects membrane excitability by acting on voltage-gated sodium channels

b. Match each drug (A–E) with the appropriate description (1–5).

A. Buprenorphine	1. A partial agonist at $\mu$ (mu) opioid receptors and an antagonist at $\kappa$ (kappa) opioid receptors.
B. Codeine	2. A full opioid agonist with the highest oral bioavailability. It is used in the treatment of heroin addiction.
C. Naltrexone	3. A narcotic antagonist that is effective when taken orally. It is long-acting and it has been proposed for the treatment of heroin addiction and alcohol dependence.
D. Methadone	4. A weak agonist of opioid receptors. It is used to treat cough.
E. Naloxone	5. A drug with high affinity but no intrinsic activity at opioid receptors. It is short-acting.

**Task 4.** Topics for report.

1. New antiepileptic drugs: neuropharmacology and clinical indications.
2. New approaches in the treatment of neuropathic pain.
3. A TRPV1 agonist: capsaicin.
4. Features of paracetamol biotransformation in children and adults.

**QUESTIONS AND TASKS IN CLASS**

**Task 1.** Analyze the tasks that illustrate the mechanisms of action and characteristics of opioids and antiepileptic drugs (the set of graphic tasks).

**Task 2.** Analyze the following case tasks.

1. A 64-year-old man suffering from advanced heart failure was admitted to the emergency department because of severe dyspnea over the past hour. After physical examination, a diagnosis of impending pulmonary edema was made. The patient was prescribed an appropriate therapy that included an intramuscular injection of morphine. Describe the actions of morphine that most likely contributed to its therapeutic effect in the patient's condition.
2. A 39-year-old woman was admitted to the hospital because of gripping and burning abdominal pain that had been worsening over the past 4 hours. The patient was suffering from stage 4 ovarian cancer with metastases to the pelvis. A treatment with sustained release morphine was started. Which of the following effects on the patient's respiratory system could be observed within the first few days of the therapy?
  - a. Stimulation of the cough reflex
  - b. Bronchodilation
  - c. Increased vital capacity
  - d. Decreased tidal volume
  - e. Increased respiratory rate
3. A 28-year-old woman was admitted unconscious to the emergency department. Her friend reported that the woman had taken an analgesic prescribed following multiple fractures that she had sustained in a car accident. She had injected the drug approximately 45 minutes prior to admission. Vital signs: blood pressure 90/50 mm Hg, heart rate 40 bpm, respiratory rate 5/min. Physical examination revealed cyanosis and pinpoint pupils. What drug did the woman most likely take? Explain the symptoms of the overdose.
4. A 32-year-old woman reported experiencing two breakthrough seizures last week. One month earlier, the woman had been diagnosed with simple partial seizures and had started treatment with an antiepileptic drug. The physician increased the dosage, suspecting that the reduced effectiveness was most likely due to the drug's being a potent enzyme inducer and having an ability to

induce its own metabolism. What drug was the patient most likely taking?

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 receiving a treatment for 6 months. Physical examination revealed mild hirsutism, wider lips and nose, and thicker, bleeding gums. What drug most likely caused these adverse effects?
6. A 14-month-old boy had been exhibiting jerking movements of the upper limbs for a few weeks. The jerking movements never caused him to fall but occurred several dozens of times a day, including when falling asleep. An electroencephalogram showed that the jerking movements always coincided with spike-and-wave discharges, and that their frequency increased during sleep onset. What most likely caused the patient's symptoms? Which drug would be the most appropriate treatment for this patient?

**Task 3.** Answer the test questions (in the ICT classroom).

## **Lesson 20**

### **Drugs for Neurodegenerative Diseases. Drugs for Migraine Treatment. Drugs for Spasticity Treatment**

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

#### **KEY TOPICS FOR PREPARATION**

1. The importance of dopamine, acetylcholine and glutamic acid in the regulation of muscle tone and cognitive processes. Metabolic dysfunction in Parkinson's disease and Alzheimer's disease.
2. Antiparkinsonian drugs: mechanisms of action, classification (dopaminomimetics, M-cholinoblockers, antagonists of NMDA-receptors).
3. Dopaminomimetics: mechanisms of action, pharmacokinetics, use, adverse effects, contraindications in Parkinson's disease:
  - a) levodopa, combination of levodopa with carbidopa and benserazide;
  - b) MAO-B inhibitors – selegiline, rasagiline;
  - c) Catechol-O-methyltransferase (COMT) inhibitors – entacapone;
  - d) D-receptor agonists:
    - ergoline agonists – bromocriptine;
    - non-ergoline agonists – pramipexole, ropinirole, rotigotine.
4. M-cholinoblockers: mechanisms of action, pharmacokinetics, use, adverse effects, contraindications in Parkinson's disease – trihexyphenidyl, biperiden.
5. NMDA-receptor antagonists: mechanisms of action, pharmacokinetics, use, adverse effects, contraindications 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: mechanisms of action, adverse effects and contraindications:
  - precursors of acetylcholine – choline alfoscerate;
  - cholinesterase inhibitors – rivastigmine, donepezil, galantamine, ipidacrine;
  - NMDA-receptor antagonist and AMPA-receptor agonist– memantine;
  - anti-amyloid treatment– aducanumab.
8. 5-HT-receptors: localization, functions.
9. Drugs for migraine attacks: mechanisms of action, pharmacokinetics, adverse effects and contraindications:
  - ergot alkaloids – ergotamine;
  - triptans – sumatriptan, naratriptan, eletriptan, zolmitriptan;
  - paracetamol (acetaminophen) and NSAIDs – acetylsalicylic acid, ibuprofen, naproxen;
  - antiemetics – metoclopramide.
10. Pharmacotherapy for migraine in the interictal phase (the interval between two migraine attacks) – propranolol, metoprolol, topiramate, cinnarizine, erenumab.
11. Drugs for the symptomatic treatment of spasticity and dystonia: mechanisms of action, pharmacokinetics, use, adverse effects and contraindications:
  - centrally acting muscle relaxants – anxiolytics (diazepam), tolperisone, baclofen, tizanidine, dantrolene;
  - Peripherally acting muscle relaxants – botulinum neurotoxin type A.
12. Neuroprotective agents: mechanisms of action, pharmacokinetics, use, adverse effects and contraindications – citicoline, acetylcarnitine, cerebrolysin.

## PRESCRIPTIONS

**Levodopum + Carbidopum** – tablets containing 250 mg of Levodopa and 25 mg of Carbidopa. TD: orally, 1–2 tablets 2–3 times a day.

**Pramipexole** – tablets, 0.25 and 1 mg. TD: orally, 0.25–1 mg 3 times a day.

**Trihexyphenidyl** – tablets, 2 mg. TD: orally, 1–4 mg 3–4 times a day.

**Rivastigmine** — capsules, 1.5 and 6 mg; solution in 50 and 120 ml bottles containing 2 mg per ml (drops for oral administration); TTS patches, 9.5 mg. TD: orally, 0.0015–0.006 2 times a day with meals, apply 1 patch once a day.

**Sumatriptan** — tablets, 50 and 100 mg. TD: orally, 50–100 mg once.

**Choline alfoscerate** – 400 mg capsules; solution for injection in 4 ml ampoules containing 250 mg per ml. TD: orally, 400 mg 2 times a day, intravenously, 1000 mg in 50 ml of isotonic sodium chloride solution once a day.

**Metoprolol** – tablets, 50 and 100 mg; solution in 5 ml ampoules containing 1 mg per ml. TD: orally, 50–100 mg 1 or 2 times a day; intravenously, 2–5 mg in 10 – 20 ml of 5% glucose solution slowly.

**Paracetamol** – 500 mg tablets; rectal suppositories, 250 mg; solution in 100 ml bottles containing 10 mg per ml. TD: orally, 500 mg 2–3 times a day 1–2 hours after meals; rectally, 250 mg 2–3 times a day; intravenously, 1000 mg slowly.

**Metoclopramide** – tablets, 10 mg; solution in 2 ml ampoules containing 5 mg per ml. TD: orally, 10 mg 3 times a day before a meal; intramuscularly, 10 mg 1–2 times a day; intravenously, 10 mg in 10 ml of isotonic sodium chloride solution.

## SELF-ASSESSMENT TASKS

**Task 1.** Questions on pharmacotherapy. Write the prescriptions, justifying the choice of drugs.

1. Combination therapy Parkinson's disease.
2. Drug that increases dopamine accumulation 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 that rarely causes dyskinesia.
5. Drug for Parkinson's disease that has neuroprotective properties.
6. Drug for the treatment of Parkinson's disease that reduces tremor.

7. Drug for drug-induced parkinsonism.
8. Selective acetylcholinesterase inhibitor for treatment of Alzheimer's disease.
9. Drug that improves memory and attention in Alzheimer's disease.
10. Drug for the treatment of senile dementia.
11. Drug for the treatment of Alzheimer's disease.
12. Drug 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. Non-opioid analgesic for the relief of migraine headaches.
16. Neuroprotective drug for the treatment of ischemic stroke.
17. Drug for the long-term treatment of migraine in patients with arterial hypertension.
18. Neuroprotective agent for recovery after cerebral stroke.

**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? Describe 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 affecting 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 in Alzheimer's disease.

7. What types of 5-HT receptors are known? Where are they located and how do they function? Which medications affecting 5-HT receptors are used for migraines?
8. Why does sumatriptan have advantages over ergotamine in the treatment of 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 an anti-excitotoxic effect?

**Task 3.**

a. Match each drug (A–E) with the appropriate description (1–5).

A. Trihexyphenidyl	1. Central muscarinic receptor blocker
B. Entacapone	2. Metabolic precursor of dopamine
C. Levodopa	3. Component of phosphatidylcholines, in which the two hydroxyl groups of glycerol are esterified with fatty acids
D. Choline alfoscerate	4. Selective monoamine oxidase B (MAO-B) inhibitor
E. Selegiline	5. Peripheral inhibitor of catechol- <i>O</i> -methyltransferase (COMT)

b. Match each drug with the appropriate description.

A. Sumatriptan	1. Triptan that is administered subcutaneously, intranasally, or orally
B. Acetylsalicylic acid	2. Drug that binds to 5-HT <sub>1</sub> receptors, $\alpha$ receptors, and dopamine receptors
C. Naratriptan	3. Longest-acting triptan associated with fewer cardiac adverse effects
D. Ergotamine	4. Weak organic acid that irreversibly acetylates (and, thus, inactivates) cyclooxygenase

**Task 4.** Topics for report.

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

**QUESTIONS AND TASKS IN CLASS**

**Task 1.** Analyze the tasks that illustrate the mechanisms of action and key characteristics of drugs for the treatment of neurodegenerative diseases and migraine (the set of graphic tasks).

**Task 2.** Analyze the following case tasks.

1. A 62-year-old man complained to his physician about facial grimacing, lip smacking, and trunk rocking that occurred 1 to 2 hours after taking his prescribed medication. The patient, who has Parkinson's disease, had been receiving an antiparkinsonian drug for three years. What type of adverse effect was this patient experiencing? Which drug is most likely responsible for the reported adverse effects?
2. A 78-year-old man has been experiencing increasing memory impairment and recognition deficits over the past two years. Recently, he became disoriented and confused at night. A physical examination revealed that he was alert and oriented to place, with no focal neurological deficits. His physician prescribed a medication that might help slow the progression of his symptoms. What is the patient's disease? Which drug would be appropriate for his treatment?
3. A 63-year-old woman complained to her physician of frequent palpitations. She had recently been diagnosed with Parkinson's disease and had been receiving levodopa/carbidopa for three weeks. Subsequent examinations led to a diagnosis of sinus tachycardia, likely induced by her antiparkinsonian therapy. Which of the following mechanisms is most likely responsible for the adverse effect reported by this patient?
  - a. Activation of cardiac dopamine receptors
  - b. Decreased acetylcholine release from cholinergic terminals

- c. Activation of cardiac  $\beta$  receptors
  - d. Blockade of cardiac  $M_2$  receptors
4. A 64-year-old man with Parkinson's disease reported episodes of complete immobility lasting a few minutes, followed by sudden onset of involuntary movements such as twitching, nodding, and jerking. He had been receiving levodopa/carbidopa. To reduce these rapid fluctuations, his neurologist reduced his daily dose of levodopa/carbidopa and added another medication. What type of phenomenon was this patient experiencing? Which drug was most likely prescribed?
5. A 30-year-old man visited the clinic with a two-month history of recurrent right-sided headaches occurring weekly. His headaches were usually preceded by flashes of light, bilaterally, and were associated with nausea, vomiting, and photophobia. The headaches did not respond to aspirin or ibuprofen and typically lasted all day unless he was able to sleep. Which type of receptor should the drug work on to effectively stop a migraine attack in this patient?
- a.  $\beta_2$  adrenergic
  - b. GABAergic
  - c.  $M_1$  cholinergic
  - d.  $5\text{-HT}_{1B/1D}$  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 for this patient?
- a. Aspirin
  - b. Acetaminophen
  - c. Ergotamine
  - d. Propranolol

**Task 3.** Answer the test questions (in the ICT classroom).

## **Lesson 21**

### **Antipsychotic, Anxiolytic, and Sedative Agents**

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

#### **KEY TOPICS FOR PREPARATION**

1. Psychotropic drugs: classification and history of development.
2. Schizophrenia: positive and negative symptoms.
3. Antipsychotic agents: chemical structure; mechanisms of antipsychotic and sedative actions.
4. Influence of antipsychotic agents on vegetative functions (hypothermic, antiemetic, hypotensive effects; changes in hormone secretion; blockade of M-cholinergic receptors).
5. Classification, mechanisms of action, features, and pharmacokinetics of antipsychotics:
  - a) First generation (typical):
    - Phenothiazine derivatives – chlorpromazine, levomepromazine, pericyazine, thioridazine, perphenazine, trifluoperazine, fluphenazine
    - Butyrophenone derivatives – droperidol, haloperidol
    - Substituted benzamide derivatives – sulpiride
  - b) Second generation (atypical):
    - Benzodiazepine derivatives – clozapine, quetiapine, olanzapine
    - Benzisoxazole derivatives – risperidone
    - Substituted benzamide derivatives – amisulpride
    - Imidazolidinone derivatives – sertindole
6. The use of antipsychotic drugs in psychiatry, anesthesiology, and internal diseases.
7. Adverse effects of antipsychotic drugs and methods for their correction; contraindications to their use.

8. Acute chlorpromazine poisoning: pathogenesis, symptoms, treatment.
9. Structure, functions and localization of GABA-receptors; role of benzodiazepine receptors,  $\sigma$ 1-receptors and MT-receptors in the anxiolytics action.
10. Anxiolytics: mechanism of action.
11. Anxiolytics: classification, mechanism of action, pharmacokinetics, uses, adverse effects, and contraindications:
  - benzodiazepine derivatives – alprazolam, diazepam, lorazepam, medazolam;
  - modified benzodiazepine – tofizopam;
  - anxiolytics with another chemical structure – buspirone, etifoxine.
12. Acute benzodiazepine anxiolytic group: pathogenesis, symptoms, treatment.
13. Chronic anxiolytic poisoning: mechanisms of addiction, prevention of drug addiction.
14. Sedatives: mechanism of action; differences from anxiolytics.

## **PRESCRIPTIONS**

**Droperidole** – solution in ampoules of 5 and 10 ml, containing 2.5 mg per 1 ml. TD: into muscles 2.5 mg; into a vein 5 mg in 20 ml of 5% glucose solution slowly.

**Clozapine** – tablets of 25 and 100 mg. TD: orally 50–200 mg 2–3 times a day after meals.

**Quetiapine** – tablets of 200 and 400 mg. TD: orally 200–400 mg twice daily.

**Trihexyphenidyl** – tablets, 2 mg. TD: orally, 1–4 mg 3–4 times a day.

**Diazepam** – 5 mg tablets; solution in ampoules of 2 ml containing 5 mg in 1 ml. TD: orally 5 mg 1–3 times a day; into muscles 10 mg; into a vein slowly 10 mg in 20 ml of isotonic sodium chloride solution.

**Tofisopam** – 50 mg tablets. TD: orally 50 mg 2 times a day in the morning and early afternoon.

**Flumazenil** – solution in ampoules of 5 ml containing 0.5 mg in 5 ml.  
TD: 0,5 mg into a vein; repeat injections as needed up to a daily dose of 2 mg.

## QUESTIONS AND TASKS FOR SELF-CONTROL

**Task 1.** Pharmacotherapeutic questions. Write 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 used in shock complex therapy.
8. Drug for schizophrenia resistant to first-generation antipsychotics.
9. Drug for generalized anxiety disorder.
10. Drug for post-traumatic stress disorder (PTSD).
11. Anxiolytic for anxiety without sedative (drowsiness) effect.
12. Drug for phobias.
13. Drug for ataralgesia.
14. Drug for convulsions.
15. Drug for spasticity treatment.
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. Which receptor actions underlie the antipsychotic and sedative effects of antipsychotics?
2. What effects of antipsychotics are attributed to: a) dopamine-blocking activity, b) adrenergic blocking activity, c) effect on 5-HT receptors?
3. What are behavior correctors? When are they prescribed?

4. Suggest ways to correct side effects of antipsychotic drugs without reducing their therapeutic effects. What type of antagonism underlies this interaction?
5. Which antipsychotics rarely cause parkinsonism and hyperprolactinemia? Why?
6. What antipsychotic can be prescribed for tardive dyskinesia after long-term haloperidol use?
7. What effect is common to both antipsychotic and anxiolytic drugs?
8. Antianxiety, anticonvulsant, sedative, hypnotic, and muscle relaxant effects of anxiolytics share a common mechanism. What is it?
9. How do peripheral muscle relaxants differ from anxiolytics in terms of muscle relaxation?

**Task 3.**

a. Match each drug (A–D) with the appropriate description (1–4).

A. Clozapine	1. A typical antipsychotic effective in treatment-resistant cases
B. Fluphenazine	2. Atypical antipsychotic effective in treatment-resistant cases
C. Haloperidol	3. High-potency antipsychotic
D. Chlorpromazine	4. Phenothiazine antipsychotic that does not cause obstructive jaundice

b. Match each drug (A–E) with the appropriate description (1–5).

