

**Ministry of health of Republic Belarus**  
**Educational institution**  
**«Gomel state medical university»**

Department of General and Clinical Pharmacology

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**METHODICAL RECOMMENDATIONS**

for a practical lesson on the discipline "Pharmacology"  
for the third-year students of the Faculty of Foreign Students,  
studying at the specialty 1-79 01 01 "General medicine"

**TOPIC 14: « ANXIOLYTICS. SEDATIVES. ANTIDEPRESSANTS.**  
**NORMOTHYMIC, NOOTROPIC, PSYCHOSTIMULATING AGENTS.**  
**ANALEPTIC DRUGS»**

Time is 3 hours

Approved at the meeting of the department of general and clinical pharmacology  
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## **LEARNING AND EDUCATIONAL GOALS, OBJECTIVES, MOTIVATION FOR LEARNING THE TOPIC**

The theme "Anxiolytics. Sedatives. Antidepressants. Normotimic, nootropic, psychostimulating agents. Analeptic agents" continues the topic of drugs that regulate the functions of the central nervous system. Mental disorders are one of the most important problems of modern medicine, primarily because of their high prevalence, which is steadily increasing every year. In this case, the number of patients with psychoses increases to a lesser extent in comparison with the number of patients with neurotic disorders. As a result, the prevalence of neurotic disorders takes an increasing place in the structure of mental illness. Thus, according to WHO (2016), about 100 million experience anxiety and depression among 870 million people living in the European Region; over 21 million people suffer from alcohol-related disorders; more than 7 million have Alzheimer's disease and other types of dementia; about 4 million have schizophrenia; 4 million bipolar affective disorders and 4 million more panic disorders. Such a wide spread of neurotic and mental disorders leads to the fact that doctors of many specialties have to face with such patients in their practice. Consequently, every future doctor, regardless of the future profile chosen, should know their pharmacological properties, rules for storage, prescribing and use.

### **Learning purpose:**

-to learn to evaluate the possibilities of using psychotropic drugs and analeptics taking into account their pharmacokinetic and pharmacodynamic features, indications and contraindications to the use. To know the complications arising from the use of these medicines in practical medicine and their overdose treatment. Be able to prescribe in the prescriptions the main drugs from the above groups, taking into account the presence of concomitant disease and, if necessary, calculating the doses, depending on the age and body weight of the patients.

### **Educational purpose:**

- to develop one's value-personal, spiritual potential, to form the qualities of a patriot and a citizen, ready for active participation in the economic, industrial, socio-cultural and public life of the country; to realize the social significance of their future professional activities, to learn to observe educational and labor discipline, the norms of medical ethics and deontology.

### **Tasks:**

As a result of the training session, the student must

#### **know:**

- the basis of information on the anatomy and physiology of the central nervous system;
- the concept of neuroses, affective-emotional disorders, violations of cognitive functions of the brain;
- classifications, pharmacokinetic and pharmacodynamic features of medicines on the topic of the class;
- complications with the use of these medicines, assistance with their overdose, indications and contraindications to the use.

#### **be able to:**

- to make an informed choice of medicines taking into account the clinical diagnosis of the patient, information about concomitant diseases, individual intolerance, features of pharmacodynamics and pharmacokinetics of the drug;
- substantially replace one drug with another;
- determine the dose and frequency of medication taking into account the concomitant pathology and individual characteristics of the patient;
- prescribe medications on the topic of the lesson;
- analyze the medical prescriptions and make the necessary adjustments;
- analyze "instructions for specialists" and "instructions for patients" of drugs.

**own:**

- skills in using basic pharmacokinetic parameters and information about the dependence of pharmacodynamics on the properties of the antidepressants, nootropic, psychostimulating drugs, anxiolytics, sedatives, normothymic drugs, analeptics, conditions of their use, features of their release forms, dose regimen and ways of delivering drugs to the body;
- the rules of prescribing the studied drugs for the treatment, prevention of various diseases and pathological conditions, taking into account the indications;
- skills in choosing the antidepressants, nootropic, psychostimulating drugs, anxiolytics, sedatives, normothymic drugs, analeptics for medical measures for the most common diseases and conditions in the adult population and adolescents;
- skills of searching, analyzing and summarizing information about the use and operation of tools on the topic of the lesson.

