

Ministry of health of the Republic of Belarus
Educational institution
«Gomel State Medical University»

Department of general and clinical pharmacology

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METHODOLOGICAL RECOMMENDATIONS

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

**TOPIC 3: « CLINICAL PHARMACOLOGY OF
DRUGS FOR RESPIRATORY DISEASES»**

Time: 6 hours

Approved at the meeting of the department of general and clinical pharmacology
the protocol № 18 of 30.06.2022

LEARNING AND EDUCATIONAL GOALS, OBJECTIVES, MOTIVATION FOR LEARNING THE TOPIC

Respiratory diseases are among the most pressing problems of modern-term practical medicine. According to the World Health Organization, in the developed world, they are comparable to a pandemic. However, despite the relevance of pharmacological development, international guidelines and recommendations on therapy of respiratory diseases, the issue is far from solution and often patients do not receive adequate treatment. For this reason, knowledge and skillful use of drugs for respiratory diseases is one of the most important tasks of pharmacology.

Learning objective:

- determine the role of analgesic and antiinflammatory drugs in the practice of a modern doctor. To study the characteristics of pain and inflammation syndromes pharmacotherapy in view of features of pharmacokinetics and pharmacodynamics of antiinflammatory and pain medication.

Educational purpose:

- to develop their value-personal, spiritual potential, to form the qualities of a patriot and 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 follow academic and work discipline, standards of medical ethics and deontology.

Tasks:

As a result of the study lesson, the student should

know:

- clinical-pharmacological classification of antiinflammatory and analgesic agents, their pharmacokinetic and pharmacodynamic characteristics;
- indications and contraindications to drugs, especially their use in different age groups and various associated diseases;
- drug dosing regimen and their interaction with other drugs;
- principles of efficacy and safety control of anti-inflammatory and analgesic drugs, potential side effects, methods for their prophylaxis and correction;

be able to:

- select the most effective and safe drugs based on their pharmacokinetic and pharmacodynamic features, possible side effects and drug interactions, on the one hand, the features of the disease, the age and sex of the patient, presence of concomitant diseases and degree of disturbance of the main functions of the organism, on the other hand;
- hold the objective control of the efficacy and safety of drugs, analyze their pharmacokinetic parameters and pharmacokinetic parameters based on the received data count single and course doses;
- determine the optimal route of drugs administration, administer them based on time of day, reception and food composition, predict, prevent and detect side effects of drugs and to avoid polypharmacy;
- prescribe drugs;
- Inform patients about the action of drugs, their administration rules and possible

side effects;

possess:

- skills in choice of drugs on the topic of the lesson;
- the rules of prescribing the studied drugs in the treatment of various diseases and pathological conditions, taking into account the indications;
- skills of dosage regime correction in case of pathological changes in functions of organs or systems responsible for biotransformation and elimination of drugs or in case of joint use of different drugs;
- skills to search, analyze and summarize information about the use and effects of the studied drugs.

Motivation for learning the topic:

- the specifics of training doctors in this specialty determines the need for students to purposefully study the main pharmacological effects, providing therapeutic and preventive effects of drugs on the topic of the class, indications and contraindications for their use, the interaction of drugs, their combined use, which will successfully complete the specialized disciplines of the specialty.

MATERIAL EQUIPMENT

Reference and informational literature, charts, tables, presentations, drug collections.

CONTROL QUESTIONS FROM RELATED DISCIPLINES

Successful study of the topic of discipline "Clinical Pharmacology" takes into account the students acquired knowledge and skills in the following sections of the disciplines:

- **general chemistry:** basics of chemical thermodynamics, chemical kinetics and catalysis, buffer solutions and pH calculation;

- **medical biology and general genetics:** molecular genetic and cellular levels of the organization, the genetic basis for the development of biological species, genetic disorders and their manifestations, ecology;

- **biological chemistry:** structure, function, metabolism of proteins, lipids, carbohydrates, biochemistry of muscle, the connective, nervous tissues, biochemistry of blood, water and mineral metabolism, biochemical processes in healthy and sick organisms, features of the biochemical processes in diseases in different age categories;

