FEDERAL STATE BUDGET EDUCATIONAL INSTITUTION OF HIGHER EDUCATION "NORTH-OSSETIAN STATE MEDICAL ACADEMY OF THE MINISTRY OF HEALTH OF THE RUSSIAN FEDERATION

Department of pharmacology with clinical pharmacology

MEDICINES, INFLUENCING THE FUNCTIONS OF EXECUTIVE BODIES, INFLAMMATION AND METABOLISM

Educational and methodical manual for students

Bolieva L.Z., Vyalkova A.B. drugs AFFECTING FUNCTIONS of the EXECUTIVE BODIES AND INFLAMMATION. Educational and methodical manual.- Vladikavkaz.

This manual is intended for independent classroom and extracurricular work of students of the 3rd year of medical, pediatric, medical and preventive, pharmaceutical and dental faculties of medical Schools. The manual contains training and control elements under " Drugs that affect the functions of the Executive organs and inflammation."

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PRACTICAL CLASS № 1

The theme of the lesson. MEDICINE USED FOR DISEASES OF THE RESPIRATORY SYSTEM.

The General purpose of the lesson. Get acquainted with the basic principles of treatment of respiratory diseases. To study the pharmacokinetics and pharmacodynamics of drugs used in various pathological conditions of the respiratory system, side effects, contraindications to the appointment.

Specific objectives of the lesson

The student should know:

- the main groups of drugs used in respiratory diseases;
- mechanisms of action of antitussives, expectorants, stimulants dy-Hania;
- basic principles of treatment of bronchial obstruction;
- side effects of the main groups of drugs used in the treatment of respiratory organs.

The student should know:

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- mechanisms of action of antitussives, expectorants, stimulants dy-Hania;
- basic principles of treatment of bronchial obstruction;
- side effects of the main groups of drugs used in the treatment of respiratory organs.

The student must be able to:

- to justify the choice of the drug taking into account the absolute and relative contraindications;
- select the drug in the appropriate dosage form and dosage regimen based on age, appropriate pathology and other features;
- prescriptions for drugs studied groups.

Control question:

1. Respiratory stimulants: classification, mechanisms of action, application.
2. Anti-cough agents: classification, mechanism of action, application.
3. Expectorant and mucolytic means: classification, mechanisms of action, application.
4. Means used in bronchial asthma. Classification.
5. Drugs inhaled glucocorticoids, the mechanism of action, the use.
6. Stabilizers of membranes of fat cells: mechanism of action, application.

7. Antileukotriene tools: classification, mechanisms of action, application.

8. Bronchodilators: classification by mechanism and duration of action, especially the use of beta-adrenomimetics, M-holinoblokatorov, combined preparations.

9. Methylxanthines: mechanism of action, application.

10. The basic principles of treatment of acute respiratory failure.

1.1 breathing Stimulators

1.2 Antitussives

1.3 Expectorant and mucolytic agents

1.4 Agents used in asthma

1.5 Means used in acute respiratory failure

1.1 AGENTS THAT STIMULATE BREATHING

Table 1.1. Means, stimulating breath

Preparations	Mechanism of action, pharmacological effects	Indications for use	Side Effects
Direct action: *bemegride, etimizol, caffeine, camphor*	Direct stimulating effect on the respiratory and vasomotor centers. *Etimizol* has also a depressing effect on the cerebral cortex.	Currently, they are rarely used. Oppression of the respiratory center, poisoning with hypnotics and narcotic analgesics of mild degree, poisoning with carbon monoxide, asphyxia of the newly-born, restoration of pulmonary ventilation in the post-Marx period. Etimizol in psychiatric practice.	Nausea, vomiting, seizures, muscle twitching, anxiety. Bemegrid, cordiamine, camphor have a small breadth of therapeutic action.
Reflex action: *cititon, lobeline hydrochloride*	Excitation of N-cholinoreceptors-ditch sinocarotidna zone → afferent impulses to the medulla → increased activity of the respiratory center.		
Mixed: *kordiamin, Carbogen*	The Central effect + reflex action of chemoreceptors sinocarotidna zone.		

1.2 ANTITUSSIVES

Preparations of this group reduce the intensity and frequency of cough. They are used for unproductive, debilitating cough, sleep disturbance and normal daily activity. Are symptomatic means.

Table 1.2. Antitussives

Preparations	Mechanism of action	Side Effects
Central action		
Narcotic type of action: *codeine, Ethylmorphine hydrochloride*	Direct inhibition of the neurons of the cough center.	Respiratory depression, drug dependence, addiction, constipation, increased bronchial tone.