**Motivation for mastering the topic:**

The specifics of the training of doctors in this specialty determines the need for students to purposefully study knowledge about the classification, pharmacokinetic and pharmacodynamic properties, indications for prescribing and side effects of the antidepressants, nootropic, psychostimulating drugs, anxiolytics, sedatives, normothymic drugs, analeptics.

## **MATERIAL EQUIPMENT**

Reference and information literature, diagrams, tables, presentations, collection of medicines.

## **CONTROL QUESTIONS FROM RELATED DISCIPLINES**

1. Serotonergic, dopaminergic and adrenergic processes in the central nervous system.
2. Limbic system, its structure and functions.

## **CONTROL QUESTIONS ON THE TOPIC OF THE LESSON**

1. Anxiolytic, sedative and hypnogenic effects - essence, similarities and differences. Chemical classes and pharmacological groups of drugs used in psychoneurotic disorders.
2. Anxiolytics: alprazolam, diazepam, oxazepam, chlordiazepoxide, buspirone hydrochloride. The role of the GABA mediator in the development of inhibitory processes in the central nervous system and the receptor mechanisms of the action of anxiolytics. The concept of "daytime" anxiolytics. Indications for use of anxiolytics. Differences in the side effects of neuroleptics and anxiolytics.

3. Sedatives (sedatives): phytopreparations of valerian, motherwort; bromides (sodium bromide); combined funds (Corvalol). The concept of sedative action. Classification of sedatives by origin. Features of the action of bromides (the work of the school of Pavlov). Pharmacology of salts of bromine, magnesium sulfate. Complications of therapy. Antidotes. Features of the use of plant and mixed sedatives.

4. Neurophysiological and molecular mechanisms of action of anxiolytic and sedatives, pharmacological effects, pharmacokinetics, side and toxic effects. Fields of application of anxiolytics and sedatives, restrictions on their use.

5. Antidepressants (thymoanaleptics). Classification. Tricyclic antidepressants (imipramine, amitriptyline). Selective inhibitors of neuronal reuptake of norepinephrine and serotonin (venlafaxine). Selective inhibitors of neuronal reuptake of serotonin (fluoxetine, sertraline). Selective norepinephrine reuptake inhibitors (maprotiline, reboxetine). Atypical antidepressants (mirtazapine, mianserin, tianeptine, trazadone). Monoamine oxidase inhibitors (moclobemide). Principles of pharmacotherapy for depressive states, pharmacodynamics (influence on biogenic brain amines, receptor and post-receptor effects) and pharmacokinetics of antidepressants, use and side effects.

6. Normotimic (antimanic) drugs: lithium salts (lithium carbonate), anticonvulsants, antipsychotics, benzodiazepines. Mechanism of action and pharmacokinetics of lithium salts. The use of lithium preparations in medicine: indications, side effects, contraindications. Differences in indications for the use of antidepressants and normotimics.

7. Nootropics: piracetam, vinpocetine, nimodipine, donepezil hydrochloride, memantine. Mechanism of action, the role of GABA in the realization of the cognitive functions of the central nervous system.

8. Psychostimulants: caffeine, mesocarb. Differences in the use of nootropic drugs and psychostimulants.

9. Analeptic agents: almitrin, doxapram hydrochloride, bemegrid, niketamide, caffeine sodium benzoate. Selectivity of pharmacological effects and indications for the use of various drugs in this group.

10. Molecular and neurophysiological mechanisms of action, pharmacological effects, use, side effects, indications and contraindications for the use of nootropic, psychostimulating, analeptic drugs.

11. Comparative characteristics of the main drugs – representatives of anxiolytics, sedatives, antidepressants, normotimic, nootropic, psychostimulating and analeptic agents for pharmacological properties, indications, side effects.

## **THE COURSE OF THE LESSON**

### **The theoretical part**

Theoretical questions are set out in the appendix to the methodological recommendations.

### **The practical part**

1. Take notes of the theoretical material demonstrated by the teacher;
2. To master the methodology of solving problems and prescribing prescriptions on the topic of employment.