- **normal physiology:** reactivity role in causing disease, especially in the reactivity of different age categories, physiology of the circulatory, respiratory, digestive, endocrine, excretory systems, price-central and peripheral nervous systems, blood and lymphatic systems;

- **pathological physiology:** cell damage, disorders of protein, fat, carbohydrate, and mineral metabolism, disorders of local and general blood circulation, immunopathological processes, allergy, inflammation, pathology of respiratory, digestive, endocrine, excretory systems, the central and peripheral nervous systems, blood and lymphatic systems;

- **microbiology, virology, immunology:** microbial flora and viruses that cause disease in patients of different age the categories, the immune system, antigens, specific and nonspecific defensive factors of protection;

- **general health care and military hygiene:** influence of the environment on the occurrence and the course of pathological processes, hygienic regulations of environment, food and water;

- **pharmacology:** general issues of pharmacology, pharmacokinetics and pharmacodynamics of drugs, medicines regulating function of the central and peripheral nervous systems, drugs that affect the function of the respiratory, cardiovascular and gastrointestinal system, antimicrobial, antiviral, and antiparasitic agents, hormones and vitamins, agents used for the hemostasis system correction;

- **therapy:** principles of patient examination, basics of semiotics, diagnosis and treatment of diseases of the cardiovascular, respiratory, digestive and endocrine systems, diseases of kidneys and urinary tract, blood and blood-forming organs, musculoskeletal and connective tissues, clinical manifestations, diagnostics and emergency medical care to patients with life-threatening conditions, clinical manifestations of occupational diseases;

- **pediatrics:** principles of examination of a child, the basics of semiotics, diagnostics and treatment of cardiovascular, respiratory, digestive, endocrine diseases, diseases of kidneys and urinary tract, blood and blood-forming organs, musculoskeletal and connective tissues, clinic, diagnostics and emergency medical care in life-threatening conditions, premature baby, disease of the newborn and care for them;

- **immunology:** organs, cells, molecules of the immune system, allergy, hypersensitivity, especially the immune system in patients of different age groups;

- **infectious diseases:** general issues of infectology, intestinal infections, acute respiratory viral infection, viral hepatitis, transmitted infections, infectious diseases, infections of the central nervous system;

- **surgery:** sepsis, antisepsis, bleeding, hemostasis, general violations of vital activity in surgery and treatment, acute surgical pathology, wounds and wound infections, infusion and transfusion, general and local anesthesia;

- **obstetrics and gynecology:** physiology and pathology of pregnancy, gynecology.

CONTROL QUESTIONS ON THE TOPIC OF THE CLASS

1. Clinical and pharmacological characteristics of antitussive drugs of central, peripheral, mixed action. Expectorant and mucolytic drugs, features of their use.

2. Drugs for bronchial obstruction syndrome (beta-2 adrenergic agonists, muscarinic antagonists, xanthines, combined agents).

3. Basic antiinflammatory therapy for bronchial asthma (inhaled glucocorticoids, leukotriene receptor antagonists, recombination monoclonal antibodies). Use of mast cell stabilizers in pediatrics.

4. Phytotherapy in pulmonology.

5. Treatment of status asthmaticus. Drugs for pulmonary edema.

PROCESS OF THE STUDY

- 1.
- 2.
- 3.
- 4.
- 5.

Theoretical part

Theoretical questions are described in the appendix to the methodological recommendations.

Practical part

1. Take notes on theoretical material demonstrated by the teacher.
2. Master the methods of solving the tasks and writing out prescriptions on the topic of the class.

Theme learning control

Conducted in the form of independent written work (solution of practical problems and prescriptions for individual task).

METHODOLOGICAL RECOMMENDATIONS FOR ORGANIZATION AND EXECUTION OF STUDENTS' INDEPENDENT WORK (SIW)

The time given for independent work can be used by students for:

- preparing for the practical classes;
- writing an educational medical history;
- preparing thematic reports, essays and presentations;
- taking notes from academic literature.

The main methods of organizing independent work:

- completing tests and practical tasks of the electronic educational-methodical complex (EEMC) for self-monitoring and self-assessment;
- writing an educational medical history.