A. Midazolam	1. Benzodiazepine with a long duration (24–48h) used as anxiolytic, muscle relaxant, and anticonvulsant
B. Lorazepam	2. Ultrashort-acting intravenous anaesthetic
C. Diazepam	3. Short-acting (12–18 h) drug which is used as hypnotic

D. Buspirone	4. Medium-acting (24 h) drug used as anxiolytic and antidepressant
E. Alprazolam	5. Partial agonist at 5-HT <sub>1A</sub> receptors used to treat generalized anxiety disorders

**Task 4.** Topics for report.

1. History of psychopharmacology.
2. Animal models of schizophrenia.
3. Measurement of anxiolytic activity: animal models of anxiety and human tests.
4. Functions of  $\sigma_1$ -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 was admitted to the psychiatric emergency department after being brought in by the police due to assaultive behavior toward his mother. He had hit her after a heavy drinking episode, believing she was about to kill him with a knife. On day two of his admission, he presented with brief episodes of tongue protrusion, grimacing, and spasmodic torticollis. A treatment regimen was initiated to manage his aggressive behavior, which included three intramuscular injections over a 24-hour period. Which drug is most likely responsible for the adverse effects observed in this patient? What specific adverse effect is presented?
2. A 39-year-old man, residing in a psychiatric unit for disorganized schizophrenia, displayed profound lack of motivation, notably blunted affect, reduced speech, and psychomotor retardation. He has been hospitalized three times since his diagnosis and had partially responded to treatments with haloperidol, chlorpromazine, and risperidone. What psychotropic drug would be the most appropriate choice at this stage, and why?
3. A 24-year-old woman reported to her physician experiencing amenorrhea for the past two months, alongside a white breast

discharge over the past week. She had been compliant with her medications, which included haloperidol and paroxetine for the treatment of schizoaffective disorder for three months, and her condition was well managed. What mechanism most likely contributed to the symptoms she is experiencing?

4. A 33-year-old woman was brought to the emergency department exhibiting increased agitation and confusion. Physical examination revealed a temperature of 40°C (104°F), a pulse of 125 bpm, labile blood pressure, and muscle rigidity. She had recently been diagnosed with schizophrenia and started new therapy just a few days earlier. What adverse effect is evident in this patient? Which drug is most likely responsible for her condition?
5. A 41-year-old man was admitted to a psychiatric hospital due to worsening psychosis. Recently diagnosed with paranoid schizophrenia, he had been treated with risperidone without success. A new treatment was initiated. A week later, lab results showed:
  - White blood cell count: 1200/mm<sup>3</sup> (normal 4500–11,000/mm<sup>3</sup>)
  - Neutrophils 12% (normal 54–62%)
  - Red blood cell count: 4.3 million/mm<sup>3</sup> (normal 4.0–5.5 million/mm<sup>3</sup>)
  - Platelet count: 145,000/mm<sup>3</sup> (normal 150,000–400,000/mm<sup>3</sup>)
  - Hemoglobin (Hb): 15 g/dL (normal >12 g/dL)

What drug did the patient most likely receive as the new treatment?  
What specific adverse effect did this drug cause?

6. A 56-year-old homeless alcoholic man was brought to the emergency department by police after being found wandering the streets. He was nauseated, tremulous, and hallucinating, stating he was out of money and unable to purchase his usual daily amount of whiskey. What would be an appropriate drug to treat this patient's acute alcohol withdrawal symptoms?

**Task 3.** Answer the test questions (in the ICT classroom).

## **Lesson 22**

### **Antidepressants, Psychostimulants, and Nootropic Drugs**

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

#### **KEY TOPICS FOR PREPARATION**

1. Antidepressants: general characteristics, spectrum, and mechanisms of psychotropic action.
2. Antidepressants: classification, chemical structure, mechanisms of action, indications, side effects, and contraindications for use:
  - a) nonselective monoamine reuptake inhibitors
    - tricyclic antidepressants – amitriptyline, imipramine, clomipramine;
    - tetracyclic antidepressants – maprotiline;
    - antidepressants with another chemical structure – venlafaxine, duloxetine;
  - b) selective serotonin reuptake inhibitors (SSRIs) – citalopram, escitalopram, paroxetine, fluvoxamine, fluoxetine, sertraline, trazodone;
  - c) MAO inhibitors
    - irreversible inhibitors – phenelzine;
    - reversible inhibitors – moclobemide, pirlindole;
  - d) atypical antidepressants – mirtazapine, tianeptine, agomelatine.
3. Lithium drugs: mechanism of action, uses, adverse effects, and contraindications – lithium carbonate.
4. Psychostimulants: characteristic, classification.
5. Neurophysiological mechanism of action of psychomotor stimulants: influence on the brain, emotional-motivational response, and motor skills.
6. Effects of psychomotor stimulants on psychophysiological processes: memory, attention, and quality of mental work.

7. Natural sources, chemical structure, spectrum, and mechanisms of the psychostimulating action of caffeine; effects of caffeine and methylxanthines (theophylline, theobromine) on cardiovascular, renal, and digestive functions; uses, adverse effects, and contraindications of methylxanthines.
8. Acute and chronic poisoning with amphetamines and caffeine: pathogenesis, symptoms, and treatment.
9. Psychostimulant-adaptogens: origin, active substances, mechanisms of action, features, and applications:
  - Plant-derived products: rhodiola rosea, levsea, eleutherococcus, aralia, ginseng
10. Nootropics (neurometabolic stimulants): mechanisms of action, uses, side effects, contraindications, and differences from psychostimulants:
  - GABA derivatives: gamma-aminobutyric acid, aminophenylbutyric acid, nicotinylgamma-aminobutyric acid
  - Piracetam

## PRESCRIPTIONS

**Duloxetine** – capsules of 30 and 60 mg. TD: orally 30–60 mg once daily.

**Sertraline** – tablets of 50 and 100 mg. TD: orally 25–200 mg once daily.

**Coffeinum** – tablets of 100 and 200 mg; solution in ampoules of 1 and 2 ml, containing 200 mg per 1 ml. TD: 100–200 mg orally 2–3 times per day (preferably in the morning); 100–200 mg subcutaneously.

**Extractum Rhodiolae fluidum** – 30 ml bottles. TD: 10–20 drops orally 2–3 times a day in the morning.

**Piracetam** – 400 mg capsules; 800 mg coated tablets; solution in 5 ml ampoules containing 200 mg per 1 ml. TD: orally 800–1600 mg three times a day; into the vein 800–1600 mg in 250 ml 5% glucose solution 1–2 times a day.

## SELF-ASSESSMENT TASKS

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

1. Drug for bipolar affective disorder.
2. Drug for somatized depression.
3. Drug for depression associated with pain syndrome.
4. Drug for panic disorder.
5. Psychomotor stimulant for asthenia.
6. Psychomotor stimulant for chronic arterial hypotension.
7. Psychostimulant-adaptogen for asthenia.
8. Psychostimulant-adaptogen for chronic arterial hypotension.
9. Drug for chronic fatigue syndrome.
10. Analeptic for respiratory failure.
11. Drug for the consequences of traumatic brain injury.
12. Drug for coma.
13. Drug for post-traumatic stress disorder (PTSD).
14. Drug for cerebral atherosclerosis.
15. Drug for cognitive impairment in patients with alcoholism.
16. Drug for hypertensive encephalopathy.
17. Drug for anxiety disorders of vascular origin.
18. Drug for withdrawal symptoms.

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

1. What is “neuroplasticity”? How does it change in depression and under the influence of antidepressants?
2. Which antidepressants have multitarget effects? Should these be considered therapeutic or adverse effects?
3. Name antidepressants with additional sedative or psychostimulant properties. Why should these effects be considered when prescribing?
4. What is the role of  $\sigma_1$ -receptors in the mechanisms of antidepressant action?
5. Why are psychostimulant-adaptogens prescribed for diabetes, immunodeficiency states, and cancer?

6. Explain the mechanism of action of nootropic drugs in cases of cerebral circulation disorders, vertigo, and chronic fatigue syndrome. Why are nootropics ineffective in healthy individuals?
7. Which nootropic drugs can be prescribed to reduce cognitive disorders in patients with epilepsy?

**Task 3.**

a. Match each drug (A–E) with the appropriate description (1–5).

A. Amitriptyline	1. Drug with pronounced anticholinergic properties
B. Fluoxetine	2. Nonselective monoamine oxidase inhibitor
C. Phenelzine	3. Active metabolite of this drug has a half-life of about 10 days
D. Selegiline	4. Selective monoamine oxidase inhibitor type A
E. Trazodone	5. Serotonin 5-HT <sub>2A</sub> presynaptic receptor blocker

b. Match each drug (A–C) with the appropriate description (1–3).

A. Amphetamine	1. Naturally occurring xanthine derivative, increasing alertness and produces agitation
B. Caffeine	2. Psychostimulant that acts by releasing monoamines from nerve terminals in the brain
C. Piracetam	3. Nootropic drug in the racetam group, with neuroprotective and anticonvulsant properties, reported to improve neural plasticity

**Task 4.** Topics for report.

1. Theories of depression.
2. Future antidepressant drugs.
3. Functions of purine receptors.
4. Brain stimulation therapies.

## QUESTIONS AND TASKS IN CLASS

**Task 1.** Analyze the mechanisms and features of action of antidepressants, psychostimulants, and nootropic drugs through a collection of graphic tasks.

**Task 2.** Analyze case tasks.

1. A 25-year-old woman visited a psychiatrist because she felt very anxious when eating or drinking in public. She recognized that her fear of being watched by others was irrational, but she could not overcome it. She also noted that alcohol helped her cope with her anxiety, leading her to drink two or three glasses of brandy every day. After further questioning, a preliminary diagnosis was made, and cognitive behavioral therapy was prescribed alongside 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 that she had taken several pills of amitriptyline in a suicide attempt. What symptoms did the patient most likely exhibit? Describe the effects of poisoning with tricyclic antidepressants.

3. A 53-year-old woman with a long history of depression was admitted to the hospital due to agitation, insomnia, and tremors. She had been taking fluoxetine, lorazepam, and mirtazapine for several months, with recent increases in the doses of fluoxetine and mirtazapine. Physical examination revealed a confused patient with hyperhidrosis, hyperreflexia, and myoclonus, but no focal neurological deficits. Vital signs showed blood pressure at 105/60 mm Hg, heart rate at 130 bpm, respirations at 32/min, and body

temperature at 39.8°C (103.8°F). Qualitative plasma tests for alcohol, opioids, benzodiazepines, and tricyclic antidepressants were negative, and an electrocardiogram indicated sinus tachycardia. A brain computed tomography scan was normal. What disorder most likely caused the patient's signs and symptoms? Indicate the appropriate therapy for this case.

4. A 36-year-old woman presented at an outpatient psychiatric clinic complaining of extreme lethargy and a depressed mood for the past five weeks. During the interview, she reported an intense fear of being in confined spaces and carefully avoided elevators and airplane travel. Her psychiatric history indicated two similar episodes in the past, treated 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 this patient?

5. A 30-year-old woman was brought to a psychiatric hospital by her parents because she had been in bed for most of the day for the last two weeks. The woman had been admitted to the hospital four months ago due to an acute manic episode and was discharged on valproic acid with a favorable response. Upon questioning, she stated that she discontinued her therapy two weeks ago because she felt cured, but now she admitted to being depressed most of the time and expressed thoughts of wanting to die. The patient was discharged from the hospital one week later with an appropriate maintenance therapy. Which drug would be suitable for this patient at this time?

**Task 3.** Answer the test questions (in the ICT classroom).

## **Lesson 23**

### **Final Class on Drugs Affecting the Central Nervous System**

*Learning objectives are to assess and reinforce prescription writing skills; to evaluate and consolidate knowledge of mechanisms of action, classifications, pharmacokinetics, uses, adverse effects, and drug poisoning related to previously studied topics.*

#### **TOPICS TO PREPARE FOR THE FINAL LESSON**

1. Inhalation anesthetic drugs: classification, mechanisms of action, stages of anesthesia.
2. Volatile (gas-forming) inhalation anesthetic agents: mechanisms of action; effects on autonomic functions and metabolism.
3. Non-inhalation anesthetic agents: classification, mechanisms of action, uses, adverse effects, and contraindications.
4. Acute ethanol poisoning: pathogenesis, symptoms, and treatment.
5. Hypnotic drugs: classification, mechanisms of action, adverse effects, and contraindications.
6. Treatment of insomnia: selection of hypnotic agents based on the type of insomnia.
7. Acute and chronic poisoning with hypnotics.
8. Antiepileptic drugs: classification, mechanisms of action, adverse effects, and contraindications.
9. Opioid analgesics: opioid receptors; mechanisms of analgesic action; classification.
10. Uses, adverse effects, and contraindications of opioid analgesics.
11. Acute and chronic opioid analgesic poisoning.
12. Antiparkinsonian drugs: mechanisms of action, classification, and adverse effects.
13. Mechanisms of action, adverse effects, and contraindications of M-anticholinergics and NMDA receptor antagonists used in Parkinson's disease.
14. Mechanisms of action, adverse effects, and contraindications of drugs used to treat Alzheimer's disease.
15. Mechanisms of action, side effects, and contraindications of drugs used to treat migraine.
16. Psychotropic drugs: principles of action, classification, and uses.

17. Antipsychotics: classification, chemical structure, mechanisms of action, and uses.
18. Anxiolytics: classification, mechanisms of action, uses, adverse effects, contraindications.
19. Acute and chronic anxiolytic poisoning.
20. Antidepressants: classification, mechanisms of action.
21. Antidepressants – monoamine reuptake inhibitors: classification, mechanisms of action, uses, adverse effects, and contraindications.
22. Antidepressants – MAO inhibitors: classification, mechanisms of action, uses, adverse effects, and contraindications.
23. Psychostimulants: classification, mechanisms of action, uses, and adverse effects.
24. Caffeine: origin, mechanisms of action, uses, adverse effects, and contraindications.

### **PRESCRIPTIONS**

Prescribe: Propofol, Ethanol, Nitrazepam, Zolpidem, Doxylamine, Flumazenil, Benzobarbital, Carbamazepine, Pregabalin, Ethosuximide, Valproic Acid, Morphine, Fentanyl, Tramadol, Buprenorphine, Naloxone, Paracetamol, Levodopa + [Carbidopa], Pramipexole, Trihexyphenidyl, Rivastigmine, Choline Alfoscerate, Sumatriptan, Droperidol, Clozapine, Diazepam, Duloxetine, 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 long-term treatment of epilepsy.
5. Drug for managing status epilepticus.
6. Drug for trigeminal neuralgia.
7. Analgesic for preventing shock in traumatic injury.
8. Analgesic for myocardial infarction.
9. Drug for treating Parkinson's disease.
10. Drug for treating Alzheimer's disease.
11. Drug for treating migraine.

12. Drug for relieving psychomotor agitation.
13. Drug for long-term treatment of schizophrenia.
14. Antipsychotic used in complex shock therapy.
15. Drug for treating anxiety.
16. Drug for treating depression.
17. Drug for treating asthenia.
18. Drug that stimulates the respiratory center in cases 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 24**

### **Drugs Affecting Functions of the Respiratory System**

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

#### **KEY TOPICS FOR PREPARATION**

1. Analeptics (central respiratory stimulants): classification, mechanism of action, uses, adverse effects, and contraindications to the use
  - analeptics with direct tonic action – caffeine.
2. Antitussive agents: classification, origin, mechanism of action, pharmacokinetics, uses, routes of administration, adverse effects, and contraindications for use
  - a) Centrally acting
    - opioid – codeine;
    - non-opioid – butamirate, dextromethorphan;
  - b) peripherally acting – benzonatate.
3. Expectorants: classification, origin, mechanism of action, uses, routes of administration, adverse effects, and 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, adverse effects, and contraindications to the use

- $\beta_2$ -adrenomimetics  
short-acting – salbutamol, 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 the basic therapy of bronchial asthma: mechanism of action, pharmacokinetics, uses, adverse effects, and 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 – digoxin, levosimendan.

## PRESCRIPTIONS

**Codeinum** 8 mg + **Natrii hydrocarbonas** 250 mg + **Terpinum hydratum** 250 mg. TD: orally 1 tablet two–three times a day.

**Butamirate** – coated tablets 20 mg; syrup in 200 ml vials containing 1,5 mg in 1 ml. TD: orally, 20 mg 3 times a day (tablets); adults 22,5 mg 4 times a day, children under 12 years of age 15 mg 3 times a day (syrup).

**Ambroxol** – 30 mg tablets; syrup in 100 ml vials containing 3 mg in 1 ml; inhalation solution in 100 ml vials containing 7,5 mg in 1 ml; solution in 2 ml ampoules containing 15 mg in 2 ml. TD: orally 30 mg 3 times a day (tablets); adults 30 mg 3 times a day, children under 12 years of age 15 mg three times a day (syrup); inhalation 15 mg 1–2 times a day; into a vein slowly 15 mg in 20 ml of 5% glucose solution.

**Acetylcysteine** – powder and granules of 600 mg for the preparation of a solution for oral administration; solution in 200 ml bottles containing 40 mg in 1 ml; solution in ampoules of 3 ml containing 100 mg in 1 ml. TD: orally 600 mg in ½ glass of water 1 time per day (powder, granules), 400 mg once daily (solution); 150 mg/kg body weight in 100 ml of 5% glucose intravenously.

**Aminophyllinum** – 150 mg tablets; solution in 10 ml ampoules containing 24 mg per 1 ml. TD: orally 150 mg 1–3 times a day after meals; into a vein 120–240 mg in 20 ml of isotonic sodium chloride solution.

**Prednisolonum** – tablets 5 mg; solution in ampoules of 1 ml, containing 3 mg in 1 ml; 0,5% ointment in tubes of 10,0. TD: orally 5–20 mg 1 time per day in the morning with meals; into a vein 0,075–0,15 in 500 ml of 5% glucose solution.

**Beclometasone** – aerosol containing 50 and 100 mcg in 1 dose; spray containing 50 mcg in 1 dose of TD: inhalation 100–300 mcg 2 times a day; 100–400 mcg in each nasal passage twice daily.