### **Monitoring the assimilation of the topic**

It is carried out in the form of independent written work (solving practical tasks and prescribing prescriptions for individual tasks).

## **METHODOLOGICAL RECOMMENDATIONS FOR THE ORGANIZATION AND IMPLEMENTATION OF THE INDEPENDENT WORK OF STUDENTS**

**The time allotted for independent work can be used by students on:**

- preparation for practical classes;
- completing assignments on the topic of the lesson in the workbook;
- preparation of thematic reports, abstracts, presentations;
- taking notes of educational literature.

**The main methods of organizing independent work:**

– performing test tasks and practical tasks of the EEMC for self-control and self-assessment.

**The list of tasks of the independent work of students:**

- solving practical tasks of the EEMC;
- execution of test tasks of the EEMC.

**The control of the independent work of students is carried out in the form of:**

- evaluation of an oral answer to a question, a message, a report or a solution to a problem in practical classes;
- individual conversation.

## **METHODOLOGICAL RECOMMENDATIONS FOR THE ORGANIZATION AND IMPLEMENTATION OF THE USRS**

**Recommended forms of independent work of students organization:**

- completing assignments on the topic of the lesson in the workbook;
- writing an abstract on a given topic;
- preparation of a report and multimedia presentation on a given topic.

**List of independent work of students tasks:**

Topics of abstracts / multimedia presentations:

1. Modern directions of synthesis of effective neurotropic drugs against the background of widespread psychoemotional disorders and neuralgic pain syndrome (complete the teaching workbooks).
2. Pharmacological and social consequences of the use of hallucinogens.

**Forms of control over the implementation of independent work of students:**

- review and evaluation of the abstract on a given topic;
- checking and evaluating a multimedia presentation on a given topic.

## **LIST OF REFERENCES**

1. Kharkevitch, D. A. Pharmacology : textbook for med. students : transl. of 12th ed. of Russ. textbook "Pharmacology" (2017) / D.A. Kharkevitch. - 2nd ed. - Москва : ГЭОТАР-Медиа, 2019. - 676 с. : ил., табл. - Рек. ФГАУ "ФИРО".–Режим доступа: <http://www.studmedlib.ru/book/ISBN5970402648.html> – Дата доступа: 03.05.2021.
2. Конорев, М. Р. Курс лекций по фармакологии. В 2 т. Т. 2, ч. 1: для студентов 3 и 4 курсов фармацевт. фак. учреждений высш. образования, обучающихся по специальности 1 - 79 01 08 "Фармация" / М. Р. Конорев, И. И. Крапивко, Д. А. Рождественский ; УО "ВГМУ", Каф. общей и клинической

фармакологии с курсом ФПКиПК. - Витебск: ВГМУ, 2019. - 294 с.: ил., табл. - Рек. УМО по высш. мед., фармацевт. образованию.

3. Конорев, М. Р. Курс лекций по фармакологии. В 2 т. Т. 2, ч. 2: для студентов 3 и 4 курсов фармацевт. фак. учреждений высш. образования, обучающихся по специальности 1 - 79 01 08 "Фармация" / М. Р. Конорев, И. И. Крапивко, Д. А. Рождественский ; УО "ВГМУ", Каф. общей и клинической фармакологии с курсом ФПКиПК. - Витебск: ВГМУ, 2019. - 165 с.: ил. - Рек. УМО по высш. мед., фармацевт. образованию.