The list of tasks of the SIW:

- solving practical problems in the EEMC;
- completing the test tasks of the EEMC;
- writing an educational medical history.

Control of the SIW is carried out in the form of:

- assessment of an oral answer to a question, report, report, or solution of a task in a practical class;
- individual conversation;
- checking up for medical history.

METHODOLOGICAL RECOMMENDATIONS FOR ORGANIZATION AND EXECUTION OF CONTROLLED INDEPENDENT WORK OF STUDENTS (CIWS)

Recommended forms of CIWS organization:

- writing an educational medical history;
- writing an essay on a given topic;

- preparing a report and a multimedia presentation on a given topic.

The list of tasks of the CIWS:

Topics of essays / multimedia presentations:

1. Emergencies in respiratory diseases and their drug treatment.
2. Drugs used for the treatment of respiratory diseases in a power nebulizer.
3. Features of use of antitussives in pediatrics.

Forms of control of CIWS realization:

- checking up for medical history;
- checking and grading an essay on a given topic;
- checking and grading 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: 23.05.2022.

2. Кратко о лекарственных средствах: учебно – методическое пособие для студентов 3 и 6 курсов факультета иностранных студентов, учреждений высшего мед. образования: в 2 ч.=Drugs in short: partical workbook for 3 and 6 year students Faculty for International Students of medical higher educational institutions: in 2 parts / Е.И. Михайлова [и др.]. – Ч. 1. – Гомель: ГомГМУ, 2020. – 56с. – Режим доступа: <http://elib.gsmu.by/xmlui/handle/GomSMU/7128> – Дата доступа: 23.05.2022.

3. Кратко о лекарственных средствах: учебно – методическое пособие для студентов 3 и 6 курсов факультета иностранных студентов, учреждений высшего мед. образования: в 2 ч.=Drugs in short: partical workbook for 3 and 6 year students Faculty for International Students of medical higher educational institutions: in 2 parts / Е.И. Михайлова [и др.]. – Ч. 2. – Гомель: ГомГМУ, 2020. – 76с. – Режим доступа: <http://elib.gsmu.by/xmlui/handle/GomSMU/7129> – Дата доступа: 23.05.2022.

4. Rang and Dale's Pharmacology / J.M. Ritter [et al.]. - 9th ed. - Edinburg [et al.]: Elsevier, 2020. - xvi, 789 p.: ill., tab. + Student consult online.

Antitussives are cough suppressants [1-8].

Classification	Centrally acting		Perypherally acting
	Addicting	Non-addicting	
Drugs	<i>Less addicting:</i> 1. Codeine 2. Dihydrocodeine <i>Potent addicting:</i> 3. Morphine 4. Hydromorphone	<i>Opioid</i> 4. Dextrometorphan <i>Non-opioid</i> 5. Glaucone 6. Oxeladine 7. Butamirate	<i>Mixed-action drugs:</i> 8. Prenoxdiazine 9. Bithiodine <i>Local anesthetics:</i> 10. Lidocaine
Mechanism of action	Directly suppress the cough and respiratory centers.		Block sensitive receptors of the bronchial mucosa. 8-9 + block cough center
Pharmacological effects	1. Antitussive 2. Analgesic (1-3, 10) 3. Locally anesthetic (8-10) 4. Antiinflammatory (5, 6) 5. Bronchodilating (6.7)		
Indications	1. Non-productive cough (rhinopharyngitis, laryngitis, tracheitis or tumor of the bronchi) 2. Dry pleurisy 3. Postoperative period 4. Cough of central origin (pathologic irritation of the cough center) 5. Tuberculosis		
Side effects	1. Tolerance+dependence 2. Constipation 3. Arterial hypotension 4. Inhibition of respiration.	1. Dizziness 2. Nausea 3. Allergic reactions	1. Dry mouth and throat mucosa 2. Nausea 3. Diarrhea 4. Allergy
Contraindications	1. Respiratory failure 2. Alcohol intoxication 3. Craniocerebral trauma 4. Arterial hypotension 5. Pregnancy 6. Impaired liver and kidney function	1. Productive cough 2. Hypersensitivity to the drug components	1. Intensive secretion in the respiratory tract (in the postoperative period after inhalation anesthesia) 2. Hypersensitivity to the components of the drug
NB!		<u>Do not affect the respiratory center, do not cause drug dependence.</u> <u>Combined drug: broncholitine</u> (Glaucin + ephedrine + sage oil + citric acid)	