Non-narcotic actions: *hydrochloride glaucine, oxeladin citrate (tusupreks)*		Nausea, dizziness.
Peripheral action		
Prenoxdiazine (libexin)	Local anesthetic effect on the mucous membrane of the upper respiratory tract; lowering of bronchial tone	Nausea, diarrhea, numbness of the mouth and pharynx, allergic reactions.

1.3 EXPECTORANTS AND MUCOLYTIC AGENT

Preparations of this group contribute to the removal of the respiratory tract viscous, difficult to separate sputum.

Table 1.3. Expectorants and mucolytics

Preparations	Mechanism of action	Side effect, Contraindications
Expectorants		
Reflex action: *the drug grass thermopsis, ipecac, liquorice, istoda, Althea, sodium benzoate*	When ingestion have an irritating effect on the receptors of the gastric mucosa → reflex increase in the activity of the respiratory epithelium atrial fibrillation, increased secretion of the bronchial glands, increased muscle contractions of the bronchi. A number of products (marshmallow, licorice) have an additional anti-inflammatory effect.	Nausea. Drugs thermopsis, ipecac reflexly stimulate the vomiting center, and in high doses cause vomiting. *Contraindications:* peptic ulcer disease
Direct action: *potassium iodide, sodium iodide, sodium bicarbonate*	When ingestion secreted airway mucosa → stimulation of secretion of the bronchial glands, dilution of sputum, increased motor activity of the atrial epithelium	Irritation of mucous membranes. Contraindications: hypersensitivity to iodine
Mucolytics *Directly act on the sputum, reduce its viscosity, liquefy and facilitate, thereby, the allocation of*		
Acetylcysteine (ACC), carbocysteine,	Due to the presence of free sulfhydryl groups lead to the rupture of disulfide bonds of proteoglycans → depolymerization and decrease in the viscosity of sputum	Rarely-nausea, vomiting, tinnitus. Contraindications: peptic ulcer, liver, kidney, adrenal dysfunction, pregnancy, lactation.
Bromhexine, ambroxol	Depolymerization of mucoproteins and mucopolysaccharides of sputum → liquefaction. Stimulation of formation of pulmonary surfactant → normalization of rheological properties of bronchial secretions, relief of sputum.	Rarely-nausea, vomiting, skin rash.

Enzymes: trypsin, chymotrypsin	Break peptide bonds in protein molecules	Irritation of the mucous membranes of the respiratory tract, hoarseness, allergic reactions
Dornase Alfa (Pulmozyme)	Recombinant α-deoxyribonuclease (α-DNase) is a depolymerization of extracellular DNA in patients with cystic fibrosis	Pharyngitis, laryngitis, skin itching, rash, hives, voice changes.

1.4 DRUGS USED IN BRONCHIAL ASTHMA

Bronchial asthma (BA) is a chronic inflammatory disease of the respiratory tract, accompanied by hyperreactivity of the bronchi, cough, shortness of breath and attacks of suffocation caused by a violation of bronchial patency of varying degrees and duration. Treatment for asthma consists of systematic (basic) therapy for the prevention of exacerbations, and emergency Thera-PY exacerbations of ASTHMA (asthma attacks). Accordingly, medicines are divided into drugs intended for prevention or for relief of drugs.

Classification of funds for the treatment of asthma

I. anti-inflammatory and anti-allergic Agents
- Preparations of glucocorticoids
- inhalation: *beclomethasone, budesonide, fluticasone*
- System*: hydrocortisone, prednisone, dexamethasone, betamethasone*
- Stabilizers fat cell membranes: cremony *(kromoglicieva acid, sodium nedocromil); ketotifen*
- Antileukotriene funds:

leukotriene synthesis Inhibitors (5-lipoxygenase): *zileuton*
- leukotriene receptor Blockers: *zafirlukast, montelukast*

II. Tools that expand the bronchi (bronchodilators)
- A means of stimulating β2-adrenergic receptors (β2-agonists or β2-agonists)
- Short-acting: *salbutamol, fenoterol, terbutaline*
- Long-acting: *salmeterol, formoterol*
- M-cholinoblockers: *ipratropia bromide, tiotropia bromide*
- Antispasmodics myotropic action
- Methylxanthines: *theophylline, aminophylline (aminophylline)*

MEANS OF BASIC THERAPY OF BRONCHIAL ASTHMA

Glucocorticoids (ha) are by far the most effective anti-asthmatic agents. Their clinical effect is expressed in the inhibition of the early and late phase of allergic response, in improving the performance of external respiration, reducing the need for β2-agonists, inhibition of non-specific armorchial hyperreactivity, in reducing the frequency of exacerbations of the disease and pre-prevention of irreversible bronchopulmonary changes.
The mechanism of action, pharmacological effects and side effects of glucocorticoids are described in detail in section

3.1.The problem of undesirable side effects of systemic application of ha is largely solved by the development of highly active dosage forms for topical use. Advantage-the ability to create a high

concentration of the active substance in the pathological focus with a slight systemic action of the drug. With comparable efficacy of topical corticosteroids cause substantially fewer side effects. In bronchial asthma, GCS dosage forms are used for inhalation administration.