**Anxiolytics (minor tranquilizers)** are drugs that inhibits anxiety [1-15]

Classification	Benzodiazepine derivatives	Diphenylmethane derivatives	Other chemical groups ("daytime" tranquilizers)
Drugs	<b>1. Diazepam</b> (Seduxen, Sibazon, Relanium) <b>2. Chlordiazepoxide</b> (Elenium, Chlosepide) <b>3. Alprosolam</b> (Xanax) <b>4. Oxazepam</b> (Nozepam, Tazepam) <b>5. Phenazepam</b>	<b>6. Hydroxysin</b> (Atarax)	<b>7. Trimethozine</b> (Trioxazine) <b>8. Mebicar</b> (Adaptol) <b>9. Benzoacidine</b> (oxylidine)
Mechanism of action	1. Stimulation of the benzodiazepine site of the chloride channel of the GABA <sub>A</sub> receptor complex → conformational changes in the GABA-receptor → ↑ the number of individual chlorine channels and the chloride ions flow inside cells → hyperpolarization and inhibition of neuronal sensitivity, ↑ GABA-ergic inhibition in the central nervous system (1-5). 2. ↓ excitability of subcortical areas of the brain (thalamus, hypothalamus, limbic system, reticular formation) and their connection with the cortex. 3. It blocks central and peripheral muscarinic receptors (6)		
Pharmacological effects	<b>1. Anxiolytic</b> <b>2. Sedative</b> (elimination of irritability, ↓ attention and speed of thought) <b>3. Hypnotic</b> (acceleration of the onset of sleep and increase in its duration) <b>4. Miorelaxing</b> (↓tone of skeletal musculature) <b>5. Anticonvulsant</b> <b>6. Potentiating</b> (potentiation of drugs depressing the central nervous system)	<b>1. Anxiolytic</b> <b>2. Cholinolytic</b> <b>3. Antihistamine</b>	<b>1. Anxiolytic</b> 2. Activating (7) 3. Potentiating (8,9) 4. Spasmolytic (9) 5. Hypotensive (9)
Indications for use	<b>1. Neurosis and neurosis-like (reactive) conditions</b> <b>2. Sleep disorders</b> 3. Premedication (1, 2, 4, 5) 4. Hyperkinesis, tics, epilepsy (1, 5) 5. Alcohol withdrawal syndrome (1, 2, 5-7)		
Side effects	1. Hypersedation – daytime sleepiness 2. Muscle relaxation 3. "Behavioral toxicity" – mild violations of cognitive functions and psychomotor skills 4. "Paradoxical" reactions – intensification of agitation and aggressiveness, sleep disorders 5. Mental and physical dependence	1. Hypersedation 2. Dry mouth	1. Indigestion 2. Hypersedation 3. Dry mouth
Contraindications	1. Diseases of the liver and kidneys	1. Diseases of the liver and kidneys 2. Hypertrophy of the prostate	1. Diseases of the liver and kidneys 2. Arterial hypotension (9)
NB!	Classification of benzodiazepines by duration of action: T <sub>1/2</sub> 24-48 hours: diazepam, phenazepam; T <sub>1/2</sub> 6-24 hours: oxazepam, nitrazepam; T <sub>1/2</sub> <6 hours: triazolam, midazolam. <b><i>The antagonist of benzodiazepines is flumazenil.</i></b>		

**Sedatives** are medicines that can reduce increased irritability and have a pronounced general calming effect [1-15].

Classification	Bromine preparations	Preparations of medicinal plants	Mixed preparations
Drugs	1. Sodium bromide 2. Potassium bromide 3. Bromocaphora	4. Valerian 5. Motherwort 6. Peony	Phenobarbital-containing: 7. Corvalol (Valocordin) Mixed drugs of plant origin: 8. Novo-Passit 9. Persen
Mechanism of action	Strengthen and concentrate the processes of inhibition in the cerebral cortex, weaken the excitation processes in the central nervous system		
Pharmacological effects	1. Sedative 2. Spasmolytic (4-9) 3. Anticonvulsant (1,2)		
Indications for use	1. Neuroses, neurosis-like conditions 2. Insomnia 3. Spasms of the digestive tract (4-9) 4. Epilepsy, chorea (1,2)		
Side effects	<u>" Bromism ":</u> <ul style="list-style-type: none"><li>✓ General inhibition, apathy, weakening of memory.</li><li>✓ Inflammation of mucous membranes: cough, runny nose, bronchitis, conjunctivitis, diarrhea.</li><li>✓ Skin rash (acne bromica)</li></ul> <u>Treatment:</u> brome discontinuation, increased fluid (3-5 liters per day) andsodium chloride (10.0 - 20.0 per day) intake.	1. Drowsiness 2. Dizziness 3. Reducing concentration	
Contraindications	1. Hypersensitivity to the drug		
NB!	Bromides are practically not used today.		