Drugs interaction	Mixed operation: tipepidin (bitiodin). Affects the respiratory tract mucosa receptors, as well as the centers of medulla oblongata.		
	Combination of antitussives and mucolytic expectorants is not recommended as it will cause sputum stagnation in the respiratory tract.		
	<ol style="list-style-type: none"> 1. CNS suppressants (opioid analgesics, barbiturates, benzodiazepines, clonidine, anesthetics): enhance their action (1-3) 2. Morphine derivatives: increased inhibitory action on the respiratory center; ibuprofen - enhanced analgesic effect; carbamazepine - increase in analgesic action is possible. Codeine + quinidine: analgesic effect of codeine ↓ or virtually disappears (1) 3. Systematic use of barbiturates - ↓ analgesic effect (2,3) 4. Amitriptyline, doxepin, chlorpromazine, haloperidol, indomethacin, naproxen, piroxicam, acetylsalicylic acid in oncological patients: myoclonus is possible (3) 6. Dopamine: ↓ analgesic effect; ketamine - ↑ respiratory suppression; ketoprofene - ↓ morphine-induced respiratory suppression; lidocaine - ↑ analgesic effect (3) 7. Metoclopramide - ↑ absorption rate in oral administration and amplified sedative effect (3) 8. Naloxone and nalorphine eliminate analgesia and respiratory depression (1-3) 	1. Combination with CNS suppressants isn't recommended (hypnotics, antipsychotics, tranquilizers) (6)	1. No data

Expectorants and mucolytics are drugs which aid in the clearance of mucus from the airways and are used for productive cough [1-8].

Classification	Expectorants (mucokinetics)		Mucolytics	
	Directly acting	Reflex acting	A) Synthetic mucolytics	B) proteolytic enzymes
Drugs	<u>Vegetable:</u> 1. Terpene hydrate 2. Fruits of anise 3. Eucalyptus oil 4. Pine buds <u>Synthetic:</u> 5. Potassium and sodium iodides 6. Guaiphenesin 7. Potassium and sodium citrates 8. Guaifenesin	<u>Vegetable:</u> 8. Grass of thermopsis, Ledum bogberry, Viola tricolor 9. Leaves of coltsfoot 10. Root of Althea and Glycyrrhiza glabra <u>Synthetic:</u> 11. Sodium benzoate	12. Acetylcysteine 14. Carbocysteine 14. Bromhexine 15. Ambroxol	16. Trypsin 17. Chymotrypsin 18. Ribonuclease 19. Deoxyribonuclease (dornase-alpha)
Mechanism of action	Are absorbed in the gastrointestinal tract → are secreted by bronchial mucosa → stimulate the secretion of bronchial glands, dilute sputum and promote drainage of mucus	Irritant gastric mucosal receptors → form the initial stage of excitation of the vomiting center → ↑ (through the vagus nerve) separation of mucus in the gastrointestinal tract and liquid secretion in the respiratory tract → ↑ peristalsis of the bronchi and flicker of the cilia → ↑ sputum discharge.	Cause depolymerization of protein and other sputum molecules (fibrin, mucopolysaccharides, DNA, RNA, etc.) → reduce its viscosity. Increase the formation of surfactant in the lungs – a substance that prevents alveoli collapse and improves gas exchange in the lungs.	
Pharmacological effects	1. Expectorant, 2. Mucolytic, 3. Surfactant-like (14,15)			
Indications	1. Cough with sputum during bronchitis, tracheitis, tracheobronchitis, and pneumonia 2. Bronchoectatic disease, bronchial asthma exacerbation 3. Infant respiratory distress syndrome (14,15), cystic fibrosis 4. Preventive maintenance of complications after operations on respiratory organs			
Side effects	1. Allergy	1. Nausea, vomiting (high doses) 2. Allergy	1. Dyspeptic disorders 2. Allergy (rarely)	1. Bronchospasm, allergy 2. Pulmonary haemorrhage
Contraindications	1. Open pulmonary tuberculosis 2. Diseases with a tendency to pulmonary hemorrhage	1. Gastroduodenal ulcer 2. Open pulmonary tuberculosis 3. Diseases of the nervous system with violation of the reflex mechanism of expectoration	1. Gastroduodenal ulcer 2. Pregnancy, lactation 3. Childhood 4. Open pulmonary tuberculosis	1. Open pulmonary tuberculosis 2. Pulmonary emphysema with respiratory insufficiency