Table 1.4. Drugs of inhaled glucocorticoids

Preparation	Average daily doses, μg		
	Low	Average	High
Budesonide (Pulmicort) – dosed aerosol for inhalation, suspension for inhalation	200-500	500-1000	Further 1000
Beclomethasone (Beclazone, Beklaget) is a metered-dose aerosol or powder for inhalation	200-400	400-800	Further 800
Fluticasone (Flixotide) is a measured aerosol for inhalations	100-250	250-500	Further 500

In mast cells and basophils, biologically active substances (including leukotrienes, histamine) are synthesized, the release of which provokes bronchospasm. The isolation of biologically active substances from mast cells occurs as a result of their degranulation due to the interaction of antigen with immunoglobulin E adsorbed on the cell surface.at the same time, calcium ions enter the mast cells, contributing to the release of mediators of allergic inflammation.
Membrane stabilizers prevent degranulation of mast cells.

Table 1.5. Stabilizers of membranes of fat cells

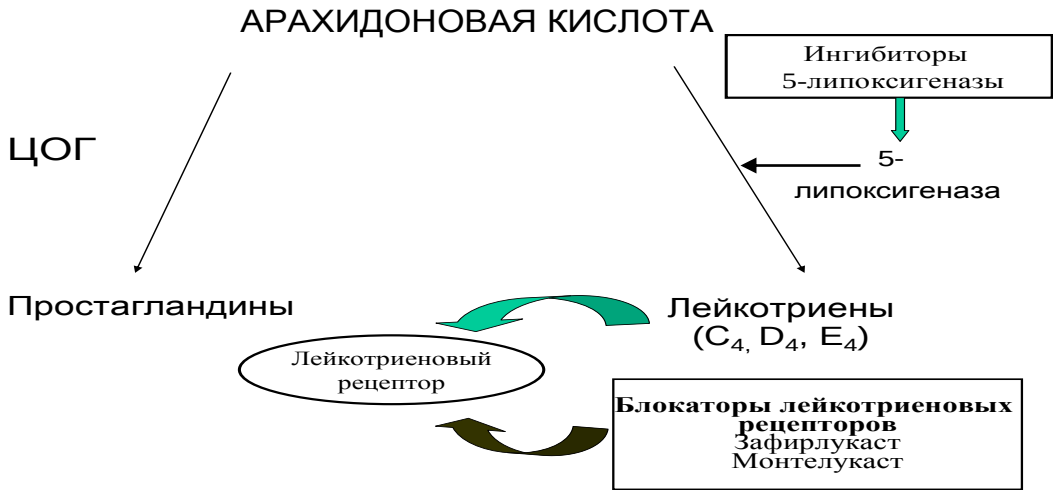
Preparation	Mechanism of action	Side effect, Contraindications
Sodium chromoglycate (Intal) - dosed aerosol for inhalation	Blocks the entry of calcium ions into the fat cell → inhibition of degranulation and release of biologically active substances - mediators of allergic inflammation	Cough, short-term bronchospasm. Very rarely – bronchospasm with decline in respiratory function. Contraindications: hypersensitivity, pregnancy, children under 5 years.
Nedocromil (tayled) is a measured aerosol for inhalations	Stabilizer of membranes of fat cells. Inhibits histamine release from mast cells and beta-glucuronidase from macrophages.	Rarely: headache, bad taste, cough, bronchospasm, nausea, vomiting, abdominal pain. *Contraindications:* hypersensitivity, age up to 12 years.
Ketotifen (zaditen) – tablets and syrup for oral administration	The membrane stabilizer of mast cells, reduces the release of histamine. Blocks H1-histamine receptors.	Drowsiness, dry mouth, dizziness, slowing mental reactions, passing through a few days of therapy. Rarely: increased appetite, thrombocytopenia, dyspepsia.

! The peculiarity of the action of the stabilizers of the membranes of mast cells is the slow development of the therapeutic effect - within 1-3 weeks of systematic application

Leukotrienes (LT) are synthesized in mast cells from arachidonic acid with the participation of the enzyme 5-lipoxygenase. Secreted by cell degranulation, LT stimulates specific recep-

tors in the bronchi, which leads to bronchospasm. Their effect can be reduced by disrupting the synthesis or blockade of specific receptors.