**Fenoterol** – aerosol containing 100 mcg per dose. TD: inhalation 100–200 mcg mg.

**Salmeterol + Fluticasone** – aerosol containing 25 mcg of salmeterol and 125 mcg of fluticasone in one dose. TD: 1 dose by inhalation twice daily.

**Tiotropii bromidum** – powder for inhalation in capsules 18 mcg. TD: inhalation 18 mcg once daily.

**Morphinum** – tablets, 10 mg; solution in 10 ml bottles containing 20 mg per ml (drops for oral administration); solution in 1 ml ampoules containing 10 mg per ml. TD: orally, subcutaneously, intramuscularly, 10 mg.

### **SELF-ASSESSMENT TASKS**

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

1. Combined drug for the treatment of bronchitis.
2. Cough medicine containing an opioid analgesic.
3. Drug for bronchitis with both antitussive and expectorant effects.
4. Antitussive drug for bronchitis that also acts as a bronchodilator.
5. Drug that reduces the viscosity of bronchial mucus.
6. Drug that increases surfactant synthesis in respiratory distress syndrome.
7. Drug for cystic fibrosis.
8. Adrenomimetic to prevent exercise-induced bronchospasm.
9. M-cholinoblocker for chronic obstructive pulmonary disease (COPD).
10. Myotropic antispasmodic for bronchial asthma.
11. Drug for prophylactic therapy of bronchial asthma.
12. Hormonal drug for basic anti-inflammatory therapy of asthma.
13. Hormonal drug for inhalation in asthma.
14. Drug for long-term prevention of bronchial asthma.
15. Opioid analgetic for pulmonary edema.
16. Drug that inhibits inflammatory mediator release in asthma.
17. Hormonal drug for pulmonary edema.
18. Combined drug for the preventive therapy of bronchial asthma.

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

1. Which expectorants are used for respiratory diseases with scant sputum, and which for viscous sputum?
2. Analyze the pros and cons of inhaled bronchodilators and anti-inflammatory drugs in asthma treatment.

3. Identify bronchodilators that increase and decrease mucociliary clearance.
4. What is bronchial remodeling? Which drugs inhibit this process and prevent microbial adhesion to the bronchial epithelium?
5. Which medications prevent nighttime asthma attacks and why?
6. Why is it rational to combine  $\beta_2$ -adrenomimetics with M-cholinoblockers in broncho-obstructive syndromes? What is their route of administration?

**Task 3.** Match each drug (A–E) with the appropriate description (1–5).

a. Match each drug with the appropriate description

A. Ipratropium	1. Long-acting $\beta_2$ adrenoceptor agonist
B. Omalizumab	2. Bronchodilator drug that can block neuronal n-acetylcholine receptors
C. Salmeterol	3. Anti-inflammatory agent that inhibits mast cell degranulation and release of histamine
D. Cromolyn	4. Drug that blocks high-affinity immunoglobulin E (IgE) receptors of sensitized mast cells

b. Match each drug (A–E) with the appropriate description (1–5).

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

E. Bromhexine

5. Drug that decreases mucus viscosity by increasing lysosomal activity

**Task 4.** Topics for reports.

1. Glucocorticoids in bronchial asthma: Inhaled vs. systemic administration.
2. Advantages and disadvantages of inhaled drug delivery.
3. Modern inhalation drug delivery systems.

## QUESTIONS AND TASKS IN CLASS

**Task 1.** Analyze the tasks that reflect the mechanisms and features of action of drugs that affect the functions of the respiratory system and the myometrium (this includes a collection of graphic tasks).

**Task 2.** Analyze case tasks.

1. A 34-year-old man with asthma was brought to the emergency department experiencing a severe asthma exacerbation. The patient's forced expiratory volume in one second (FEV1) did not improve after the administration of inhaled salbutamol. Consequently, the attending physician decided to administer parenteral triamcinolone. What is the benefit of using parenteral glucocorticoids in this situation?
2. A 45-year-old man has been suffering from chronic obstructive pulmonary disease (COPD) that has not been adequately controlled by inhaled salmeterol and ipratropium. His physician decided to add a third medication that acts through multiple mechanisms, including the inhibition of phosphodiesterase 4 in inflammatory cells and the enhancement of histone deacetylation. What drug was most likely added to this patient's therapeutic regimen?
3. A 43-year-old man reported to his physician that while his current therapy improved his breathing, he still experienced an annoying cough from time to time. Two weeks prior, he had been diagnosed with moderate persistent asthma and started treatment with inhaled salbutamol and fluticasone. What medication would be appropriate to address this patient's cough?

4. A 21-year-old man with severe persistent asthma had been using daily inhaled salmeterol, inhaled beclomethasone, and oral zafirlukast for two months, alongside inhaled salbutamol as needed. However, his asthma remained poorly controlled, leading his physician to consider adding another drug to his treatment plan. What medication would be most appropriate for this patient at this time?

5. A 32-year-old male with a history of opioid addiction presents with symptoms of an upper respiratory infection that has lasted for the past five days. It has been determined that the infection is viral in nature, and no specific treatment for the underlying infection is indicated. Which of the following is an appropriate symptomatic treatment for this patient's cough?

**Task 3.** Answer the test questions (in the ICT classroom).

## **Lesson 25**

### **Drugs Affecting Functions of the Digestive System**

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

#### **KEY TOPICS FOR PREPARATION**

1. Origin, mechanisms, features of action, pharmacokinetics, uses, adverse effects, and contraindications to the use of drugs affecting the appetite and function of the gastrointestinal tract.
2. Drugs affecting appetite:
  - drugs that increase appetite – genetically engineered insulin;
  - anorectic drugs (diet pills) – orlistat, sibutramine.
3. Drug replacement therapy for gastric – betaine + pepsin.
4. Drugs used to inhibit gastric acid secretion:
  - m-cholinoblockers – metocinia iodide, pyrensepin;
  - H<sub>2</sub>-receptor blockers – famotidine;
  - proton pump inhibitors (PPIs) – omeprazole, lansoprazole, pantoprazole, rabeprazole, esomeprazole.
5. Antacid agents – sodium hydrogen carbonate, magnesium oxide, hydroxide and carbonate, aluminum hydroxide, oxide and phosphate, calcium carbonate.
6. Drugs with protective effects on the mucous membrane of the stomach and intestine – bismuth tripotassium dicitrate, sucralfate, misoprostol.
7. Antiemetic drugs:
  - non-selective antagonists of D-receptors – chlorpromazine, sulphiride;
  - antagonists of D<sub>2</sub>-receptors – domperidone;
  - 5-HT<sub>3</sub>-receptor antagonists – tropisetron, ondansetron, granisetron;
  - antagonists of D<sub>2</sub>-receptors and 5-HT<sub>3</sub>-receptors –

- metoclopramide;
  - H<sub>1</sub>-receptor antagonists – dimenhydrinate;
  - NK-receptor antagonists – aprepitant.
8. Laxatives:
- irritants of intestinal chemoreceptors – castor oil, senna, bisacodyl, sodium picosulphate;
  - osmotic agents (irritants of mechanoreceptors) – lactulose, sodium and magnesium sulfates, macrogol.
9. Drugs that increase gastrointestinal tone and motility:
- a) M-cholinomimetics – aceclidine;
  - b) cholinesterase inhibitors – neostigmine methylsulfate;
  - c) prokinetics
    - stimulants of the acetylcholine release, cholinesterase inhibitors and D<sub>2</sub>-receptor antagonists – itopride;
    - antagonists of D<sub>2</sub>-receptors and 5-HT<sub>3</sub>-receptors – metoclopramide;
    - antagonists of D<sub>2</sub>-receptors – domperidone.
10. Drugs that reduce the tone and motility of the stomach and intestines:
- a) M-cholinoblockers – atropine, platyphyllin, metocinia iodide;
  - b) myotropic antispasmodics
    - phosphodiesterase inhibitors – bencyclane, drotaverine;
    - sodium channel blockers – mebeverine;
  - c) antidiarrheal agents
    - opioid receptor agonists – loperamide;
    - adsorbents – activated charcoal;
11. Origin, mechanisms, features of action, uses, adverse effects, and contraindications of drugs affecting liver function.
1. Cholergics (bile formation stimulants):
    - true cholergics – garlic, tansy flowers, ursodeoxycholic acid;
    - hydrocholergics mineral waters.
  2. Cholekinetics (bile secretion stimulants):
    - cholecystokinetics magnesium sulfate.
  3. Hepatoprotective agents:

- drugs that improve the detoxifying function of the liver and antioxidants ademetionine, ornithine.
4. Drugs for dissolution of cholesterol gallstones:
- ursodeoxycholic acid.

## PRESCRIPTIONS

**Omeprazole** – 20 mg capsules; powder 40 mg in bottles. TD: orally 20–40 mg once a day; 40 mg drip into a vein in 100 ml of isotonic sodium chloride solution.

«**Maalox**» — official tablets and suspension in a bottle of 250 ml. TD: orally 1 tablet or 1 tablespoon 1—1,5 hours after meals or with stomach pain

**Metoclopramide** — 10 mg tablets; solution in ampoules of 2 ml containing 5 mg in 1 ml. TD: orally 10 mg three times a day before meals into the muscles 10 mg one–two times a day; into the vein 10 mg in 10 ml of isotonic sodium chloride solution.

**Bisacodyl** – 5 mg tablets; rectal suppositories: 10 mg. TD: 5–10 mg. orally at bedtime; 10 mg. rectally.

**Drotaverine** – 40 mg tablets; solution in ampoules of 2 ml containing 20 mg in 1 ml. TD: orally 40–80 mg two–three times a day; into the muscles 40–80 mg; into the vein 40–80 mg in 10–20 ml isotonic sodium chloride solution slowly.

**Acidum ursodeoxycholicum** — 500 mg coated tablets; suspension in 250 ml bottles containing 250 mg in 5 ml. TD: 250–750 mg orally once daily at bedtime.

**Neostigmini methylsulfas** – tablets 15 mg; solution in 1 ml ampoules containing 0,5 mg per 1 ml. TD: 15 mg orally 30 minutes before meals; under the skin 0,5 mg one–two times a day.

**Platyphyllinum** – solution in ampoules of 1 ml containing 2 mg in 1 ml. TD: 2–4 mg subcutaneously 1–2 times daily.

**Bismuthi trikalii dicitras** – 120 mg tablets. TD: orally 120–240 mg three times a day half an hour before meals and at bedtime.

## SELF-ASSESSMENT TASKS

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

1. Proton pump inhibitor for peptic ulcers.
2. Drug to reduce NSAID-induced ulcerogenic risk.
3. Antacid for neutralizing gastric acid.
4. Drug for hyperacid gastritis.
5. Anti-*Helicobacter pylori* agent for ulcers.
6. Drug for treating peptic ulcers.
7. Antiemetic for general prevention of vomiting.
8. Antiemetic for chemotherapy-induced nausea.
9. Antiemetic for postoperative vomiting.
10. Antidiarrheal for non-infectious diarrhea.
11. Drug for traveler's diarrhea.
12. Laxative for chronic constipation.
13. Drug for intestinal atony.
14. Myotropic antispasmodic for abdominal pain.
15. M-anticholinergic for cramping abdominal pain.
16. Drug for biliary colic.
17. Drug for primary biliary cirrhosis.
18. Drug for dissolving gallstones.

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

1. How do antacids affect intestinal tone and motility? What are rational antacid combinations?
2. Explain the mechanisms of gastroprotection. Which drugs have gastroprotective effects?
3. Choose antiemetics for:
  - Gastroduodenal reflux
  - Motion sickness
  - Endogenous/exogenous intoxication
4. What are the pleiotropic effects of aprotinin?
5. What is the mechanism of selective action of anthraquinone laxatives on the colon?
6. Which laxatives should be used preoperatively?

7. Why should long-term laxative use be avoided?

**Task 3.**

a. Match each drug (A–E) with the appropriate description (1–5).

A. Famotidine	1. Selective histamine H <sub>2</sub> -receptor antagonists act selectively on H <sub>2</sub> receptors in the stomach
B. Misoprostol	2. Proton pump inhibitor that blocks H <sup>+</sup> /K <sup>+</sup> -ATPase
C. Omeprazole	3. Neutralizes gastric acid via water and salt formation
D. Sucralfate	4. Forms protective gels with epithelial cells
E. Aluminum hydroxide	5. Approved for prevention of NSAID-induced gastric ulcers

b. Match each drug (A–E) with the appropriate description (1–5).

A. Ondansetron	1. Neurokinin receptor antagonist in the brain
B. Loperamide	2. 5-HT <sub>3</sub> receptor antagonist antiemetic
C. Senna	3. Drug that activates presynaptic opioid receptors in the enteric nervous system to inhibit acetylcholine release and reduce peristalsis
D. Castor oil	4. 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. Medications for nausea and vomiting in pregnancy.

3. Enzyme replacement therapy in pancreatic insufficiency.
4. Antienzyme and hormonal therapy for acute pancreatitis (e.g., aprotinin, octreotide).
5. Natural products with hepatoprotective effects.
6. Hepatoprotective agents: benefits and limitations.

### QUESTIONS AND TASKS IN CLASS

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

**Task 2.** Analyze case tasks.

1. A 45-year-old woman had been self-medicating for heartburn. The physician decided to prescribe her 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 using a single product?
2. A 50-year-old woman complained to her physician about regurgitation of foul-tasting fluid into her mouth, as well as occasional nausea and vomiting. The physician prescribed a drug that can both prevent nausea and vomiting, and promote upper gastrointestinal motility. Which receptors' blockade most likely contributed to the therapeutic effect of the drug in the patient's condition? What drug was prescribed?
  - a) M<sub>3</sub>-cholinergic
  - b) N-cholinergic
  - c) β<sub>2</sub> adrenergic
  - d) H<sub>2</sub> histaminergic
  - e) D<sub>2</sub> dopaminergic
3. A 60-year-old man suffering from recurrent heartburn routinely took large quantities of different antacid preparations. Which antacid poses 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 taking bisacodyl, one tablet daily for a week. What is the best advice to give this patient?

- a) There is no cause for alarm; the situation is self-limiting.
- 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 she has gastroesophageal reflux disease and advises her to raise the head of her bed 6 to 8 inches, avoid eating for several hours before bedtime, and eat smaller meals. Two weeks later, she returns and reports that her symptoms have slightly subsided but still remain a concern. Which drug is the clinician likely to prescribe?

**Task 3.** Answer the test questions (in the ICT classroom).

## **Lesson 26**

### **Cardiotonic and Antiarrhythmic Drugs**

*Learning objectives are to study classifications, mechanisms of action, antimicrobial spectrum, pharmacokinetics, uses, adverse effects, and contraindications of cardiotonic and antiarrhythmic drugs; to learn about cardiac glycoside toxicity; to practice prescription writing.*

#### **KEY TOPICS FOR PREPARATION**

1. Characteristics of cardiac glycosides. Overview of plants containing cardiac glycosides.
2. Pharmacodynamics of cardiac glycosides: mechanism of action, effects on myocardial contractility and the cardiac conduction system.
3. Hemodynamic effects of cardiac glycosides: impact under normal conditions and in heart failure; diuretic properties.
4. Pharmacokinetics of digoxin.
5. Indications, adverse effects, and contraindications for digoxin use.
6. Glycoside intoxication (transitional and toxic stages): pathogenesis, clinical manifestations, treatment strategies. Use of Digoxin Immune Fab.
7. Non-steroidal cardiotonic drugs: mechanism of action and clinical application of levosimendan.
8. Antiarrhythmic drugs: classification
  - a) Class I – sodium channel blockers
    - IA – drugs that prolong the effective refractory period (ERP) – procainamide;
    - IC – with a multidirectional effect on ERP, –propafenone;
  - b) Class II –  $\beta$ -adrenoblockers – propranolol, atenolol, metoprolol, esmolol;
  - c) Class III – potassium channel blockers prolonging ERP – amiodarone, sotalol;
  - d) Class IV – calcium channel blockers – verapamil, diltiazem.
9. Unclassified antiarrhythmic drugs
  - adenosine;

- potassium and magnesium asparaginate.
10. Mechanism of action, pharmacokinetics of antiarrhythmic drugs; drug selection for different forms of supraventricular and ventricular arrhythmias; adverse effects and contraindications. Arrhythmogenic effect of antiarrhythmic drugs.
  11. Antiarrhythmic drugs for bradycardia treatment: use of atropine.

## PRESCRIPTIONS

**Digoxinum** – available in 0.25 mg tablets and as a solution in 1 ml ampoules containing 0.25 mg per ml. TD: 0.125–0.25 mg orally once or twice daily; 0.25 mg intravenously in 10–20 ml of 5% glucose solution, administered slowly.

**Procainamide** – available in 250 mg tablets and as a solution in 5 ml ampoules containing 100 mg per ml. TD: 250–500 mg orally every 4 hours; 100–500 mg intravenously in 20 ml of 5% glucose solution, administered slowly.

**Esmolol** – provided as a solution in 10 ml ampoules, containing 10 mg per ml. TD: 80 mg intravenously over 15–30 seconds.

**Amiodarone** – available as 200 mg tablets and a solution in 3 ml ampoules containing 50 mg per ml. TD: 200–400 mg orally, twice daily before meals; intravenously, 250–500 mg in 250 ml of 5% glucose solution, administered dropwise.

**Verapamil** – available as coated tablets of 40 mg and 80 mg, and as a solution in 2 ml ampoules containing 2.5 mg per ml. TD: 40–80 mg orally three to four times daily; intravenously, 5–10 mg in 100 ml of isotonic sodium chloride solution, administered slowly.

**Metoprolol** – available as tablets of 50 mg and 100 mg, and as a solution in 5 ml ampoules containing 1 mg per ml. TD: 50–100 mg orally once or twice daily; intravenously, 2–5 mg in 10–20 ml of 5% glucose solution, administered slowly.

**Atropinum** – available as a solution in 1 ml ampoules, containing 1 mg per ml. TD: 0.25–0.5 mg subcutaneously or intramuscularly, once or twice daily.