Drug interactions

1. High dose therapy with iodine and potassium-sparing diuretics: hyperkalemia, preparations of lithium - goiter and hypothyroidism. Antithyroid drugs weaken the effect (6)
2. Lithium carbonate: ↓ lithium concentration in the blood plasma caused sodium ions (7)
3. Methotrexate: enhanced urine elimination of methotrexate and ↓ its renal toxicity due to ↑ urine pH (7)
4. ↓ absorption of tetracyclines (7)
5. ↑ pH ↓ ephedrine elimination and ↑ the risk of side effects (tremor, anxiety, sleep disorders, tachycardia) (7)

1. Inhalations and other expectorant drugs ↑ efficiency (12)

1. ↓ absorption of penicillins, cephalosporins, tetracyclines, erythromycin (2h administration interval is needed) (13)
2. Inhalations + antibiotics: mutual inactivation (13)
3. ↑ vasodilating effect of nitroglycerine, administration interval is needed (13)
4. ↓ toxic effects of paracetamol (13)
5. ↑ the effects of β₂-agonists, antibacterials, xanthines and glucocorticoids (14)
6. Interaction with alkaline solutions leads to inactivation (15)
7. ↑ penetration into the bronchial secret of amoxicillin, cefuroxime, erythromycin and doxycycline (15,16)

1. Iron preparations: ↓ iron absorption (18)

Pharmacotherapy of bronchial asthma, part 1 [1-8]

Bronchial asthma is a disease marked by recurrent attacks of dyspnea, with airway inflammation and wheezing due to spasmodic constriction of the bronchi. Can be allergic (atopic) and intrinsic (secondary to chronic or recurrent infections of the bronchi, sinuses, or tonsils and adenoids).

Bronchodilators and anti-inflammatory agents are used.