Figure 1.1. The mechanism of action antileukotrienes funds



FUNDS FOR THE RELIEF OF BRONCHIAL ASTHMA ATTACKS

Table 1.6. Bronchodilator

Preparations	Mechanism of action	Side effect, Contraindications
short-acting β2-adrenomimetics: *salbutamol*, *phenoterol*-dosed inhalation aerosol, tablets and syrup for oral administration	Activation of bronchial β2-adrenergic receptors → reduction of smooth muscle tone	Tremor, tachycardia, arrhythmias, tension, anxiety, headache, dizziness, nausea, vomiting. *Contraindications:* tachyarrhythmia, myocarditis, heart disease, hyperthyroidism, diabetes, glaucoma, children under 2 years
M-anticholinergics: ipratropium bromide metered-dose aerosol for inhalation	Blockade of M3-cholinoreceptors → reduction of smooth muscle tone	Rare: dryness of mucous membranes. With caution in glaucoma.
Flomax - fenoterol + ipratropium bromide	Activation of β2-adrenoreceptors of bronchi + blockade of M3-cholinoreceptors → reduction of smooth muscle tone	- // -
Methylxanthines: theophylline, aminophylline	Inhibition of all isoforms of phosphodiesterase→↑ camp. Blockade of the A1 adenosine receptors.	Dizziness, heartbeat, arrhythmias, sleep disorders, nausea, vomiting, anxiety, seizures, exacerbation of

	↑ level of circulating adrenaline. ↓ transport of calcium ions ↓ release of histamine	peptic ulcer disease. At/in the introduction-a sharp decrease in blood PRESSURE.

It should be emphasized that, despite the fact that short-and long-acting β2-agonists have a common mechanism of action and are bronchodilators, the long-acting preparation of salmeterol and formoterol belong to the means of basic therapy of bronchial asthma and are used to prevent attacks of pain necessarily in combination with IGCs.

Combined preparations containing IGCs and long-acting β2-agonist:

• **Seretide** is fluticasone + salmeterol

*** Symbicort**-budesonide + formoterol

There are extended formulations of theophylline - tablets retard (teopek, teotard, feostat), which are also used for the systematic ones-rapii and prevention of attacks BA.

1.5. DRUGS USED IN ACUTE RESPIRATORY LACK OF NEWS

Therapy of pulmonary edema

- Adequate oxygenation with the oxygen supply with a mask

- Morphine hydrochloride 2-5 mg / V to suppress the excess activity of the respiratory center

- Furosemide 40-100 mg IV for reduction of BCC, the extension of venous vessels, decreasing venous return to the heart

- high blood PRESSURE:

- sodium nitroprusside at a dose of 20-30 μg / min to reduce postload in systolic blood PRESSURE above 100 mm Hg.up to the resolution of pulmonary edema

-ganglioplegic (pentamin, benzogeksony)

-α-blockers (phentolamine)

- Aminophylline at a dose of 240-480 mg/V to reduce bronchoconstriction, increase renal blood flow, increase sodium excretion

- Defoamers: ethyl alcohol inhalation.

- Glucocorticoids

Treatment of respiratory distress syndrome in newborns

- surfactant Preparations of artificial surfactant - *colfosceril palmitate*, beractant; of animal origin (from pigs easy) – *Curosurf.*

Tasks for self-training

Task 1. Note the indications for the use of anti-asthmatic agents.

Indications for application Preparations	Cupping attacks BA	Caution attacks BA
Budesonide		
Salbutamol		
Formoterol		
Fluticasone		
Cromolyn sodium		
Fenoterol		
Montelukast		
Aminophylline		
Ipratropium		
Theophylline		

Task 2. Note the side effects of anti-asthmatic agents.

Preparations **Side Reactions**	Budesonide	Salbutamol	Theophylline	cromolyn sodium	Montelukast
Dizziness					
Tachycardia					
Arrhythmias					
Nausea					
Vomiting					
Cough					
Bronchospasm					
Convulsion					
Candidiasis of the oral mucosa					
Pharyngitis, laryngitis					
Anxiety					
Dry mouth					
Tremor					

Task 3. Note the side effects of antitussives and expectorants.