**Antidepressants** – medicines that eliminate the symptoms of depression (a psychiatric disorder characterized by a prolonged deterioration in mood, loss of interest in life, a decrease in appetite, a violation of sleep, thinking and concentration, a sense of guilt and constant thoughts of death and suicidal attempts) [1-15].

Classification	Tricyclic and other heterocyclic drugs	Monoamine oxidase inhibitors (MAO)	Selective serotonin reuptake inhibitors (SSRIs)	Other antidepressants
Drugs	<b>1. Myanserin (Lerivon)</b> <b>2. Amitriptyline (Amizol)</b> <b>3. Imipramine (Melipramine)</b> <b>4. Maprotiline (Ludomil)</b>	<i>Irreversible:</i> <b>5. Nialamide (Niamid, Nuredal)</b> <i>Reversible:</i> <b>6. Pirlindole</b> <b>7. Moclobemide</b>	<b>8. Fluoxetine (Prozac)</b> <b>9. Sertraline (Zoloft)</b> <b>10. Paroxetine (Paxil)</b>	<b>11. Ademethionine (Heptral)</b> <b>12. Mirtazapine (Remeron)</b>
Mechanism of action	↓ re-uptake of norepinephrine, dopamine, serotonin → ↑ their concentrations in the synaptic cleft	1. It blocks the MAO-A and MAO-B enzymes (5) 2. It blocks the MAO-A enzyme (6, 7)	Inhibit the re-uptake of serotonin in the synaptic cleft\	1. The methyl group donor in biochemical reactions of the transfer of a given radical to the central nervous system. 2. Improves central serotonergic and noradrenergic activity by blocking presynaptic (inhibitory) α <sub>2</sub> -adrenergic receptors (12)
Pharmacological effects	<b>1. Antidepressant (improving mood, appearance of interest in life, elimination of suicidal attempts),</b> 2. Sedative (1,2,4,6,7,10,12), 3. Stimulating (3,5,8), 4. Cholinolytic (2-4,8,12), 5. Adrenoblocking (4)			
Indications for use	1. Depressive conditions 2. Alzheimer's disease (6) 3. Neuralgia of the trigeminal nerve (5) 4. Manic-depressive psychosis (6,7) 5. Enuresis (2,3)			
Side effects	1. Vegetative disorders (tachycardia, dry mouth, disruption of accommodation, constipation, urinary retention). 2. Allergic reactions (skin rash, itching of the skin, dermatitis, eosinophilia, agranulocytosis). 3. On the cardiovascular system (arterial hypotension, arrhythmia). 4. On the liver (drug hepatitis, intrahepatic jaundice). 5. Neurological disorders (type of extrapyramidal disorders - tremor of fingers, increased muscle tone, dysarthria).			
Contraindications	1. Dysfunction of the liver and kidneys 2. Diseases of the hematopoietic organs			
NB!	<i>Serotonin syndrome = SSRIs + MAO inhibitor.</i> • Clinic: tremor, myoclonic seizures, vomiting, diarrhea, cardiovascular disorders, further - hyperthermia, death. • Treatment: antagonists of serotonin receptors - cyproheptadine, metisergide; β-blocker - propranolol • Prevention: a sufficient interval between administration of MAO inhibitors and selective serotonin reuptake inhibitors, for example, 2 weeks after administration of MAO inhibitors and 5 weeks after administration of fluoxetine. <i>«Cheese Syndrome» = MAO inhibitor + food containing tyramine (cheese, legumes, bananas, smoked products, coffee, beer, chocolate)</i> Clinic: hypertensive crises			