Classification	Bronchodilators of neurotropic action			Bronchodilators of myotropic action
	Non-selective adrenergic	Selective β_2 -agonists	Muscarinic antagonists	Methylxanthines
Drugs	<u>Universal adrenergic agonists:</u> 1. Epinephrine 2. Ephedrine <u>Non-selective β-agonists:</u> 3. Isoprenaline 4. Orciprenaline	<u>Short-acting (до 3-4 h):</u> 5. Salbutamol 6. Terbutaline 7. Fenoterol <u>Long-acting (~ 12 h):</u> 8. Salmeterol 9. Clenbuterol 10. Formoterol	<u>Non-selective:</u> 11. Atropine 12. Metacin 13. Platifillin <u>Selective:</u> 14. Ipratropium bromide (atrovent) 15. Tiotropium bromide (spiriva)	<u>Short-acting:</u> 16. Aminophylline 17. Theophylline <u>Long-acting:</u> 18. Euphyllong 19. Theotard
Mechanism of action	1. Stimulates α - and β -adrenoceptors (1, 2) 2. Increase release of norepinephrine (2) 3. Stimulate β_1 - and β_2 -adrenoceptors (3, 4)	Stimulation of β_2 -adrenoceptors \rightarrow activation of adenylate cyclase \rightarrow \uparrow cAMP \rightarrow stimulation of protein kinase \rightarrow cleavage of kinase catalyzing phosphorylation of myosin kinase, its activity \downarrow \rightarrow no myosin phosphorylation \rightarrow relaxation of smooth muscles.	Blockage of the transmission in the postganglionic muscarinic receptors \rightarrow the tone of the smooth muscles of the bronchi decreases, the reflex bronchoconstriction is prevented, and the secretion of bronchial glands is suppressed.	1. Blockage of adenosine receptors involved in bronchospasm \rightarrow \uparrow release of catecholamines into the synaptic cleft \rightarrow relaxation of the bronchi. 2. Inhibition of PDE \rightarrow \uparrow cAMP, \downarrow intracellular concentration of Ca^{2+} ions and stabilization of mast cells \rightarrow dilatation of bronchi.
Pharmacological effects	1. Bronchodilating 2. Cardiostimulating	1. Bronchodilating 2. Improve mucociliary clearance 3. Tocolytic	1. Bronchodilating 2. \downarrow gland secretion (11-13)	1. Bronchodilating 2. Vasodilating 3. Antiplatelet
Indications	1. Acute attack treatment 2. Asthmatic status (1,2) 3. Anaphylactic shock (1,2)	1. Acute attack treatment (5-7) 2. Prevention of an attack of asthma (8-10) 3. Asthmatic status (5-7) 4. Emphysema of the lungs (9) 5. Threat of premature birth (5.7)	1. Bronchial asthma 2. Chronic obstructive pulmonary disease (15) 3. Bronchoobstruction induced by physical exertion, cold, inhalation of dust	1. Bronchospasm 2. Violation of cerebral circulation 3. Pulmonary hypertension 4. Hypertensive crisis (16)
Side effects	1. Tachycardia, arrhythmia 2. \uparrow blood pressure 3. Nausea	1. Tachycardia 2. Tremor, headache	1. Dry mouth, \uparrow sputum viscosity 2. Tachycardia, mydriasis, \uparrow IOP	1. Dyspeptic disorders 2. Arrhythmia, tachycardia 3. Headache, insomnia
Contraindications	1. AH, IHD (1-2) 2. DM, pregnancy (1-2) 3. Tachyarrhythmias (3-4)	1. Individual intolerance 2. Diabetes mellitus 3. Arrhythmias	1. Closed-angle glaucoma 2. Pregnancy	1. Pregnancy and lactation 2. Paroxysmal tachycardia, myocardial infarction

NB!

Berodual = Fenoterol + Ipratropium bromide. Indecaterol - selective β_2 -agonist (~72 h)

Drug interactions

1. Opioids and hypnotics: ↓ their effects;
cardiac glycosides, quinidine, tricyclic antidepressants, dopamine, inhalation anesthetic - ↑ risk of arrhythmias;
other sympathomimetics — ↑ cardiac side effects;
antihypertensives (including diuretics) - ↓ their effectiveness; nitrates - ↓ their effects;
Hypoglycemic agents (including insulin) - ↓ hypoglycemic effect; potassium-lowering drugs (including corticosteroids, loop diuretics, aminophylline and theophylline) - ↑ hypokalemic effect (1,2)
2. β -blockers: ↓ efficiency (3,4)

1. β -blockers - weakening of the effectiveness of selective β_2 -agonists
2. Theophylline - ↑ the risk of tachycardia and arrhythmia, particularly supraventricular extrasystoles
3. Xanthine derivatives, glucocorticoids, diuretics: ↑ risk of hypokalemia
4. MAO inhibitors and tricyclic antidepressants: ↑ cardiac risk
5. Halothane, enflurane: ↑ cardiac risk

1. ↑ bronchodilator effect of β -agonists and xanthines
2. Drugs with antimuscarinic activity (including amantadine, haloperidol, phenothiazines, MAO inhibitors, tricyclic antidepressants, some antihistamines): ↑ risk of side effects
3. Nitrates: ↑ IOP
4. ↓ absorption of zopiclone, mexelitine, ↓ nitrofurantoin absorption and renal excretion. Probably ↑ therapeutic and side effects of nitrofurantoin (11)
5. Antacids containing Al^{3+} or Ca^{2+} , ↓ atropine absorption from the GIT ↓ (11)
6. Neostigmine: antagonists (11-13)

1. Phenobarbital, rifampicin, carbamazepine, isoniazid and other microsomal liver enzymes inducers can ↑ elimination.
2. macrolides (erythromycin, etc.), cimetidine, allopurinol, fluoroquinolones, verapamil can ↑ methylxanthines effects.
3. ↑ action of β -agonists and diuretics
4. Gluco- and mineralocorticoids: ↑ the risk of hypernatremia;
General anesthetics: the risk of ventricular arrhythmias.
5. Acyclovir: ↑ theophylline plasma concentrations and adverse reactions (17,19)
6. ↓ effectiveness of lithium drugs and β blockers.