## SELF-ASSESSMENT TASKS

**Task 1.** Pharmacotherapeutic questions. Write the prescriptions, justifying the drug selection for each case.

1. Drug for chronic heart failure.
2. Intravenous drug for chronic heart failure.
3. Cardiac glycoside used in atrial fibrillation.
4. Drug for arrhythmia due to glycoside toxicity.
5. Drug for arrhythmia in a patient with thyrotoxicosis.
6. Drug used to stop tachycardia during surgery.
7. Drug for sinus tachycardia.
8. Adrenergic blocking agent for atrial fibrillation.
9. Calcium channel blocker for atrial fibrillation.
10. Drug for treating paroxysmal supraventricular tachycardia.
11. Potassium drug for treating ventricular tachycardia.
12. Drug for arrhythmia during halothane anesthesia.
13. Drug increases the duration of the effective refractory period for myocytes.
14. Drug for arrhythmia in a patient with arterial hypertension.
15. Drug for arrhythmia in a patient with angina.
16. Drug for arrhythmia associated 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 do cardiac glycosides, despite increasing myocardial contractility, not improve blood flow to organs in healthy individuals?
3. What are the common electrophysiological mechanisms of action of antiarrhythmic drugs?
4. Why do both ERP-prolonging and ERP-shortening antiarrhythmic drugs prevent re-entry circuits in the myocardium?
5. Why are Class IB antiarrhythmic drugs effective only for ventricular arrhythmias, and why do they not impair conduction?

6. Which antiarrhythmic drugs are effective exclusively for supraventricular arrhythmias? Why?
7. Both verapamil and nifedipine block L-type calcium channels. Why is only verapamil used as an antiarrhythmic?
8. Why do propranolol and verapamil, despite good intestinal absorption, have low oral bioavailability?

**Task 3.**

a. Match each drug (A–E) with the appropriate description (1–5).

A. Amiodarone	1. Blocks L-type pf calcium channel
B. Verapamil	2. Acts on acetylcholine-sensitive K <sup>+</sup> channels
C. Adenosine	3. Blocks inactivated Na <sup>+</sup> channels and is the most effective antiarrhythmic agent for both supraventricular and ventricular arrhythmias
D. Metoprolol	4. Blocks both β receptors and K <sup>+</sup> channels
E. Sotalol	5. Blocks β receptors

b. Match each drug (A–D) with the appropriate description (1–4).

A. Digitoxin	1. Drug can cause cardiotoxic effect by blocking phosphodiesterase type 3 and sensitization of troponin C to calcium ions
B. Digoxin	2. Drug can increase the synthesis of cyclic adenosine monophosphate (cAMP) in the heart
C. Dobutamine	3. Cardiac glycoside with longer half-life than digoxin
D. Levosimendan	4. Drug that inhibits the Na <sup>+</sup> -K <sup>+</sup> -ATPase membrane pump

**Task 4.** Topics for report.

1. Dronedarone is an amiodarone-like compound.
2. Arrhythmogenic effect of antiarrhythmic drugs.
3. Digoxin immune Fab.

## QUESTIONS AND TASKS IN CLASS

**Task 1.** Analyze the tasks that illustrate the mechanisms and features of the action of cardiogenic and antiarrhythmic drugs (collection of graphic tasks).

**Task 2.** Analyze case tasks.

**Task 3.** Answer the test questions (in the ICT classroom).

1. A 78-year-old man was admitted to the hospital due to dyspnea, a nonproductive cough, and fever. He had been receiving an antiarrhythmic drug for 2 months to treat refractory supraventricular tachycardia. A chest X-ray revealed diffuse bilateral infiltrates. Bacterial, fungal, and viral cultures were negative. Which drug is most likely responsible for the patient's pulmonary disorder?

2. A 54-year-old woman was admitted to the hospital after experiencing dizziness and near-syncope. Her medical history included a urinary tract infection, currently being treated with ciprofloxacin. A few days ago, she was diagnosed with atrial fibrillation and started receiving treatment with sotalol. An electrocardiogram strip recorded by a Holter monitor during another episode of near-syncope clarified the diagnosis. What disorder is she most likely suffering from?

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 appeared to be hallucinating. The patient had been suffering from severe chronic heart failure for 2 years, and his wife reported finding an empty bottle of digoxin tablets near his bed. His vital signs showed a blood pressure of 100/50 mm Hg and a heart rate of 45 bpm. Emergency treatment was initiated, and a drug was administered intravenously. Which of the following drugs was most likely given?

- a) Lidocaine
- b) Atropine
- c) Phenytoin
- d) Potassium chloride

- e) Digoxin immune Fab
- f) Amiodarone

4. A 61-year-old man with a history of alcoholism was admitted to the hospital with a 2-day history of epigastric pain accompanied by nausea and vomiting. He had been managing systolic heart failure for 1 year, which was well controlled with captopril, furosemide, and digoxin. Key laboratory results upon admission showed a potassium level of 2.8 mEq/L (normal range 3.5–5.0 mEq/L) and a creatinine level of 3.2 mg/dL (normal range 0.6–1.2 mg/dL). An electrocardiogram displayed a heart rate of 65 bpm with occasional premature ventricular contractions and runs of bigeminy. What appropriate therapeutic adjustment should be made for this patient?

**Task 3.** Answer the test questions (in the ICT classroom).

## **Lesson 27**

### **Antianginal Drugs. Lipid-lowering Agents**

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

#### **KEY TOPICS FOR PREPARATION**

1. Antianginal drugs: classification based on the effect on the imbalance between myocardial oxygen demand and supply; clinical 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 – diltiazem.
3. Mechanism of action, pharmacokinetics, clinical use of drugs that reduce myocardial oxygen demand:
  - a)  $\beta$ -blockers
    - nonselective  $\beta$ -blockers – propranolol;
    - cardioselective  $\beta_1$ -blockers – atenolol, bisoprolol, metoprolol;
    - $\beta$ -blockers with additional vasodilatory effects – nebivolol;
  - b) bradycardic agents – ivabradine (selective sinus node If channel inhibitor), ranolazine (late sodium current inhibitors).
4. Nitrite and nitrate poisoning: pathogenesis, symptoms, treatment.
5. Cardioprotective drugs – trimetazidine, meldonium.

6. Drugs that improve cerebral circulation: mechanisms, features of action, pharmacokinetics, uses, side effects and contraindications
  - drugs reducing contractile function of cerebral vascular pericytes – vinpocetine, vinpocetine + piracetam;
  - Cerebral vasodilating calcium channel blockers – nimodipine, cinnarizine, piracetam + cinnarizine;
  - $\alpha$ -blockers – nicergoline;
  - nicotinic acid derivatives – xanthinol nicotinate.
  - Cyclic nucleotide phosphodiesterase inhibitors – aminophylline, vinpocetine.
7. Drugs selectively improving cochlear blood flow – betahistine.
8. Lipid-lowering agents: mechanism of action, clinical significance, classification
  - statins (3-hydroxy-3-methylglutaryl-coenzyme A reductase inhibitors) – atorvastatin, lovastatin, pitavastatin, pravastatin, rosuvastatin, simvastatin;
  - fibrates – gemfibrozil, fenofibrate;
  - nicotinic acid;
  - Cholesterol absorption inhibitors– ezetemibe;
  - proprotein convertase subtilisin kexin type 9 inhibitor – evolocumab, alirocumab, inclisiran.
9. Mechanism of action, pharmacokinetics, drug selection for different hyperlipidemia types, side effects, and contraindications of lipid-lowering drugs.

## PRESCRIPTIONS

**Nitroglycerin** – 0.5 mg tablets; spray (0.4 mg / dose). TD: sublingual 0.5–1 mg (tablets); 0.4–0.8 mg (spray).

**Isosorbide mononitrate** – 20 and 40 mg tablets; 50 and 60 mg slow-release tablets or capsules. TD: orally 20–40 mg 2 twice daily (tablets), 50–60 mg once daily in the morning or evening (tablets and slow-release capsules).

**Nifedipine** – 10 mg tablets; 40 mg slow-release tablets. TD: orally after meals 10–20 mg twice daily or 40 mg once daily.

**Vinpocetine** – 5 and 10 mg tablets; solution in ampoules of 2 and 5 mL (5 mg/mL). TD: orally 5–10 mg thrice daily after meals; 10–20 mg drip into a vein in 1 mL of isotonic sodium chloride solution, administered slowly.

**Betahistine** – 8 and 16 mg tablets; 24 mg capsules; oral solution in 30 mL bottles (12.5 mg/mL). TD: orally 8–16 mg thrice daily (tablets); 24 mg twice daily (capsules); 10 mg 2–4 times daily with meals (drops for oral use).

**Rosuvastatine** – 10 and 20 mg tablets. TD: 10–20 mg orally once daily with dinner.

**Ezetimibe** – 10 mg tablets. TD: orally 10 mg once daily.

**Metoprolol** – 50 and 100 mg tablets; solution in ampoules of 5 mL (1 mg/mL). TD: orally 50–100 mg twice daily (morning and evening); into a vein 5 mg in 10–20 ml of 5% glucose solution slowly.

**Verapamil** – 40 and 80 mg coated tablets; solution in 2 ml ampoules (2,5 mg/mL). TD: orally 40–80 mg 3–4 times daily; 5–10 mg drip into a vein in 100 mL of isotonic sodium chloride solution, administered slowly.

## SELF-ASSESSMENT TASKS

**Task 1.** Pharmacotherapeutic questions. Write prescriptions, justifying the choice of drugs for the following clinical scenarios.

1. Drug for arresting angina.
2. Drug for acute relief of an attack of angina pectoris due to coronary artery disease.
3. Drug for course treatment of stable angina.
4. Drug for course treatment of unstable angina.
5. Drug for myocardial infarction.
6. Drug for IHD with thyrotoxicosis.
7. Drug for heart failure.
8. Calcium channel blocker (open-channel type) for IHD.
9. Calcium channel blocker (inactivated channel type) for IHD.
10. Cardioselective  $\beta$ -blocker for IHD.
11. Drug for IHD with arrhythmia.

12. Drug for post-ischemic stroke.
13. Drug for hypertensive encephalopathy.
14. Drug for dizziness.
15. Drug for visual impairment of vascular etiology.
16. Statin for atherosclerosis.
17. Drug for mixed hyperlipidemia.
18. Cholesterol absorption inhibitor for atherosclerosis.

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

1. Explain the mechanisms by which antianginal drugs reduce myocardial oxygen demand. Classify these drugs and describe how each group achieves this effect?
2. Define coronary steal syndrome. What drugs can induce this condition?
3. What antianginal agents have the greatest bioavailability — nitroglycerin with prolong action, isosorbide dinitrate or isosorbide mononitrate? Why?
4. Why does prolonged nitrate therapy lead to tolerance? Under what conditions is tolerance to molsidomine less likely to develop?
5. What drugs cause dilation of blood vessels with the participation of nitric oxide?
6. What are the advantages of ivabradine?
7. Meldonium inhibits  $\gamma$ -butyrobetaine-hydroxylase, which converts  $\gamma$ -butyrobetaine to carnitine, trimetazidine inhibits the mitochondrial  $\beta$ -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. Define “pleiotropic effect”. Identify the pleiotropic effects of statins and fibrates. Are they related to hypolipidemic action?

10. What is the mechanism of action of new lipid-lowering drugs – proprotein convertase subtilisin kexin type 9 inhibitors. Identify the route of administration for drugs in this group.

**Task 3.**

a. Match each antianginal drug (A–E) with the appropriate description (1–5).

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

b. Match each lipid-lowering drug (A–E) with the appropriate description (1–5).

A. Evolocumab	1. Drug which is IgG against proprotein convertase subtilisin kexin type 9
B. Ezetimibe	2. Facial flushing is the most common adverse effect of this drug
C. Gemfibrozil	3. Drug prevents intestinal absorption of cholesterol
D. Niacin	4. 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. 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 afterload and coronary vascular tone
  - b. Decreased myocardial contractility
  - c. Increased heart rate.
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 ICT classroom).

## **Lesson 28**

### **Diuretics. Drugs Affecting Myometrium**

*Learning objectives are to study classifications, mechanisms of action, antimicrobial spectrum, pharmacokinetics, clinical uses, side effects and contraindications of diuretics; to practice prescription writing.*

#### **KEY TOPICS FOR PREPARATION**

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 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, chlorthalidone;  
thiazide-like diuretics – indapamide;
  - diuretics that inhibit reabsorption in distal convoluted tubules  
and collecting ducts
  - potassium-sparing diuretics:  
antagonists of aldosterone – spironolactone, eplerenone;  
sodium channels blockers – triamterene.
3. Clinical uses of diuretics.
4. Specialized uses of diuretics for glaucoma, epilepsy, heart failure and hypertension.
5. Side effects and contraindications to diuretics. Neural and humoral controlling mechanisms of the tone and contractile function of the uterus.
6. 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<sub>2α</sub>), dinoprostone (prostaglandin E<sub>2</sub>);
- Drugs, that increase myometrium tone (uterotonic drugs) – ergometrine, ergotamine;
- Drugs, that decrease the contractile function of the myometrium (tocolytics) – fenoterol, sodium oxybutyrate, magnesium sulfate;
- β<sub>2</sub>-adrenergic agonist – hexoprenaline;
- oxytocin receptor antagonist – atosiban;
- magnesium sulfate;
- Drugs, that reduce the tone of the cervix – atropine, dinoprost, dinoprostone.

## PRESCRIPTIONS

**Mannitolum** – solution in bottles of 200 and 400 mL (150 mg/mL). TD: drip into a vein at a prophylactic dose of 500 mg/kg body weight, at a therapeutic dose – 1500–2000 mg/kg body weight.

**Furosemidum** – 40 mg tablets; solution in ampoules of 2 mL containing (10 mg/mL). TD: orally 40 mg one–two times daily; into the muscles 20–40 mg one–two times daily; into the vein 20–40 mg in 20 mL of isotonic sodium chloride solution.

**Torasemide** – 5 and 10 mg tablets. TD: orally 5–10 mg one–two times daily.

**Hydrochlorothiazide** – 25 mg tablets. TD: orally 25–50 mg one–two times daily for 3–7 days, then break for 3–4 days.

**Indapamide** – 2.5 mg tablets. TD: orally 2.5 mg in the morning before a meal.

**Spirolactone** – 25 mg tablets. TD: orally 25 mg two–four times daily.

**Oxytocinum** – 1 ml ampoules (5 IU / mL). TD: 5 IU drops into a vein in 500 mL of a 5% glucose solution; into muscles 2–5 IU.

**Hexoprenaline** – 0.5 mg tablets; solution in 2 mL ampoules containing (5mcg/mL). TD: orally 0.5 mg every 3–4 hours; into a vein 10 mcg in 10 mL of isotonic sodium chloride solution, administered slowly.

## SELF-ASSESSMENT TASKS

**Task 1.** Pharmacotherapeutic questions. Write prescriptions with justification for drug choice in the following clinical scenarios

1. Diuretic for acute renal failure.
2. Diuretic for chronic renal failure.
3. Diuretic for the prevention of renal ischemia.
4. Diuretic for non-traumatic cerebral edema.
5. Diuretic for forced diuresis.
6. Diuretic for heart failure.
7. Diuretic for hypertensive crisis.
8. A potent diuretic for the course treatment of arterial hypertension.
9. A diuretic of the thiazide group for the course treatment of arterial hypertension.
10. Thiazide-like diuretic for course treatment of arterial hypertension.
11. Diuretic for nephrogenic diabetes insipidus.
12. Diuretic for ascites in a patient with cirrhosis of the liver.
13. Diuretic for the correction of hypokalemia.
14. Diuretic for hyperaldosteronism.
15. Hormonal agent for stimulating labor.
16. Medicine for stopping postpartum uterine bleeding.
17. Drug that reduces the risk of preterm labor.
18. Tocolytic for preterm labor.

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

1. Compare ion transport mechanisms (symport vs. antiport) in the apical versus basolateral membranes of nephron epithelial cells, highlighting key functional differences.
2. What diuretic is indicated for central sleep apnea?
3. Why is mannitol is preferred for preventing and treating 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 in glaucoma management? Why?

6. What diuretics are used for heart failure?
7. Why diuretics remain first-line agents for arterial hypertension?
8. It is known that the diuretic action of potassium-sparing agents is moderate. What is the clinical significance of this group of diuretics?
9. Identify cardioprotective mechanisms of spironolactone. What receptor types are involved in this effect?
10. Why is the onset of spironolactone action 2-3 days, and the onset of triamterene action – 2-4 hours after administration?
11. What cytoceptors are localized in the myometrium and how do the tone and contractile activity of the myometrium change when activated?

**Task 3.**

- a. Match each diuretic (A–F) with the appropriate description (1–6).

A. Acetazolamide	1. Drug inhibits Na <sup>+</sup> reabsorption in the proximal tubule
B. Eplerenone	2. Drug inhibits the synthesis of new Na <sup>+</sup> channels in the collecting duct
C. Furosemide	3. Drug causes an initial extracellular volume expansion in normal subjects
D. Indapamide	4. Drug increases the renal reabsorption of Ca <sup>2+</sup>
E. Mannitol	5. Drug blocks Na <sup>+</sup> transport channels
F. Spironolactone	6. Drug is the most likely to cause deafness

- b. Match each diuretic (A–E) with the appropriate description (1–5).

A. Acetazolamide	1. Clinically, this drug is a mainstay of antihypertensive medication
B. Spironolactone	2. Diuretic of choice in reducing extracellular volume in heart failure
C. Indapamide	3. Drug is a mainstay of treatment for patients with increased intracranial pressure
D. Furosemide	4. Drug which is used in the prophylaxis of

	acute mountain sickness
E. Mannitol	5. Drug is particularly effective in clinical situations associated with secondary hyperaldosteronism

c. Match each diuretic (A–E) with its target (1–5).