**Nootropics** are medicines that improve mental performance (memory, training) [1-15].

<b>Classification</b>	<b>Derivatives of GABA</b>	<b>Derivatives of vitamin B6</b>	<b>Means that promote the synthesis of biologically active substances</b>
<b>Drugs</b>	<b>1. Piracetam (Nootropil, Lucetam)</b> <b>2. Gamma-aminobutyric acid (Aminalon, Gamalon)</b> <b>3. Sodium oxybutyrate</b> <b>4. Phenibut (Noofen)</b>	<b>5. Pyridinol (Encephabol)</b>	<b>6. Meclofenoxate (Acefen, Deanol)</b>
<b>Mechanism of action</b>	1. Stimulation of metabolic processes and transmission of excitation in the central nervous system due to activation of GABAergic processes (1-4) 2. Improve energy processes and blood supply to the brain, ↑ its resistance to hypoxia.		1. Activates metabolic processes, facilitates synaptic transmission in the hypothalamic and other areas of the brain 2. ↑ content of acetylcholine in synaptic endings and increases the density of the cholinceptors
<b>Pharmacological effects</b>	1. Improve cerebral circulation (1,2) 2. ↑ Brain resistance to hypoxia and aggressive influences (1-5) 3. Activates the regenerative processes in the brain after TBI, stroke, neurointoxication (1-3) 4. Eliminate memory impairments, activate intellectual and cognitive functions, stimulate learning processes (1,2,5,6) 5. Tranquilizing (4) 6. Sedative (3,5)		
<b>Indications for use</b>	1. TBI, chronic cerebrovascular disorders, atherosclerosis, vegetovascular dystonia (1-3,5,6) 2. Senile dementia (1,2,5,6) 3. Non-inhalational anesthesia (3) 4. Sleep disorder (4)		
<b>Side effects</b>	1. Dyspeptic disorders 2. Excitation phenomena (1,3,5,6)		
<b>Contraindications</b>	1. Renal failure (1,5) 2. Hypokalemia (3) 3. Myasthenia gravis (3,5) 4. Infectious diseases of the central nervous system (6)		
<b>NB!</b>	Piracetam is a part of the combined medicines: «Fezam», «Piracesine», «Zinnotropyl».		

TBI - traumatic brain injury

**Psychostimulants** are medicines that reduce the feeling of fatigue and drowsiness, increase mental and physical performance.

Classification	Phenylalkylamine derivatives and similar structure drugs	Methylxanthines (Purine Derivatives)
Drugs	<ol style="list-style-type: none"> <li>1. Amphetamine sulfate (Phenamine)</li> <li>2. Mesocarb (Sydnocarb)</li> <li>3. Meridil (Methylphenidate)</li> </ol>	<ol style="list-style-type: none"> <li>4. Caffeine</li> </ol>
Mechanism of action	<ol style="list-style-type: none"> <li>1. Cause release of granules of norepinephrine and dopamine from the presynaptic nerve endings → stimulation of central noradrenergic and dopaminergic receptors</li> <li>2. Inhibit MAO and inhibit the reverse neuronal seizure of dopamine and norepinephrine.</li> </ol>	<ol style="list-style-type: none"> <li>1. Blockade of phosphodiesterase (PDE) → accumulation of cyclic adenosine monophosphate (cAMP)</li> <li>2. Blockade of adenosine (A1, and A2) receptors → ↑ excitation processes in the cerebral cortex</li> </ol>
Pharmacological effects	<ol style="list-style-type: none"> <li>1. ↑ mental and physical performance, ↓ fatigue and drowsiness</li> <li>2. ↑ blood pressure</li> <li>3. ↓ aggregation of platelets (4)</li> <li>4. ↑ secretion of gastric juice (4)</li> <li>5. Analeptic effect (4)</li> <li>6. Dilation of coronary vessels, spasm of cerebral arteries (4)</li> </ol>	
Indications for use	<ol style="list-style-type: none"> <li>1. Physical and mental fatigue</li> <li>2. Migraine, hypotension (4)</li> <li>3. Depression, narcolepsy (1-3)</li> <li>4. Asthenic and neurasthenic disorders (2)</li> <li>5. Poisoning with substances depressing the central nervous system</li> </ol>	
Side effects	<ol style="list-style-type: none"> <li>1. Excitation</li> <li>2. Arterial hypertension</li> <li>3. Violation of higher nervous activity (1)</li> <li>4. Risk of addiction (1)</li> </ol>	
Contraindications	<ol style="list-style-type: none"> <li>1. Insomnia</li> <li>2. Arterial hypertension</li> <li>3. Organic diseases of the cardiovascular system</li> </ol>	
NB!	<p><i>Amphetamine</i> is not used in the Republic of Belarus as a medicine.  <i>Caffeine</i> is a part of the combined preparations – citramone, cofetamine.</p>	