Pharmacotherapy of bronchial asthma, part 2 [1-8]

Anti-inflammatory agents

Classification	Glucocorticoids		Mast cells stabilizers	Leukotriene receptor antagonists	Monoclonal anti-IgE antibodies
	Inhalational	Systemic			
Drugs	1. Beclomethasone 2. Budesonide 3. Fluticasone 4. Flunisolide	5. Prednisolone 6. Methylprednisolone	7. Cromolyn 8. Nedocromil 9. Ketotifen	10. Montelukast 11. Zafirlukast	12. Omalizumab
Mechanism of action	1. Inhibit phospholipase A2 → violate the formation of leukotrienes, serotonin, and prostaglandins. 2. Stabilize the membranes of lysosomes. 3. ↓ release of histamine by basophils.		1. Inhibition of PDE → ↑ cAMP → ↓ contractility of myofibrils of protein and stabilization of mast cells. 2. Blockage of Ca ²⁺ ions entry into the mast cell → prevention of mediator release.	Block leukotriene receptors	Inhibits binding of IgE to mast cells
Pharmacological effects	1. Anti-asthmatic 2. Anti-allergic 3. Anti-inflammatory (1-6, 10,11) 4. Immunodepressive (1-6)				
Indications	1. Bronchial asthma 2. Prevention of attacks of atopic bronchial asthma (7-9) 3. Asthmatic status (5,6) 4. Aspirin-, cold- and exercise induced asthma (7-11)				
Side effects	1. Candidiasis of the mouth 2. Dysphonia Prophylaxis: rinsing the mouth after inhalation, using a spacer.	1. Osteoporosis, myopathy 2. Puffiness, hypertension 3. Cushing's syndrome 4. Peptic ulcers 5. The withdrawal syndrome	1. Cough 2. Dry mouth 3. Bronchospasm	1. Hepatotoxicity 2. Nausea, vomiting 3. Allergic reactions	1. Local reactions in the site of administration 2. Dispeptic disorders 3. Headache
Contraindications	1. Acute bronchospasm 2. Infectious diseases	1. Osteoporosis 2. Peptic ulcers 3. Severe hypertension 4. Diabetes mellitus	1. Hypersensitivity 2. Pregnancy, lactation	1. Hypersensitivity 2. Lactation 3. Childhood (up to 5 years)	1. Hypersensitivity 2. Lactation 3. Childhood (up to 5 years)

Drug interactions	<p>1. Other nasal or systemic GCs: ↑ adrenal suppression</p> <p>2. The previous use of inhaled-beta-agonists can increase the clinical effectiveness</p> <p>3. CYP3A4 inhibitors (including ketoconazole and ritamivir) can ↑ systemic effects of GCs (2,3)</p>	<p>1. NSAIDs: ↑ GIT risks</p> <p>2. The effect of anticoagulants can be weakened</p> <p>3. Hypoglycemic drugs (including insulin), hypotensives and diuretics are GCs antagonists.</p> <p>4. ↑ risk of glycoside intoxication with the development of ventricular extrasystoles due to hypokalemia</p> <p>5. P450 inducers (phenobarbital, rifampin, carbamazepine) can ↓ the GCs effectiveness</p> <p>6. GCs ↑ hypokalemic action of diuretics and methylxantines</p>	<p>1. The effect is ↑ by beta-agonists, GCs, theophylline and other methylxanthines, anti-histamines.</p> <p>2. Combined use of cromoglicic acid and GCs allows to ↓ GCs dose, and in some cases - to discontinue</p> <p>3. Oral antidiabetic drugs: the risk of thrombocytopenia (9)</p> <p>4. Atropine and atropine-like drugs: ↑ the risk of urinary retention, constipation, dry mouth (9)</p> <p>5. Can ↑ the effects of sedatives, hypnotics and anti-histamine agents (9)</p>	<p>1. It should be used with caution with CYP 3A4, 2C8, 2C9 inducers like fenitoin, phenobarbital and rifampicine (10)</p> <p>2. The combination with warfarin prolongs prothrombin time (11)</p> <p>3. Acetylsalicylic acid ↑ concentration in blood plasma, erythromycin and theophylline ↓ the plasma concentration of the drug (11)</p>	No data
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Status asthmaticus (acute severe asthma) [1-8]