A. Acetazolamide	1. Receptors
B. Spironolactone	2. Ion channels
C. Triamterene	3. Enzymes
D. Furosemide	4. Carrier systems
E. Mannitol	5. Effects mediated by physicochemical interactions

**Task 4.** Topics for report.

1. Pleiotropic effects of diuretics.
2. Cardioprotective effects of spironolactone.

## QUESTIONS AND TASKS IN CLASS

**Task 1.** Analyze the tasks that reflect the mechanisms and features of action of diuretics (a 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 due to a sudden onset of extreme dyspnea. She presented with cyanosis, tachypnea, hyperpnea, restlessness, anxiety, and a sense of suffocation. Coughing was prominent and produced pink-tinged, frothy sputum. Her pulse was thready and fast (120 bpm), blood pressure was 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 two-week history of nausea, vomiting, and lower abdominal cramps. Physical examination revealed an afebrile, jaundiced, cachectic male in moderate distress. The abdomen was very tense with prominent veins, and 2+ ascites was noted by shifting dullness and a fluid wave. Pertinent serum values on admission were

$\text{Na}^+$  144 mEq/L (normal 136–145 mEq/L),  $\text{K}^+$  2.9 mEq/L (normal 3.0–5.0 mEq/L), bicarbonate 34 mEq/L (normal 22–28 mEq/L), and albumin 2.3 g/dL (normal 3.3–4.8 g/dL). 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 diuretic. Her blood pressure responds well, measuring 120/76 mm Hg. After several months on the medication, she complains of feeling tired and weak. An analysis of her blood indicates low values for which of the following?

- c) Calcium
- d) Glucose
- e) Potassium
- f) Sodium

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

- g) Blocks the  $\text{NaCl}$  cotransporter in the DCT
- h) Blocks aldosterone receptors in the CT
- i) Inhibits carbonic anhydrase in the PCT
- j) Inhibits the  $\text{Na}^+/\text{K}^+ / 2\text{Cl}^-$  cotransporter in the TAL
- k) Acts as an osmotic diuretic

**Task 3.** Answer the test questions (in the ICT classroom).

## **Lesson 29**

### **Drugs Affecting Blood Pressure**

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

#### **KEY TOPICS FOR PREPARATION**

1. Antihypertensive drugs: mechanism of action and classification.
2. Antihypertensive drugs: mechanism of action, pharmacokinetics, clinical use, side effects, contraindications
  - a) drugs reducing the excitability of the vasomotor center and sympathetic tone
    - central  $\alpha_2$ -adrenergic agonist – clonidine, guanfacine, methyldopa;
    - I<sub>1</sub>-imidazoline receptor agonists – moxonidine, rilmenidine;
  - b) adrenergic blockers
    - $\alpha_1$ -blockers – doxazosin;
    - $\beta$ -blockers – propranolol, atenolol, betaxolol, bisoprolol, metoprolol;
    - $\alpha$ ,  $\beta$ -blockers – carvedilol, urapidil;
  - 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. Diuretics in arterial hypertension management.
4. Drugs affecting functions of the renin-angiotensin system: mechanism of action, pharmacokinetics, use, side effects, contraindications
  - a) Antagonists (inhibitors) 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<sub>1</sub>-receptor blockers – losartan, valsartan, irbesartan, olmesartan medoxomil, azilsartan medoxomil, eprosartan.
5. Drugs of choice for the treatment of hypertension (first line drugs –  $\beta$ -blockers, 3<sup>rd</sup> generation of calcium channel blockers, ACE inhibitors, AT<sub>1</sub>-receptor blockers, thiazides and thiazide-like diuretics).
6. Rational antihypertensive drugs combinations.
7. Drugs for hypertensive crisis management – magnesium sulfate, enalaprilat, furosemide, urapidil.
8. Drugs increasing blood pressure (pressor agents): classification, mechanism of action, clinical use, side effects and contraindications
- a) drugs for collapse/hypotension and shock treatment
- analeptics – caffeine, nikethamide;
  - drugs that increase cardiac output and peripheral vascular resistance – epinephrine, dopamine;
  - drugs that increase peripheral vascular resistance – norepinephrine, phenylephrine;
- b) drugs for long-term (chronic) therapy of arterial hypotension – psychostimulants-adaptogens – rhodiola, ginseng.

## PRESCRIPTIONS

**Moxonidine** – 0.2 and 0.4 mg tablets. TD: orally 0.2–0.4 mg once daily.

**Amlodipine** – 5 and 10 mg tablets. TD: orally 5–10 mg once daily.

**Enalapril** – 5 and 10 mg tablets. TD: orally 5–10 mg once daily.

**Zofenopril** – 7.5 and 30 mg tablets. TD: orally 15–30 mg once daily.

**Losartan** – 50 and 100 mg tablets. TD: orally 50–100 mg once daily.

**Metoprolol** – 50–100 mg tablets; solution in ampules of 5 mL

(1 mg/mL). TD: orally 50–100 mg one or two times daily; into the vein 2–5 mg in 10–20 mL of 5% glucose solution, administered slowly.

**Verapamil** – 40 and 80 mg coated tablets; solution in 2 mL ampoules (2.5 mg/mL). TD: orally 40–80 mg three – four times daily; into the vein 5–10 mg in 100 mL of isotonic sodium chloride solution, administered slowly.

**Nifedipine** – 10 and 40 mg tablets. TD: orally after meals 10–20 mg 2 times daily or 40 mg once daily.

**Furosemidum** – 40 mg tablets; solution in ampoules of 2 mL (10 mg/ml). TD: orally 40 mg one–two times a day; into the muscles 20–40 mg one–two times daily; into the vein 20–40 mg in 20 mL of isotonic sodium chloride solution.

**Hydrochlorothiazide** – 25 mg tablets. TD: orally 25–50 mg one–two times daily for 3–7 days, then break for 3–4 days.

**Indapamide** – 2.5 mg tablets. TD: orally 2.5 mg in the morning before a meal.

**Spirolactone** – 25 mg tablets. TD: orally 25 mg two–four times daily.

**Phenylephrinum** – solution in 1 ml ampoules (10 mg/ml). TD: into a vein 1–5 mg in 20 mL of 5% glucose solution, administered slowly; subcutaneously, into muscles 3–5 mg.

**Coffeinum** – 100 and 200 mg tablets; solution in ampoules of 1 and 2 mL (200 mg/mL). TD: orally 100–200 mg two–three times daily in the first half of the day; subcutaneously 100–200 mg.

**Extractum Rhodiolae fluidum** – 30 ml bottles. TD: 10–20 drops orally 2–3 times daily in the morning.

## SELF-ASSESSMENT TASKS

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

1. Drug for arterial hypertension in combination with type 2 diabetes mellitus.
2. Drug for arterial hypertension caused by arterial spasm.

3. Drug for arterial hypertension in combination with angina pectoris.
4. Drug for a patient suffering from arterial hypertension with concomitant bronchial asthma.
5. Drug for high-renin arterial hypertension.
6. Drug for isolated systolic arterial hypertension.
7. Drug for chronic heart failure.
8. Drug for myocardial infarction.
9. Drug for nephropathy in patients with type 1 diabetes mellitus.
10. Drug for a patient with chronic heart failure with normal blood pressure.
11. Drug for arterial hypertension in a patient with a high level of uric acid in plasma.
12. Drug for chronic kidney disease.
13. Diuretic that reduces hypokalemia for the course treatment of arterial hypertension.
14. Thiazide-like diuretic for course treatment of arterial hypertension.
15. Diuretic for relief of hypertensive crisis.
16. Adrenergic agonist for relieving vascular collapse.
17. Analeptic for chronic arterial hypotension.
18. Psychostimulant-adaptogen for chronic arterial hypotension.

**Task 2.** 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. 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  $\alpha$ -blockers? In which cases are  $\beta$ -blockers the drugs of choice? Why?
4. What is the difference between  $\beta$ -blockers and calcium channel blockers? What do they have in common?

5. What is the difference between the derivatives of 1,4-dihydropyridine of 1<sup>st</sup>, 2<sup>nd</sup> and 3<sup>rd</sup> 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<sub>1</sub> 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 (A–E) with the appropriate description (1–5).

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 <sub>1</sub> receptors
D. Nifedipine	4. A calcium channel blocker
E. Sodium nitroprusside	5. A competitive inhibitor of renin

- a. Match each drug (A–D) which increases blood pressure with the appropriate clinical use (1-4).

A. Epinephrine	1. The immediate metabolic precursor of norepinephrine, can activate $\alpha$ - and $\beta$ adrenergic receptors
B. Dopamine	2. A direct-acting, synthetic adrenergic drug that binds primarily to $\alpha_1$ 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 membrane

**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 illustrate the mechanisms and features of action of diuretics (graphic tasks).

**Task 2.** Analyze case tasks.

1. A 65-year-old man was admitted to the emergency department due to restlessness, apprehension, tremors, sweating, and tachycardia. On admission, his vital signs were blood pressure 190/100 mm Hg, pulse 110 bpm, and respirations 18/min. His medical history revealed that he had been taking a thiazide diuretic and losartan for 3 months to manage stage 2 hypertension. However, his blood pressure remained poorly controlled, prompting his physician to add a third medication to his regimen. Recently, the patient experienced ankle edema and constipation, leading him to discontinue the newly prescribed medication a week before admission. Which drug was most likely the new medication that he decided to stop taking?

2. A 67-year-old man complained to his physician of a persistent dry cough and noted that food seemed to have lost its flavor. He had recently been diagnosed with stage 2 essential hypertension and had started a multidrug treatment one week earlier. Which drug is most likely responsible for the patient's signs and symptoms?

3. A 40-year-old male was recently diagnosed with hypertension, with pressure readings of 163/102 mm Hg and 165/100 mm Hg. He also

has well-controlled diabetes managed by oral hypoglycemic medications. What is the best initial treatment regimen for hypertension in this patient? Please explain your choice among the following options:

- a) Felodipine
- b) Furosemide
- c) Enalapril and hydrochlorothiazide
- d) Azilsartan medoxomil and chlorthalidone
- e) Metoprolol

4. A 53-year-old man was brought to the emergency department after experiencing crushing substernal pain for the past hour. Upon admission, his vital signs showed blood pressure at 88/50 mm Hg, pulse 115 bpm, and respirations 30/min. Further examinations led to a diagnosis of cardiogenic shock due to myocardial infarction, and therapy was initiated 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<sub>2</sub>
- b) Increased synthesis of inositol triphosphate (IP<sub>3</sub>) 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<sup>+</sup> channels

5. A 33-year-old man was brought to the emergency room after a car accident. Upon admission, he was lucid but completely paralyzed, with a loss of all sensation and reflex activity below the thorax. His vital signs indicated blood pressure of 80/40 mm Hg, heart rate of 42 bpm, and respirations of 36/min. A preliminary diagnosis of spinal shock due to spinal cord injury was made, and an intravenous infusion of an appropriate drug was initiated. Which drug was most likely administered?

**Task 3.** Answer the test questions (in the ICT room).

## **Lesson 30**

### **Drugs Affecting 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 practice prescription writing.*

#### **KEY TOPICS FOR PREPARATION**

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<sup>2+</sup>) sulfate;

- ferrous sulfate + ascorbic acid, folic acid, cyanocobalamin, serine;
  - ferrous gluconate;
  - ferrous fumarate;
  - Fe<sup>3+</sup> protein succinylate;
  - Fe<sup>3+</sup>-hydroxide polymaltose complex;
- b) iron oxide preparations (Fe<sup>3+</sup>) 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, edetate calcium disodium.
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, rutoside.

9. Antiplatelet agents: classification, mechanism of action, pharmacokinetics, use, side effects, contraindications
  - platelet receptor blockers
  - P2Y<sub>12</sub> platelet inhibition – ticlopidine, prasugrel, clopidogrel, cangrelor;
  - glycoprotein IIb/IIIa receptor antagonists – eptifibatide, abciximab;
  - thromboxane A<sub>2</sub> 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 etexilate;
  - selective inhibitors of the factor Xa – rivaroxaban, apixaban;
  - heparin sodium;
  - low molecular weight heparin – nadroparin calcium, enoxaparin sodium;
  - drugs with heparin-like action – 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

«**Sorbifer durules**» – official drug in coated tablets (320 mg ferrous sulphate and 60 mg ascorbic acid). TD: orally 1 tablet 2 times daily 1 hour before a meal.

**Cyanocobalaminum** – 1 mg coated tablets; solutions in 1 ml ampoules (0.2 and 0.5 mg/mL). TD: orally 1 mg once daily; under the skin, into the muscles 0,1–0,5 mg 1 time every 2 days.

**Menadioni natrii bisulfis** – 15 mg tablets; solution in ampoules of 1 ml (10 mg/ml). TD: orally 15 mg one–two times daily; into the muscles 10–15 mg.

**Acidum acetylsalicylicum** – 100 mg tablets. TD: orally 100 mg once daily after a meal.

**Clopidogrel** – 75 mg tablets and capsules. TD: orally 75 mg once daily.

**Rivaroxaban** – 10 and 20 mg tablets. TD: orally 10–20 mg once daily.

**Heparin sodium** – vials of 5 mL (1 mL – 5 000 Units); gel in tubes of 30 g (1 000 IU/1 g). TD: subcutaneously 5 000–10 000 Units four–six times daily; into the vein 20 000–30 000 Units in 1 000 mL isotonic sodium chloride solution dropwise; apply to the skin in the affected area 1-3 times daily.

**Enoxaparin sodium** – 1 ml ampoules (10 000 anti-Xa IU/ml). TD: 2 000–10 000 anti-Xa ME subcutaneously once daily.

**Warfarin** – 2.5 mg tablets. TD: orally 2.5 two times daily during 4 days, then 2.5 mg once daily in the morning.

**Deferoxamine** – powder in vials of 500 mg. TD: into the muscles 1 000 mg (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.

**Etamsylate** – 250 mg tablets; solution in 2 mL ampoules (125 mg/ml). TD: orally 250–500 mg thrice daily; into a vein 250–500 mg in 250 ml of 5% glucose solution.

**Calcii chloridum** – solution in ampoules of 5 and 10 mL (100 mg/ml). TD: 500–1000 mg into a vein, administered slowly.

## SELF-ASSESSMENT TASKS

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

1. Drug for the treatment of bleeding disorders, such as hemophilia.
2. Drug for the prevention of anemia in blood donors.
3. Drug with detoxification effect for poisoning.
4. Drug for the treatment of menorrhagia.
5. Drug for iron deficiency anemia.
6. Drug for macrocytic anemia.
7. Drug for neurological diseases.
8. Drug for hepatitis.
9. Drug for hemorrhagic syndrome.
10. Drug for the management bleeding associated with anticoagulants of indirect action.
11. Drug for angina.
12. Drug for 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 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 A<sub>2</sub> 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 these 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 (A–E) with the appropriate description (1–5).

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 etexilate	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 (A–D) with the appropriate description (1–5).

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

**Task 3.** 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  $3,4 \times 10^6/\text{mm}^3$  (normal, male  $4,3\text{--}5,9 \times 10^6/\text{mm}^3$ ), mean corpuscular volume 110 fL (normal 80–100 fL), vitamin B<sub>12</sub> 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 ICT classroom).

## **Lesson 31**

### **Final Class on Drugs Affecting Major Organs and Systems**

*Learning objectives are to assess prescription writing skills and to clarify knowledge regarding the mechanisms of action, classification, pharmacokinetics, uses, side effects of agents, and drug poisoning related to the topics that have been studied.*

#### **TOPICS TO PREPARE FOR THE FINAL LESSON**

1. Mechanism of cardiotonic action, classification, and pharmacokinetics of cardiac glycosides.
2. The effect of cardiac glycosides on the heart rate, the conduction system, hemodynamics, and kidney functions; uses and contraindications.
3. Glycoside intoxication: stages, pathogenesis, symptoms, and treatment.
4. Antiarrhythmic drugs: classification, mechanism of action, use, adverse effects, and contraindications.
5. Antianginal drugs: mechanism of action, classification, and uses.
6. Nitrates: mechanism of action, pharmacokinetics, uses, adverse effects, and contraindications. Mechanism of action of molsidomine.
7. Lipid-lowering agents: mechanism of action, classification.
8. Statins: mechanism of action, uses, adverse effects, and contraindications.
9. Diuretics: mechanism of action, classification.
10. Carbonic anhydrase inhibitors and osmotic diuretics: mechanism of action, uses, adverse effects, and contraindications.
11. Loop diuretics: mechanism of action, uses, adverse effects, and contraindications.
12. Thiazides and thiazide-like diuretics: mechanism of action, uses, adverse effects, and contraindications.
13. Potassium-sparing diuretics: mechanism of action, uses, adverse effects, and contraindications.
14. The choice and mechanism of action of diuretics for glaucoma, heart failure, and arterial hypertension.

15. Antihypertensive drugs: mechanism of action; requirements for antihypertensive drugs; classification.
16. Antihypertensive agents that reduce the excitability of the vascular center: mechanism of action, use, side effects, contraindications to the use.
17.  $\alpha$ -Adrenergic blockers: classification, mechanism of action, use, side effects, contraindications to use.
18.  $\beta$ -Adrenergic blockers: classification, mechanism of action, use in cardiology, side effects, contraindications to use.
19. Calcium channel blockers: classification, mechanism of action, uses, adverse effects, and contraindications.
20. ACE inhibitors: classification, mechanism of action, uses, adverse effects, and contraindications.
21. AT<sub>1</sub>-receptor blockers: mechanism of action, uses, adverse effects, and contraindications.
22. Iron drugs: natural sources of iron, metabolism of iron; mechanism of action, uses, adverse effects, and contraindications.
23. Acute iron poisoning: stages, pathogenesis, symptoms, and treatment.
24. Vitamin B<sub>12</sub>: natural sources of vitamin B<sub>12</sub>, chemical structure, pharmacokinetics, mechanism of action, and uses.
25. Folic acid: natural sources, mechanism of action, and uses.
26. Hemostatic agents: classification, mechanism of action, uses, and adverse effects.
27. Antiplatelet agents: classification, mechanism of action, uses, adverse effects, and contraindications.
28. Heparin: origin, chemical structure, mechanism of action, uses, adverse effects, and contraindications.
29. Indirect anticoagulants: mechanism of action, uses, adverse effects, and contraindications.
30. Indirect anticoagulant poisoning: pathogenesis, symptoms, and treatment.
31. Thrombolytic agents: classification, mechanism of action, uses, adverse effects, and contraindications.

## **PRESCRIPTIONS**

Prescribe: Digoxin, Procainamide, Esmolol, Amiodarone, Verapamil, Nitroglycerin, Isosorbide Mononitrate, Nifedipine, Vinpocetine, Betahistine, Rosuvastatin, Ezetimibe, Mannitol, Furosemide, Torasemide, Hydrochlorothiazide, Indapamide, Spironolactone, Oxytocin, Hexoprenaline, Amlodipine, Enalapril, Losartan, Sorbifer Durules\*, Cyanocobalamin, Menadione Sodium Bisulfite, Acetylsalicylic Acid, Clopidogrel, Rivaroxaban, Sodium Heparin, Warfarin, Etamsylate.

## **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 pharmacotherapeutic questions, demonstrating an understanding of the mechanisms of action and pharmacological characteristics of drugs that affect major organ systems. A computer-based test (CBT).

## **Lesson 32**

### ***Immunotropic and Antiallergic Agents, Nonsteroidal Anti-Inflammatory Drugs, and Medications for Gout***

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

#### **KEY TOPICS FOR PREPARATION**

1. Structure and functions of the immune system. Cell mediated and humoral immunity, specific and nonspecific protective factors, and mediators of immunity.
2. Primary and secondary immunodeficiency states: etiology, pathogenesis, clinical presentation, and principles of pharmacological correction.
3. Immunostimulants: classification, mechanism of action, pharmacokinetics, indications and contraindications, adverse effects
  - a) non-selective stimulants of leukopoiesis and tissue regeneration – methyluracil;
  - b) drugs of colony-stimulating factors – lenograstim, molgramostim, filgrastim, and 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, tilorone;
4. Classification of allergic reactions.
5. Immunosuppressants: classification, mechanism of action, pharmacokinetics, indications and contraindications, adverse effects
  - a) nonselective immunosuppressants

- cytostatic agents and antimetabolites – azathioprine, mercaptopurin, methotrexate;
- glucocorticoids – prednisolone, methylprednisolone, dexamethasone, 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  $\alpha$ -infliximab;  
humanized monoclonal antibodies to tumor necrosis factor- $\alpha$ -adalimumab, golimumab;  
a PEGylated Fab fragment against tumor necrosis factor – certolizumab;  
hybrid human type 2 receptor to tumor necrosis factor- $\alpha$ -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<sub>1</sub>- receptor blockers
- generation I – diphenhydramine, clemastin, mebhydroline, promethazine, chloropyramine;
  - generation II – loratadine, cetirizine, azelastine;
  - generation III – desloratadine, levocetirizine.
8. Nonsteroidal anti-inflammatory drugs (NSAIDs): classification, mechanism of action, pharmacokinetics, indications for use
- salicylates – acetylsalicylic acid;
  - pyrazole derivatives –phenylbutazone;
  - derivatives of indole acetic acid – indomethacin;
  - derivatives of phenyl alkanolic 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 towards isoenzymes of cyclooxygenase, including 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), canakinumab;
  - uric acid-lowering drugs – allopurinol, febuxostat.

## PRESCRIPTIONS

**Methotrexate** – 2.5 mg coated tablets; solution in ampoules of 1 ml containing 10 mg in 1 ml. TD: orally 7.5 mg once a week before meals; intramuscular 15–50 mg, intravenous 7.5–15 mg in 20 ml of 5% glucose solution, 1 time per week.

**Diphenhydramine** – 50 mg tablets; solution in 1 ml ampoules containing 10 mg per 1 ml; 1% gel in tubes of 20.0. TD: orally 50 mg 1–3 times a day; into muscles 10–30 mg, apply to the affected area of skin 3–4 times a day.

**Loratadine** – 10 mg tablets. TD: orally 10 mg once a day.

**Cetirizine** – 10 mg tablets; solution in 10 ml bottles containing 10 mg per 1 ml (oral drops). TD: orally 10 mg once a day.

**Acidum cromoglicicum** – 100 mg capsules; aerosol containing 5 mg per dose; nasal spray in 15 ml bottles containing 2,8 mg per dose; 2% solution in 5 ml bottles (eye drops). TD: orally 200 mg 4 times a day 15–20 minutes before meals; inhalation 10 mg 4 times a day; 2,8 mg in each nasal passage 4 times a day; 1 drop in both eyes 2–4 times a day.

**Diclofenac** – 25 mg tablets; solution in ampoules of 3 ml containing 25 mg in 1 ml; rectal suppositories 25 and 50 mg; TTS patch 30 mg; 1% gel in tubes of 50.0. TD: orally 25–50 mg 2–3 times a day after meals; intramuscular 75 mg once a day; rectally 25–50 mg 2 times a day; stick 1 patch on the skin once a day; Apply to skin 2 times a day.

**Meloxicam** – tablets of 7.5 and 15 mg; solution in 1.5 ml ampoules containing 10 mg per 1 ml; rectal suppositories 7,5 and 15 mg. TD: orally 7.5–15 mg once a day; rectally 7.5–15 mg 1 time per day; into muscles 15 mg 1 time per day.

**Etoricoxib** – tablets of 30 and 60 mg. TD: orally 30–60 mg once a day.

**Prednisolone** – 5 mg tablets; solution in ampoules of 1 ml, containing 3 mg in 1 ml; 0,5% ointment in tubes of 10.0. TD: orally 5–20 mg a day in the morning with meals; intravenous 75–150 mg in 500 ml of 5% glucose solution.

**Beclometasone** – aerosol containing 50 and 100 mcg in 1 dose; spray containing 50 mcg in 1 dose of TD: inhalation 100–300 mcg twice daily; 100–400 mcg in each nasal passage twice daily.

**Dexamethasone** – 4 mg tablets; solution in ampoules of 1 and 2 ml containing 4 mg in 1 ml, 0,1% solution in vials of 10 ml (eye drops). TD: orally 2–8 mg 1 time per day in the morning with meals; into a vein 4–12 mg in 500 ml of 5% glucose solution 2 times a day; 1–2 drops in each eye 1–2 times a day.

### **SELF-ASSESSMENT TASKS**

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

1. Immunosuppressant for the treatment of rheumatoid arthritis.
2. Immunosuppressant for the treatment of juvenile arthritis.
3. Immunosuppressant for the treatment of psoriatic arthritis.
4. Drug for itchy the treatment of dermatoses.
5. Drug for food allergies.
6. Drug for urticaria.
7. Drug for the prevention of an allergic reaction to vaccine administration.
8. Drug for the treatment of allergic conjunctivitis.
9. Drug for the treatment of allergic rhinitis.
10. Hormonal drug for the treatment of bronchial asthma.
11. Drug for the treatment of potentiating the action of analgesics for postoperative pain.
12. Anti-inflammatory drug for the treatment of rheumatoid arthritis.
13. Anti-inflammatory drug for the treatment of gout.
14. Anti-inflammatory drug for the treatment of osteoarthritis.
15. Drug for the treatment of toothache.
16. Topical drug for the treatment of bruises.
17. Topical drug for the treatment of osteochondrosis.
18. Drug for injections for the treatment of osteochondrosis.

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

1. Evaluate the advantages and disadvantages of using interferon preparations and interferon inducers in the management of chronic infections.
2. In the treatment of infectious diseases, which strategy is more effective: sequential administration or combination therapy using antibiotics and immunostimulants? Justify your answer with clinical rationale.
3. Differentiate between the immunosuppressive mechanisms of cytostatic agents and glucocorticoids. What are the clinical implications of these differences?
4. Define the term "selective immunosuppressants." How do these agents differ from non-selective immunosuppressants in terms of mechanism and therapeutic application?
5. Explain the mechanism of action of selective immunosuppressants using tacrolimus as an example. Present the steps in a logical sequence:
  - Binding to the intracellular protein FKBP12 (FK506-binding protein).
  - Formation of the tacrolimus–FKBP12 complex and inhibition of calcineurin.
  - Suppression of calcium-dependent transcription of lymphokine genes.
  - Impairment of interleukin production and interleukin receptor expression in cytotoxic lymphocytes.
  - Inhibition of proliferation and interaction of cytotoxic T lymphocytes.
  - Prevention of graft rejection responses.
6. For which types of allergic reactions are H<sub>1</sub>-receptor antagonists (antihistamines) most effective? Provide clinical examples.
7. Under what circumstances might the sedative effect of first-generation antihistamines be therapeutically beneficial?

8. Compare and contrast the pharmacological properties of first-, second-, and third-generation antihistamines. Why do second-generation antihistamines exhibit a prolonged duration of action (12–24 hours)?
9. Discuss the adverse effects of nonsteroidal anti-inflammatory drugs (NSAIDs) that are related to prostaglandin synthesis inhibition. Why do selective COX-2 inhibitors such as meloxicam, nimesulide, and celecoxib exhibit reduced gastrointestinal toxicity?
10. Which anti-inflammatory mechanisms of NSAIDs are of particular pathogenetic relevance in rheumatic diseases? Explain the clinical significance.
11. Outline the peripheral and central mechanisms of analgesia associated with NSAIDs and paracetamol. Why does paracetamol exert only a central analgesic effect?
12. Fever is a protective physiological response. Under what clinical conditions is the use of antipyretic agents justified?
13. Why does colchicine exhibit anti-inflammatory efficacy exclusively in the treatment of gout? Discuss its unique mechanism of action in this context.

### Task 3.

- a. Match each antihistamine drug (A–C) with the appropriate description (1–3)

A. Diphenhydramine	1. Antihistamine drug with pronounced sedative properties
B. Levocetirizine	2. Histamine receptor antagonist that may cause paradoxical hyperactivity in young children
C. Promethazine	3. Antihistamine drug with minimal or no sedative effect

- b. Match each NSAID (A–E) with the appropriate description (1–5)

A. Acetylsalicylic acid	1. Analgesic effect of this drug is primarily mediated by central impairment of pain transmission
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B. Celecoxib	2. Selective inhibitor of cyclooxygenase-2
C. Indomethacin	3. Irreversible inhibitor of cyclooxygenase in platelets
D. Piroxicam	4. Drug can inhibit both cyclooxygenase and phospholipase A <sub>2</sub>
E. Paracetamol	5. Long half-life of this drug (more than 50 hours) permits once-daily dosing

c. Match each immunomodulating drug (A–C) with the appropriate description (1–3)

A. Azathioprine	1. Specific inhibitor of inosine monophosphate dehydrogenase
B. Basiliximab	2. Drug binds to the CD25 $\alpha$ chain of the interleukin-2 receptor on activated T lymphocytes
C. Mycophenolate mofetil	3. Prodrug converted into mercaptopurine in the body

d. Match each drug (A–D) with the appropriate description (1–4)

A. Azathioprine	1. Antimalarial drug used in rheumatoid arthritis
B. Infliximab	2. Monoclonal antibody that binds to CD20 B lymphocytes
C. Hydroxychloroquine	3. Monoclonal antibody that binds to tumor necrosis factor- $\alpha$
D. Rituximab	4. Drug can inhibit the synthesis of inosinic acid

**Task 4.** Topics for report.

1. Toll-like receptors (TLRs): functions. Drugs targeting Toll-like receptors.
2. Combination drug therapies for immunosuppression in transplantation.

3. The role and selection 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<sub>1</sub> antagonist. Second-generation H<sub>1</sub> antagonists are used locally in the conjunctiva instead of first-generation H<sub>1</sub> antagonists. Explain the choice of drug.
3. A 44-year-old woman was checked in the coronary unit after a heart transplant performed 2 weeks earlier. Pertinent blood test results were white blood cell count  $1,2 \times 10^3/\text{mm}^3$  (normal  $4,5-11,0 \times 10^3/\text{mm}^3$ ), platelets  $40,000/\text{mm}^3$  (normal  $150,000-400,000/\text{mm}^3$ ). Which of the following drugs most likely caused these findings?
  - a. Cyclosporine
  - b. Dobutamine
  - c. Clozapine
  - 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 ICT classroom).

## **Lesson 33**

### **Acute Drug Poisoning**

*Learning objectives are to study treatment of acute poisoning; review the pathogenesis, clinical manifestations, and management strategies for various toxic exposures; to identify antidotes.*

#### **KEY TOPICS FOR PREPARATION**

1. Acute poisoning: definition and causes.
2. Use of antagonism in the treatment of poisoning (physical, chemical, physiological indirect, direct – competitive and noncompetitive).
3. Principles of management of acute drug poisoning:
  - a) measures and drugs to reduce the absorption and resorptive action of the poison
    - in case of dermal exposure – washing and decontamination;
    - inhalation exposure – lung hyperventilation;
    - parenteral (injection) exposure – ice, vasoconstrictor agents, application of a harness;
    - oral ingestion – adsorbents, emetics, laxatives with an osmotic effect, drugs for chemical neutralization of the poison in the gastrointestinal tract;
  - b) drugs that reduce toxin concentration in blood and tissues and mitigate effects on target organs
    - antidote therapy – chemical and physiological antagonists;
    - detoxification therapy – blood substitution and disinfection solutions, glucose, ascorbic acid;
  - c) measures to accelerate the elimination of toxins from the body, – forced diuresis, hemodialysis, hemosorption, and peritoneal dialysis;
  - d) symptomatic therapy – anti-shock drugs, drugs to eliminate pain syndrome, seizures, hyperthermia, respiratory disorders, cardiovascular disorders; correction of fluid, electrolyte, and acid-base balance.
4. Pathogenesis, clinical features, and treatment of poisoning or overdose with specific substances: 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 (e.g., Warfarin)**

*Symptoms:* Weakness, headache, multiple hemorrhages in the conjunctiva, mucous membranes, and skin; hemoptysis; epistaxis; uterine, gastric, and intestinal bleeding; hematemesis; hemarthrosis; hematuria.

*Treatment:* Gastric lavage (with activated charcoal); intravenous administration of vitamin K<sub>1</sub> (sodium menadione bisulfite), calcium chloride, glucose, and ascorbic acid.

### **Atropine Poisoning**

Stage 1 (Excitatory Phase): Disorientation, hallucinations, delirium, tonic-clonic seizures, tachypnea, hyperthermia, mydriasis, photophobia, cycloplegia, dry and flushed skin, mucosal dryness, rash, burning sensation in the mouth and throat, atonia, dysphagia, hydrophobia, tachycardia, arrhythmias, urinary retention, constipation.

*Treatment:* Gastric lavage (with activated charcoal); administration of neostigmine methylsulfate, droperidol or diazepam.

Stage 2 (Depressive Phase): Loss of consciousness, diminished reflexes, bradypnea, coma.

*Treatment:* Gastric lavage (with activated charcoal); intravenous neostigmine methylsulfate, glucose, and sodium bicarbonate.

### **Barbiturate Poisoning**

*Symptoms:* Apathy, ataxia, somnolence progressing to coma (resembles general anesthesia), hypothermia, depressed tendon reflexes, pathological reflexes, muscle hypotonia, miosis (later mydriasis with hypoxia), shallow or periodic respiration (Cheyne–Stokes), pulmonary edema, decreased blood pressure, congestive heart failure, anuria.

*Treatment:* Gastric lavage (with activated charcoal and sodium bicarbonate); IV administration of sodium bicarbonate, furosemide, piracetam, prednisolone, phenylephrine, and ceftazidime.

### **Cholinesterase Inhibitors (Organophosphates)**

Stage 1 (Cholinergic Crisis): Psychomotor agitation, disorientation, tonic-clonic convulsions, tremor, generalized fasciculations, miosis, accommodation spasm, profuse sweating, bronchospasm, dyspnea, tachycardia or bradycardia, labile blood pressure, hypersalivation, nausea, vomiting, abdominal pain, diarrhea, involuntary urination/defecation.

Stage 2 (Respiratory Failure): Bradypnea, respiratory muscle paralysis, pulmonary edema, bradycardia, vascular collapse, coma.  
*Treatment:* Gastric lavage (with activated charcoal and sodium bicarbonate); intramuscular or intravenous atropine (1 mg every 15 minutes), diazepam or droperidol, ceftazidime.

### **Hypoglycemic and Diabetic Coma**

*Hypoglycemic Coma Symptoms:* Anxiety, fear, weakness, dizziness, hunger, tremors, palpitations, hypersalivation, sweating; followed by loss of consciousness, tonic-clonic seizures, increased reflexes and muscle tone, pallor, cyanosis, cold sweat, tachycardia, hypertension.  
*Treatment:* IV administration of 50–75 ml of 40% glucose solution and ascorbic acid.

*Diabetic Coma Symptoms:* Severe hyperglycemia, glycosuria, metabolic acidosis, unconsciousness, depressed reflexes, reduced muscle and eyeball tone, dry/flushed skin, miosis, deep/labored breathing (Kussmaul respiration), acetone breath, tachycardia, hypotension.

*Treatment:* IV bolus of genetically engineered human insulin (0.1 IU/kg in 100 ml isotonic saline), under glucose monitoring.

### **Cocaine Poisoning**

Stage 1 (Stimulant Phase): Euphoria, agitation, headache, hallucinations, delirium, hyperthermia, increased reflexes, tremors, seizures, pallor, mydriasis, tachypnea, tachycardia, arrhythmia, hypertension.

*Treatment:* Gastric lavage (with activated charcoal), diazepam.

Stage 2 (Depressive Phase): Hyporeflexia, muscle atony, bradypnea, vascular collapse, coma.

*Treatment:* Gastric lavage (with activated charcoal).

### **Morphine Poisoning**

*Symptoms:* Euphoria, analgesia, sleepiness, hypothermia, tonic-clonic seizures, hyperreflexia, miosis, bradypnea, Cheyne–Stokes respiration, bronchospasm, pulmonary edema, hypotension, coma.

*Treatment:* Gastric lavage (with activated charcoal and potassium permanganate), naloxone, piracetam, caffeine, atropine.

### **Iron Preparations**

*Symptoms:* Hematemesis, bloody diarrhea, abdominal pain, cyanosis, seizures, tachycardia, vascular collapse, metabolic acidosis, hemolysis, coma.