An acute exacerbation of asthma that does not respond to basic treatments with bronchodilators (inhalers) and steroids.

Group	Drugs
1. Short-acting β-agonists	<i>Salbutamol</i> 2.5 mg (2.5 ml), fenoterol 1 mg (in 3 ml of 0.9% solution of sodium chloride to be inhaled, repeat up to 4 times during 1 hour. NB! Can be given as a constant inhalation
2. α, β-agonists	<i>Adrenalin</i> 0.01 mg/kg s/c as a 1:1000 solution, max 0.3-0.4 mg intravenously 0.1-1 mkg/kg/min as a constant infusion NB! 0.1 % solution (1:1000) – 1 mg in 1 ml; 0,01% solution (1:10000) – 100 mkg in 1 ml
3. Systemic glucocorticoids NB! They are used to ↓ inflammation of bronchial micosa and restore the sensitivity of β -adrenoceptors.	<i>Prednisolone</i> , methylprednisolone: starting dose is 2 mg/kg, supporting dose - 0.5-1 mg/kg every 6 h IV NB! Glucocorticoids are given in lack of effect of inhalation of β -agonists.
4. Methylxanthines	<i>Theophylline</i> : 6 mg/kg intravenously during 20 min, maintenance dose – 0.5-0.7 mg/kg/h as a constant infusion
Inhalation of <i>oxygen</i> . Infusion therapy (replenishment of circulating blood volume): intravenously by drop infusion 15% solution of glucose or 0.9% solution of sodium chloride at a infusion rate of 150 ml/h. <i>Magnesium sulfate</i> 2 g (in children 25 mg/kg) intravenously with 0.9% solution of sodium chloride during 10-20 min.	
<i>In severe cases</i> : inhalation anesthetics (isoflurane, sevoflurane)	

Drugs for pulmonary edema

When normal blood pressure	<ol style="list-style-type: none"> To sit a patient with legs down <i>Glyceryl trinitrate</i> 0.5 mg sublingually (or aerosol) repeatedly or once <i>Morphine</i> intravenously by 3 mg (0.3 ml 1% solution) until the effect appears or up to total dose 10 mg (1 ml 1% solution) NB! Depress the respiratory center → ↓ unproductive dyspnea → ↓ fear of death <i>Furocemide</i> 40-80 mg mg (4-8 ml 1% solution) intravenously NB! ↓ blood volume → facilitation of cardiac performance <i>Glyceryl trinitrate</i> intravenously (up to 10 mg in 100 ml of 0.9% sodium chloride solution by drop infusion, increase the infusion rate from 25 mkg/min until the effect appears under the control of blood pressure) NB! ↓ pre- and postload → facilitation of cardiac performance <i>Oxygenotherapy</i> with 100% oxygen and <i>defoamer</i> (ethanol 70%)
When ↑ blood pressure	+ 1 ml 2.5 % solution of <i>hexamethonium benzenesulfonate</i> in 20 ml of a 0.9% solution of sodium chloride intravenously by slow bolus injection under the control of blood pressure after every 2 ml of solution
When ↓ blood pressure	<ol style="list-style-type: none"> Lay the patient lifting the headboard <i>Oxygenotherapy</i> with 100% oxygen and <i>defoamer</i> (ethanol 70%) Dopamine 200-400 mg in 200-400 ml of 0.9% solution of sodium chloride or 5% glucose solution intravenously by drop infusion. Gradually increase the infusion rate from 5 mkg/kg/min until the blood pressure stabilizes <i>Furosemide</i> 40 mg (4 ml of 1% solution) intravenously after stabilization of blood pressure