*Treatment:* Gastric lavage (with activated charcoal and sodium bicarbonate), deferoxamine; IV sodium bicarbonate, prednisolone, phenylephrine, diazepam.

### **Cardiac Glycosides**

*Prodromal Symptoms:* Headache, anxiety, hallucinations, muscle weakness, blurred vision, xanthopsia, anorexia, nausea, vomiting, abdominal pain, bradycardia, hypertension.

*Toxic Phase:* Ventricular extrasystoles, paroxysmal tachycardia (supraventricular/ventricular), fibrillation, AV/intraventricular block, heart failure.

*Treatment:* Gastric lavage (with activated charcoal), IV metoprolol and digoxin-specific antibody fragments (digoxin immune Fab).

### **Benzodiazepine Overdose (Hypnotics and Anxiolytics)**

*Symptoms:* Lethargy, drowsiness, hallucinations, dysarthria, nystagmus, hyporeflexia, hypotonia, bradypnea, cyanosis, arrhythmia, hypotension, coma.

*Treatment:* Gastric lavage (with activated charcoal), flumazenil, caffeine, phenylephrine, furosemide.

### **Ethanol Poisoning**

*Symptoms:* Somnolence, coma, hypothermia, diminished reflexes and muscle tone, mydriasis, bradypnea, alcohol odor on breath, cyanosis, pulmonary edema, weak rapid pulse, vascular collapse.

*Treatment:* Gastric lavage (with sodium bicarbonate), naloxone, piracetam, phenylephrine, furosemide.

### **Amanita (Mushroom) Poisoning**

*Symptoms:* Delirium, hallucinations, tonic-clonic seizures, miosis, accommodation spasm, facial flushing, hyperhidrosis, bronchospasm, bronchorrhea, bradycardia, hypotension, hypersalivation, abdominal pain, diarrhea.

*Treatment:* Gastric lavage (with activated charcoal), atropine, diazepam.

### **Nitrate Poisoning**

*Symptoms:* Severe weakness, dizziness, headache, initial flushing followed by cyanosis, tachypnea, orthostatic hypotension, collapse, vomiting, methemoglobinemia.

*Treatment:* Gastric lavage (with activated charcoal), IV phenylephrine, ascorbic acid, and glucose.

### **Alkali Poisoning**

*Symptoms:* Chemical burns of lips, mouth, esophagus, and stomach; severe pain, thirst, drooling, hematemesis, bloody diarrhea, shock, bradypnea, anuria (liquefactive necrosis).

*Treatment:* Gastric lavage (with activated charcoal and weak acids—acetic or citric acid), morphine, atropine, prednisolone, IV glucose, phenylephrine, ceftazidime.

### **Iodine Poisoning**

*Symptoms:* Burning pain in the mouth, chest, and abdomen; brown discoloration of lips/tongue; hematemesis, bloody diarrhea, laryngeal edema, unconsciousness, bradypnea, weak rapid pulse, hypotension, anuria.

*Treatment:* Gastric lavage (with activated charcoal and sodium thiosulfate); IV sodium thiosulfate, sodium bicarbonate, prednisolone, morphine, atropine, norepinephrine.

### **Strong Acid Poisoning**

*Symptoms:* Burns of lips, tongue, face; sharp chest and abdominal pain; hoarseness, laryngeal edema and spasm, asphyxia, drowsiness, hematemesis, weak rapid pulse, hypotension, metabolic acidosis, hemolysis, hematuria, anuria (coagulative necrosis).

*Treatment:* Gastric lavage (with activated charcoal), magnesium oxide, IV morphine, atropine, prednisolone, glucose, sodium bicarbonate, ceftazidime.

## **Lesson 34**

### **Combination Drug Therapy and Drug Incompatibility**

*Learning objectives are to study types and mechanisms of drug incompatibility; to apply knowledge of pharmacokinetics and pharmacodynamics in evaluating the rationality of combination drug therapy.*

#### **KEY TOPICS FOR PREPARATION**

1. Types of drug interactions:
  - synergism (additive and potentiated);
  - antagonism (physical, chemical, and physiological);
  - physiological antagonism (indirect, direct competitive and non-competitive, and partial).
2. Pharmaceutical and pharmacological incompatibility of drugs.
3. Relative and absolute incompatibility. Methods for correcting relative incompatibility.
4. Pharmacokinetic incompatibility: drug interactions during absorption, distribution, biotransformation, and excretion.
5. Pharmacodynamic incompatibility: interactions resulting from synergism or antagonism at the site of action.

#### **SELF-ASSESSMENT QUESTIONS AND TASKS**

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

1. What is polypharmacy (polypragmasy), and what is its significance in modern pharmacotherapy?
2. How does the bioavailability of drugs change when co-administered with agents that enhance or inhibit intestinal motility? What are the mechanisms underlying these changes? Name pharmacological groups that affect gastrointestinal motility.
3. In which clinical situations might competition between two drugs for plasma protein binding be beneficial? Provide examples.
4. Name common inducers and inhibitors of drug biotransformation.

5. How does the excretion of weak acids and weak bases change with increasing or decreasing urine pH? Which drugs can acidify or alkalize urine?
6. What is potentiated anesthesia? Which drugs are commonly used to achieve it?
7. List examples of bactericidal and bacteriostatic antibiotics. Is it rational to use bactericidal and bacteriostatic antibiotics together? Explain your answer.
8. Can drug antagonism be therapeutically beneficial? Provide examples.

**Task 2.** Assess the outcomes and clinical significance of pharmacokinetic drug interactions.

Mechanism of action	Drug		Result of interaction
	A	B	
Change in absorption when taken orally	Alhydrate + magnesium hydroxide	Diazepam	
	Aluminum phosphate	Diclofenac	
	Ascorbic acid	Platyfillin	
	Acetylsalicylic acid	Phenytoin	
	Ferrous sulfate	Doxycycline	
	Metoclopramide	Digoxin	
	Methocinium iodide	Paracetamol	
Competition for binding to plasma proteins	Ketoprofen	Warfarin	
	Sulfadimethoxine	Glibenclamide	
Interaction during biotransformation	Carbamazepine	Propranolol	
	Rifampicin	Verapamil	
	Pefloxacin	Theophylline	
Interaction during excretion	Acetazolamide	Sulfonamides	
	Sodium bicarbonate	Lidocaine	
	Calcium chloride	Naproxen	
	Ascorbic acid	Morphine	
	Benzylpenicillin	Furosemide	

**Task 3.** Assess the outcomes and clinical significance of pharmacodynamic drug interactions.

Drug combinations	Undesirable consequences of interactions
Metoprolol + verapamil (intravenous)	
Suxamethonium iodide + neostigmine methylsulfate	
Halothane + epinephrine	
Amitriptyline + metocynium iodide	
Digoxin + acetazolamide	
Nifedipine + calcium chloride	
Warfarin + amoxicillin	
Oxacillin + doxycycline	
Gentamicin + furosemide	

**Task 4.** Determine the therapeutic value of the pharmacodynamic drug interactions. In what cases and for what diseases are combinations of drugs in the table below used for?

Drug combinations	Therapeutic effects and clinical applications <i>(to be completed by students)</i>
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 not levodopa 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? What drugs are the “first line” for pseudomembranous colitis?
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?

**Lesson 35**  
**Final Class on Medical Prescription**

**PRESCRIBE DRUGS**

1. **Adrenomimetics:** Epinephrine, Phenylephrine, Fenoterol, Salmeterol + Fluticasone
2. **Adrenergic Blocking Agents:** Tamsulosin, Metoprolol, Nebivolol
3. **M-Cholinomimetics and Cholinesterase Inhibitors:** Pilocarpine, Neostigmine Methylsulfate, Ipidacrine
4. **M-Cholinergic Blocking Agents:** Atropine, Tropicamide, Platyphylline, Tiotropium Bromide, Oxybutynin
5. **Local Anesthetics:** Lidocaine, Ropivacaine
6. **Hypnotic Drugs:** Nitrazepam, Zolpidem, Doxylamine, Flumazenil
7. **Antiepileptic Drugs:** Benzobarbital, Carbamazepine, Pregabalin, Valproic Acid
8. **Opioid Analgesics and Their Antagonists:** Morphine, Trimeperidine, Fentanyl, Tramadol, Naloxone
9. **Non-Opioid Analgesics:** Paracetamol
10. **Antiparkinsonian Drugs:** Levodopa + Carbidopa, Pramipexole, Trihexyphenidyl
11. **Drugs for the Treatment of Migraine:** Sumatriptan
12. **Psychotropic Drugs:** Droperidol, Clozapine, Diazepam, Duloxetine, Sertraline, Caffeine, Piracetam
13. **Drugs Affecting the Respiratory System:** Bromhexine, Aminophylline
14. **Cardiac Glycosides:** Digoxin
15. **Antiarrhythmic Drugs:** Procainamide, Amiodarone, Esmolol
16. **Calcium Channel Blockers:** Verapamil, Nifedipine, Amlodipine
17. **Antianginal Drugs:** Nitroglycerin, Isosorbide Mononitrate
18. **Drugs to Improve Cerebral Circulation:** Vinpocetine
19. **Lipid-Lowering Drugs:** Rosuvastatin, Ezetimibe
20. **Drugs Affecting the Renin-Angiotensin System:** Enalapril, Losartan
21. **Diuretics:** Mannitol, Furosemide, Torasemide, Hydrochlorothiazide, Indapamide, Spironolactone

22. **Drugs Affecting the Myometrium:** Oxytocin, Hexoprenaline
23. **Drugs Affecting the Digestive System:** Omeprazole, Aluminum Phosphate, Bismuth Tripotassium Dicitrate, Metoclopramide, Drotaverine, Bisacodyl, Ursodeoxycholic Acid
24. **Hematopoietic Stimulants:** Sorbifer Durules\*, Cyanocobalamin
25. **Drugs Affecting Blood Coagulation:** Clopidogrel, Acetylsalicylic Acid, Rivaroxaban, Sodium Heparin, Enoxaparin Sodium, Warfarin, Menadione Sodium Bisulfite
26. **Hormonal and Antihormonal Agents:** Levothyroxine Sodium, Thiamazole, Soluble Insulin [human recombinant], Gliclazide, Sitagliptin, Metformin, Empagliflozin, Prednisolone, Beclomethasone
27. **Non-Steroidal Anti-Inflammatory Drugs (NSAIDs):** Diclofenac, Meloxicam, Etoricoxib
28. **Antiallergic Drugs:** Diphenhydramine, Loratadine, Cetirizine, Cromoglicic Acid
29. **Antiseptics:** Potassium Permanganate, Nitrofuril
30. **Antibiotics:** Amoxicillin + Clavulanic Acid, Ceftriaxone, Ceftazidime, Meropenem, Rifampicin, Doxycycline, Azithromycin, Clarithromycin
31. **Drugs for the Treatment of Tuberculosis:** Isoniazid
32. **Fluoroquinolones:** Ciprofloxacin, Levofloxacin
33. **Antiviral Drugs:** Acyclovir, Oseltamivir
34. **Antiparasitic Drugs:** Metronidazole
35. **Anthelmintics:** Mebendazole, Praziquantel
36. **Antidotes and Drugs for the Treatment of Poisoning:** Sodium Bicarbonate, Sodium Thiosulfate, Flumazenil

### PHARMACOTHERAPEUTIC QUESTIONS

1. Drug for the management of vascular collapse.
2. Drug for the treatment of glaucoma.
3. Drug for the treatment of myasthenia gravis.
4. Drug for renal colic.
5. Drug for infiltration anesthesia.
6. Drug for the treatment of insomnia.
7. Drug for the treatment of epilepsy.

8. Analgesic for the prevention of shock in trauma.
9. Drug for the treatment of Parkinson's disease.
10. Drug for the treatment of migraine.
11. Drug for the treatment of psychosis.
12. Drug for the treatment of anxiety.
13. Drug for the treatment of depression.
14. Drug for the treatment of asthenia.
15. Drug for bronchial asthma.
16. Drug for chronic heart failure.
17. Drug for atrial fibrillation.
18. Drug for angina pectoris.
19. Drug for myocardial infarction.
20. Drug for the treatment of atherosclerosis.
21. Drug for arterial hypertension.
22. Drug for ischemic stroke.
23. Drug for peptic ulcer disease.
24. Drug for constipation.
25. Drug for anemia.
26. Drug for thrombophlebitis.
27. Drug for stimulation of labor.
28. Drug for diabetes mellitus.
29. Drug for hypothyroidism.
30. Drug for thyrotoxicosis.
31. Drug for rheumatoid arthritis.
32. Drug for allergic diseases.
33. Drug for wound irrigation.
34. Drug for the treatment of pneumonia.
35. Drug for the treatment of sepsis.
36. Drug for the treatment of dysentery.
37. Drug for the treatment of tuberculosis.
38. Drug for the treatment of influenza.
39. Drug for the treatment of herpes.
40. Drug for the treatment of trichomoniasis.

## **EXAM QUESTIONS**

### **GENERAL PHARMACOLOGY**

1. Pharmacology: objectives, research methods, and its place within the medical sciences. Pharmacokinetics and pharmacodynamics.
2. Enteral routes of drug administration: medical significance, advantages, and disadvantages.
3. First-pass metabolism and enterohepatic circulation: clinical relevance, and examples of drugs undergoing these processes.
4. Parenteral drug administration (subcutaneous, intramuscular, intravenous): characteristics and clinical relevance.
5. Parenteral administration (intra-arterial, subarachnoid, epidural, inhalation, and topical application): characteristics and clinical significance.
6. Drug absorption: types of membrane transport and factors influencing absorption. Bioavailability: clinical importance and influencing factors.
7. Biological barriers and drug permeability (capillary endothelium, blood-brain barrier, placental barrier).
8. Drug distribution in organs and tissues: influencing factors and volume of distribution.
9. Drug biotransformation: endobiotics vs xenobiotics, biological significance, metabolizing enzymes, and types of reactions.
10. Drug clearance: types, influencing factors, and metabolism kinetics. Phases I and II of drug metabolism.
11. Pharmacological effects, primary pharmacological responses, and receptor interactions: agonists and antagonists.
12. Receptor localization, classification, and functions.
13. Drug selectivity. Principles of drug classification.
14. Drug accumulation (cumulation): mechanisms and clinical significance.
15. Tolerance and tachyphylaxis: mechanisms and clinical relevance.
16. Drug abuse, addiction, and dependence: mechanisms and medical implications.

17. Individual variability in drug response: influence of ethnicity, age, comorbidities, and genetic factors.
18. Drug synergy: types, mechanisms, and clinical importance.
19. Drug antagonism: types, mechanisms, and clinical importance.
20. The importance of synergism and antagonism in the combined use of chemotherapeutic agents.

## **DRUGS AFFECTING THE AUTONOMIC NERVOUS SYSTEM**

1. Types of peripheral nerves and neurotransmitters.
2. Adrenergic synapses: localization, structure, and functions.
3. Adrenergic receptors: types, localization, and functions.
4. Epinephrine: mechanism of action, therapeutic uses, and adverse effects.
5.  $\alpha$ -Adrenergic agonists: classification, mechanisms of action, therapeutic uses, and side effects.
6.  $\beta$ -Adrenergic agonists: mechanism of action, clinical uses, and adverse effects.
7.  $\alpha$ -Adrenergic antagonists: classification, mechanisms, clinical applications, and side effects.
8.  $\beta$ -Adrenergic blockers: classification, mechanisms of action, and adverse effects.
9. Cholinergic synapses: localization, structure, and function.
10. Cholinergic receptors: types, distribution, and functions.
11. Muscarinic receptor agonists: classification, mechanisms of action, therapeutic uses, and side effects.
12. Cholinesterase inhibitors: classification, mechanisms of action, indications, and side effects.
13. Antimuscarinic agents: classification, mechanisms of action, ophthalmic applications, and adverse effects.
14. Acute atropine poisoning: stages, pathogenesis, symptoms, and management.
15. Non-depolarizing muscle relaxants: classification, mechanisms, synergists, antagonists, indications, and side effects.
16. Depolarizing muscle relaxants: mechanism of action, synergists, indications, and adverse effects.

17. Organophosphate poisoning: symptoms, pathophysiology, and treatment.

## **DRUGS AFFECTING MAJOR ORGANS AND SYSTEMS**

1. Antitussives and expectorants: classification, mechanisms of action, indications, and adverse effects.
2. Bronchodilators: classification, mechanisms, uses in asthma and obstructive syndromes, and side effects.
3. Cardiac glycosides: effects on heart rate, conduction system, hemodynamics, and renal function; indications.
4. Digitalis toxicity: stages, pathogenesis, symptoms, and management.
5. Antiarrhythmic agents (Class I): mechanisms of action, indications, and side effects.
6. Calcium channel blockers: classification, mechanisms of action, indications, and adverse effects.
7. Nitrates: mechanisms of action, clinical applications, and side effects.
8. Lipid-lowering drugs: principles, classification, statin mechanisms, indications, and side effects.
9. Diuretics: mechanisms of action and classification.
10. Carbonic anhydrase inhibitors and osmotic diuretics: mechanisms, indications, and adverse effects.
11. Loop, thiazide, and thiazide-like diuretics: mechanisms, indications, and adverse effects.
12. Potassium-sparing diuretics: mechanisms, indications, and side effects.
13. ACE inhibitors: mechanisms of action, indications, and side effects.
14. Angiotensin II receptor blockers (ARBs): mechanisms of action, indications, and side effects.
15. Antiemetics: classification, mechanisms, indications, and side effects.
16. Gastric acid-reducing drugs: classification, mechanisms, indications, and side effects.
17. Laxatives: classification, mechanisms, uses, and side effects.

18. Uterotonic and tocolytic agents: classification, mechanisms, indications, and side effects.
19. Antiplatelet agents: classification, mechanisms, indications, and side effects.
20. Heparin: origin, structure, mechanism of action, indications, and side effects. Direct thrombin and factor Xa inhibitors.
21. Low molecular weight heparins (LMWHs): mechanisms, indications, and adverse effects.
22. Warfarin: mechanism of action, indications, and side effects.
23. Thrombolytic agents: mechanisms, clinical uses, and adverse effects.
24. Fibrinolytics: classification, mechanisms, clinical uses, and side effects.
25. Iron preparations: metabolism, classification, mechanism of action, uses, and adverse effects.
26. Cyanocobalamin (Vitamin B12): metabolism, therapeutic uses, and side effects.
27. Type 1 diabetes mellitus therapy: insulin and analogues.
28. Type 2 diabetes mellitus therapy: classification, mechanisms, and side effects.

## **ANTI-INFLAMMATORY AND ANTI-ALLERGIC DRUGS**

1. Antihistamines: classification, mechanisms of action, clinical uses, and side effects.
2. NSAIDs: anti-inflammatory mechanisms and therapeutic indications.
3. NSAIDs: analgesic and antipyretic mechanisms and side effects.
4. Glucocorticoids: classification, mechanisms of anti-inflammatory, immunosuppressive, and antiallergic actions; indications and adverse effects.

## **CENTRAL NERVOUS SYSTEM PHARMACOLOGY**

1. General anesthesia: stages and classification of anesthetics.
2. Inhalation anesthetics: common features, drugs, mechanisms, and adverse effects.

3. Intravenous anesthetics: characteristics, systemic effects, and side effects.
4. Ethanol: mechanism of action and therapeutic uses.
5. Acute ethanol intoxication: pathogenesis, symptoms, and treatment.
6. Hypnotics: classification, mechanisms of action, effects on sleep stages, indications, and side effects.
7. Antiepileptic drugs: classification, mechanisms, contraindications, and side effects.
8. Opioid analgesics: receptor types, mechanisms, and classification.
9. Opioid use: therapeutic indications, side effects, and contraindications.
10. Paracetamol: mechanism of action, uses, and adverse effects.
11. Anxiolytics: GABAergic mechanisms, uses, and side effects.
12. Benzodiazepine overdose: symptoms and management.
13. Parkinson's disease: pathophysiology, dopamine pathways, and drug classification.
14. Dopaminergic agents: mechanisms, indications, and adverse effects.
15. Antimuscarinic and NMDA antagonists in Parkinson's disease: mechanisms, indications, and contraindications.
16. Alzheimer's disease drugs: mechanisms and side effects.
17. Migraine therapy: mechanisms, characteristics, and adverse effects.
18. Typical antipsychotics: classification, mechanisms of antipsychotic and sedative effects, indications.
19. Atypical antipsychotics: classification, mechanisms, therapeutic uses.
20. Antidepressants: TCAs and SSRIs – mechanisms, uses, and adverse effects.
21. MAO inhibitors: classification, mechanisms, indications, and contraindications.
22. CNS stimulants: classification, mechanisms, indications, and side effects.
23. Local anesthetics: classification, mechanisms, indications, and side effects.

## **ANTIMICROBIAL AND ANTIVIRAL DRUGS**

1. Classification of antibiotics based on mechanism of action.
2. Bacterial resistance: mechanisms, prevention, and control strategies.
3. Penicillins: mechanisms, spectrum, classification, therapeutic use, resistance, and adverse effects.
4. Cephalosporins: mechanisms, classification, uses, resistance, and adverse effects.
5. Carbapenems: mechanisms, classification, therapeutic uses, and resistance.
6. Tetracyclines: mechanisms, classification, uses, resistance, and side effects.
7. Aminoglycosides: mechanisms, classification, uses, and toxicity.
8. Macrolides: mechanisms, classification, uses, resistance, and side effects.
9. Quinolones: mechanisms, spectrum, uses, resistance, and adverse effects.
10. Sulfonamides: mechanisms, classification, therapeutic uses, resistance, and adverse effects.
11. Antitubercular drugs: classification, mechanisms, resistance, and side effects.
12. Antifungals: classification, spectrum, resistance, and adverse effects.
13. Antiviral drugs for herpes: classification, mechanisms, uses, and adverse effects.
14. Antiretroviral therapy (HIV): classification, mechanisms, uses, and side effects.
15. Antiseptics: classification, mechanisms, practical applications, resistance, and adverse effects.

## **DRUGS REGULATING METABOLIC PROCESSES**

1. Vitamins A and E: sources, metabolic significance, uses, and hypervitaminosis A.
2. Vitamin D: sources, metabolic and hormonal roles, uses, and hypervitaminosis D.

3. Vitamins B<sub>1</sub> and B<sub>6</sub>: sources, metabolic roles, and therapeutic applications.
4. Vitamin B<sub>2</sub> and niacin: sources, roles, and clinical significance.
5. Vitamin C: sources, metabolic roles, and clinical use.
6. Thyroid and antithyroid drugs: mechanisms, uses, and adverse effects.

## ANSWERS

### Lesson 5. General pharmacology. Pharmacokinetics

#### Task 2

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

#### Case tasks

1. Correct answer: 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 pKa of 4,8, will be mainly nonionized in the gastric lumen and 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. Half 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, 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” the plasma level for each half-life results in an initial plasma level at zero time ( $C_0$ ) =  $5 \text{ mg/L} \times 2 \times 2 = 20 \text{ mg/L}$ .

$$\begin{aligned} \text{Dose} &= C_0 \times V_d \\ &= 20 \text{ mg/L} \times 10 \text{ L} \\ &= 200 \text{ mg} \end{aligned}$$

1. As a result of hypoalbuminemia, the free pharmacologically active fraction of warfarin increased in the patient.
2. Correct answer: 80. The volume of distribution ( $V_d$ ) of a drug is independent of the dose.  $V_d = D \times F/C_{p0}$ , where  $D$  = dose,  $F$  = fraction absorbed, and  $C_{p0}$  = 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  $V_d$  will remain the same.
3. Correct answer: 60. The dose of a drug can be calculated using the equation  $\text{Dose} = V_d \times C_{p0}/F$ , where  $V_d$  = volume of distribution,  $C_{p0}$  = plasma concentration at time 0, and  $F$  = fraction absorbed. Because the  $V_d$  of the obese patient is twice the  $V_d$  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 2

- a. 1D, 2A, 3B, 4C, 5E
- b. 1A, 2C, 3B, 4D
- c. 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. 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 the hepatic metabolism of diazepam metabolism.
4. Correct answer: d. The 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: 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 the effects of the drugs:
7. Withdrawal syndrome
8. Withdrawal syndrome
9. 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, the 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 B2.

2. The described symptoms are retinol vitamin deficiency (vitamin A) associated with inadequate dietary intake. It binds to the cytosolic receptors (retinol-binding proteins), after which vitamin A penetrates the nucleus. In the nucleus, it causes repression, thereby regulating the biosynthesis of certain proteins (membrane glycoproteins). Retinol stimulates cell proliferation, and epithelialization and prevents keratinization of the epithelium. In retinol vitamin deficiency the skin becomes dry, and 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 the 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 a 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 D3) 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 that 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 minerals, 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 (part 1)**

### 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. 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. Hormonal and antihormonal drugs (part 2)**

### Task 3

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

### Case tasks

1. Addison's disease is a progressive hypofunctioning of the adrenal cortex. Mineralocorticoid deficiency results in increased excretion of Na<sup>+</sup> and decreased excretion of K<sup>+</sup>, whereas glucocorticoid deficiency contributes to postural hypotension and causes severe insulin sensitivity. Gluconeogenesis is impaired, and hypoglycemia results. Decreased blood cortisol causes increased pituitary adrenocorticotrophic hormone (ACTH) production and increased blood  $\beta$ -lipotropin, which has melanocyte-stimulating activity. Both ACTH and  $\beta$ -lipotropin cause hyperpigmentation of the skin and mucous membranes characteristic of Addison's 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 is used for glucocorticoid supplementation.
2. 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 muscle changes. 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.
3. Correct answer: e. Acute bursitis results from the inflammation of a fluid-filled sac, the bursa, which is located between two surfaces that rub together when moving. The inflammation has a rapid onset and can be very uncomfortable. Intra-articular

injections of glucocorticoids provide rapid relief because of their powerful anti-inflammatory activity. This effect is mediated by a vast array of actions, including the induction of the synthesis of lipocortins. These enzymes act as inhibitors of phospholipase A2, the enzyme that catalyzes the release of arachidonic acid from membrane phospholipids. Because arachidonic acid is the precursor of eicosanoids, the corticosteroid-induced induction of lipocortins leads to an inhibition of phospholipase A2 and, in turn, to an inhibition of biosynthesis of all eicosanoids, which are proinflammatory compounds.

4. Correct answer: f. Progestin alone (daily progestin tablets or implantable preparation) is the best hormonal contraceptive for women with an abnormal coagulation history, as in this case. Estrogens must be avoided because they increase blood coagulability. Mifepristone is not currently available as a regular contraceptive preparation.

## **Lesson 10. 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  $\alpha$ 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 reflex bradycardia in patients with intact innervation of the heart for the following reason: the increase in blood pressure due to activation of  $\alpha$ 1-receptors activates baroreceptors located in the carotid sinus and aortic arch (baroreceptors are stretch receptors). This increases the firing rate to the nucleus of the tractus solitaries in the medulla, which in turn increases its firing 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  $\beta$  receptors; therefore, bradycardia ensues.

3. Historically, the presence of diabetes was a contraindication for  $\beta$ -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  $\beta$ -blockers following myocardial infarction experience a 30 to 35% reduction in mortality. Therefore,  $\beta$ -blockers can be given to diabetic patients, but they must carefully control their sugar levels. In fact, hypoglycemia-associated tachycardia can be blunted by  $\beta$ -blockers, depriving the patient of an important diagnostic sign.
4. The patient was mostly given a nonselective  $\beta$ -blocker propranolol (antagonizes both  $\beta_1$  and  $\beta_2$  receptors) that made her asthma worse due to  $\beta_2$  antagonism. An alternative is to prescribe a cardioselective (antagonizes only  $\beta_1$ )  $\beta$ -blocker that does not antagonize  $\beta_2$  receptors in the bronchioles. For example, metoprolol is a cardioselective  $\beta$ -blocker.

### **Lesson 11. Drugs affecting functions of cholinergic synapses (M, N-cholinomimetics, M-cholinomimetics, cholinesterase inhibitors, M-cholinoblockers)**

#### Task 3

- a. 1G, 2D, 3E, 4F, 5B, 6C, 7A
- b. 1B, 2C, 3A, 4D

#### 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 M2 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 present 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 blackberries of deadly nightshade (*Atropa belladonna*), a plant containing antimuscarinic alkaloids (mainly atropine and scopolamine). The antimuscarinic syndrome is due to the 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 M3 receptors in sweat glands promotes sweating. By blocking M3 receptors, atropine can counteract this action.

**Lesson 12. 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

1. 1A, 2B, 3E, 4C, 5D
2. 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. Local anesthetics are weak bases; all but benzocaine have a pKa 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 a spasm of muscles around the eye that causes involuntary blinking and eye closing. Injection of botulinum toxin into 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 14. Antiseptic, disinfectant, antifungal, antiparasitic drugs**

### Task 3

1. 1A, 2B, 3D, 4C
2. 1A, 2D, 3C, 4B
3. 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. The 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. The 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 the 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. The patient's symptoms indicate that he was most likely suffering from the 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 thiosulfate — IV, ceftazidime — IM.

## **Lesson 15. Antibiotics and anticancer drugs**

### Task 3

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

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

### Case tasks

1. The 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 manifestations 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 antimicrobial therapy, which involves initial treatment with amoxicillin or trimethoprim-sulfamethoxazole. If this regimen does not reduce symptoms within 3 days, amoxicillin/clavulanate cefuroxime or ceftriaxone should be substituted for the initial therapy, as was done in this case. Potassium clavulanate is a  $\beta$ -lactamase inhibitor that blocks many, but not all,  $\beta$  lactamase enzymes, protecting amoxicillin from inactivation by  $\beta$ -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 ( $\text{Ca}^{2+}$ ,  $\text{Mg}^{2+}$ ,  $\text{Fe}^{2+}$ ,  $\text{Al}^{3+}$ ) 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 16. Sulfonamides, quinolones, antituberculosis, antiviral, antimalarial drugs**

### Task 3

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

### Case tasks

1. Oseltamivir is the best choice since it is administered orally and is not associated with resistance.
2. Correct answer: 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 infections. 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 the 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 malaria species.

## **Lesson 18. General anesthetics, sleeping pills, ethanol**

### Task 3

1. 1A, 2C, 3D, 4B, 5E
2. 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. The correct answer is b. Z-hypnotics (zolpidem, zaleplon) bind selectively to the  $\alpha 1$  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  $\text{Cl}^-$ -channels, leading to an increase in  $\text{Cl}^-$  conductance. The enhanced concentration of  $\text{Cl}^-$  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-off action that makes the withdrawal syndrome less severe but longer in duration.

1. Correct answer: c. Ethanol withdrawal can occur when an alcoholic person is forced to stop drinking because of some external event, such as 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 which typically occurs 8 to 48 hours after the last ethanol intake.

## **Lesson 19. Antiepileptic drugs. Opioid analgesics**

### Task 3

1. 1E, 2C, 3D, 4B, 5A
2. 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
1. Correct answer: 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 the partial pressure of arterial carbon dioxide ( $\text{PaCO}_2$ ).
2. 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.

3. 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. The onset of enzyme induction is at about 3 days, with maximum effect at about 30 days.
4. 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.
5. 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 20. Drugs for neurodegenerative diseases. Drugs for the treatment of migraine**

### Task 3

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

### Case tasks

1. 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. The man was most likely in the early stages of Alzheimer's 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 the treatment of AD.

3. Correct answer: 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  $\beta_1$  and  $\beta_2$ -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. The correct answer is d. Triptans (e.g., sumatriptan and zolmitriptan) are specific 5-HT<sub>1B/1D</sub> agonists that are equally as or more effective than ergot alkaloids in the acute treatment of migraine attacks.

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

- Vasoconstriction of cerebral vessels via the activation of vascular 5-HT<sub>1B</sub> receptors
- Inhibition of release of neuropeptides with inflammatory properties via the activation of presynaptic 5-HT<sub>1D</sub> receptors

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

1. Correct answer: 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 21: Antipsychotic, anxiolytic, and sedatives**

### Task 3

1. 1D, 2A, 3C, 4B
2. 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 a 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. The poor response to several neuroleptic drugs and the prevalence of negative symptoms of schizophrenia indicates 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. Amenorrhea and galactorrhea are adverse effects of neuroleptics that are related to their blockade of D2 receptors in the anterior pituitary gland. Dopamine acts as a prolactin-inhibiting factor by activating these receptors in the pituitary. When D2 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. 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 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. 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 22. Antidepressants, psychostimulants, nootropic drugs, analeptics**

### Task 3

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

### Case tasks

1. Correct answer: 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.

1. 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. John's 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),  $\beta$ -blockers for tachycardia and autonomic instability, and dantrolene for hyperthermia.

2. 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 the failure of a selective serotonin reuptake inhibitor (SSRI) therapy, as in this case.
3. The history and symptoms of the patient indicate that she was most likely suffering from the depressive phase of bipolar disorder. 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 24. Drugs affecting the functions of the respiratory system and myometrium**

### Task 3

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

### Case tasks

1. Systemic corticosteroids are given in cases of severe asthma exacerbation for two main reasons:
  1. They improve the responsiveness of  $\beta_2$  receptors.
  2. 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  $\beta_2$ -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  $\beta_2$ -agonist.

1. 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).

2. 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 sub-analgesic doses. This respiratory depression does not occur with dextromethorphan.
3. 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  $\beta_2$  receptors to  $\beta_2$ -agonists.
4. 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 25. Drugs affecting the functions of the digestive system**

### Task 3

1. 1A, 2C, 3E, 4D, 5B
2. 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. The correct answer is e. Metoclopramide is a dopamine D<sub>2</sub>-receptor antagonist, a serotonin 5-HT<sub>3</sub>-receptor antagonist, and a serotonin 5-HT<sub>4</sub>-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<sub>2</sub>-receptors and 5-HT<sub>3</sub>-receptors in the chemoreceptor trigger zone can explain the antiemetic activity of the drug.

3. NaHCO<sub>3</sub>. All antacids can cause metabolic alkalosis, due to the spared endogenous bicarbonate that is secreted in the stomach under prostaglandin E<sub>2</sub> 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 of less than 30%.
4. The 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. It is appropriate to treat this patient with a proton pump inhibitor (PPI) to reduce acid production and promote healing.

## **Lesson 26. Cardiotonic and antiarrhythmic drugs**

### Task 3

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

### Case task

1. The patient's signs and symptoms indicate a pulmonary disorder. Microbial infection 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  $\beta$ -blocker that can block potassium channels (a property not related to  $\beta$ -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: 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 mEq/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 provision of digoxin antibodies are the rational therapy for this case.

## **Lesson 27. Antianginal drugs. Lipid-lowering drugs**

### Task 3

1. 1A, 2D, 3C, 4B, 5E
2. 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: 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 patients 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 28. 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
1. 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.
1. The 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.
2. Correct answer: 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 29. Drugs affecting blood pressure

### Task 3

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

### Case tasks

1. Long-term use of amlodipine (calcium channel blocker) can cause ankle edema and constipation.
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: 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: 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  $\beta_1$ -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  $\alpha_1$ -adrenergic activity such as norepinephrine, phenylephrine, and dopamine are used to restore the arteriolar tone, thus counteracting the decreased blood pressure.

## Lesson 30. 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 B12 malabsorption due to severe atrophy of the gastric glands with loss of parietal cells and inability to secrete intrinsic factors. 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 multivitamins 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 32. 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 H1 antagonists, second-generation H1 antagonists are devoid of blocking activity on muscarinic receptors. Therefore, they do not have effects on pupil size and accommodation when applied to the conjunctiva. This explains why only second-generation is used for this disorder.
3. Correct answer: 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: 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 34. 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 D2 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 is caused by 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 inhibitors (including diclofenac), inhibiting the synthesis of substances with vasodilator and diuretic effect — prostacyclin and prostaglandin E2, prevent the decrease in blood pressure, which occurs during treatment with angiotensin-converting enzyme inhibitors and promotes hyperkalemia and nephrotoxicity.

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# **PHARMACOLOGY**

## **PRACTICAL MANUAL**

Course manual

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