Preparations **Side Reactions**	Codeine	Glaucine hydrochloride	Bromhexine	acz	Trypsin
Nausea					
Respiratory depression					
Vomiting					
Mental and physical addiction					
Constipations					
Skin eruption					
Irritation of mucous membranes					
Increase of bronchial tone					
Addictive					
Voice hoarseness					

Tasks for self-control

I. Therapeutic effect of sodium chromoglycate in bronchial asthma is due to:
1) bronchodilating action; 2) stabilization of the membranes of mast cells; 3) antihistamine action; 4) steroid-like action

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II. sodium Chromoglycate is the drug of choice in patients with:
1) severe bronchial asthma; 2) moderate and severe forms of bronchial asthma; 3) mild asthma; 4) at any degree of severity

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III. The side effects of sodium chromoglycate, requiring its cancellation in bronchial asthma, include:
1) dry mouth; 2) bad taste; 3) paroxysmal cough after inhalation; 4) bronchospasm after inhalation.

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IV. The most common side effect when using inhaled corticosteroids is:
1) the development of oropharyngeal candidiasis; 2) weight gain; 3) the development of osteoporosis; 4) subcapsular cataract.

V. Berodual is a combination Of:
1) of ipratropium bromide and fenoterol; 2) ipratropium bromide and salbutamol; 3) cromoglicate sodium and fenoterol; 4) kromoglikata sodium and salbutamol.

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VI. Side-effects of the agonists that require the termination of their employment belongs:

1) headache; 2) tremor; 3) sleep disorders; 4) increased blood PRESSURE with the development of Hy-per-tonic crisis.

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VII. The pharmacodynamic effects of theophylline include all but:
1) bronchodilating action; 2) increase of mucociliary clearance; 3) ability to stimulate breathing and cardiac activity; 4) the ability to extract an increase in pressure in the small circle of blood circulation.

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VIII. The main difference between Ambroxol and Bromhexine is:
1) greater mucolytic activity; 2) less toxicity; 3) the possibility of use in children; 4) the presence of a reflex mechanism of action

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IX. Determine the drug that:
1) inhibits cough cent; 2) reduces the activity of the respiratory center; 3) reduces motor skills and peristalsis of the gastrointestinal tract;4) can cause drug dependence; 5) may cause bronchospasm and constipation.

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X. Determine the drug that:
1) blocks M-cholinoreceptors; 2) has a more pronounced broncholytic activity than atropine; 3) less than atropine, reduces the secretion of bronchial glands; 4) virtually absorbed from the surface of the bronchial mucosa.

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Situational concerns

1. In a patient sh., 41 years old, suffering from atopic bronchial asthma of the lung, over the past 7 days, there was a progressive difficulty in breathing and the resumption of attacks of expiratory suffocation. For relief of attacks, it was called salbutamol (dosed aerosol for inhalation) up to 12-14 times a day. The effect was short-term (for 10-15 minutes). On the 3rd day, severe asphyxiation developed, aggravated after inhalation of salbutamol, tachycardia developed. What is the reason for the development of an attack after inhalation of adrenomimetics? How should the recruitment chat of inhaled β-agonists and why? What drugs should be used to eliminate the developed side effects?

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2. When taking antitussive agent, the patient felt numbness in the mouth. What medication was prescribed to the patient? What features did the patient need to communicate with the patient?

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3. In a patient suffering from peptic ulcer disease, an exacerbation of chronic bronchitis was diagnosed. Was given the drug, after taking which the patient appeared epigastric pain and heartburn. What means and for what purpose was called to the patient? What is its mechanism of action? What can explain the aggravation of venous disease? What methods can I use to replace the prescribed medication?

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Prescribe:

1. Means for relief of bronchospasm attack.
2. A means of myotropic action for the treatment of bronchial asthma.
3. Glucocorticoid for basic therapy of bronchial asthma.
4. Antitussive agent of Central action.
5. The peripheral antitussive action.
7. Expectorant of reflex action.
8. A mucolytic.
10. The Central respiratory stimulant action.

To prescribe additional in the pediatric Department:

1. Direct-acting respiratory stimulator for a newborn baby. Indications for use.
2. Antitussive drug for a child 1.5 years.
3. Antitussive drug of Central action to a child of 12 years.

PRACTICAL CLASS №2.

The theme of the lesson. DRUGS USED IN DISEASES OF THE DIGESTIVE SYSTEM.

The General purpose of the lesson. Provide a complete idea about drugs affecting appetite, used in violation of the functions of the gastric glands and the pancreas, acting on the motility of the gastrointestinal tract. Learn the material about emetic and antiemetic, choleretic and laxatives.

The student should know:

- anatomical and physiological features of the digestive system;
- mechanisms of regulation of gastrointestinal functions;
- the main causes and types of disorders of the gastrointestinal tract (production and isolation of digestive secretions, motor skills, absorption, excretion);
- classification of funds affecting the function of the digestive system;
- classification, the mechanism of stimulating action on gastric secretion and indications for use of bitterness;
- the mechanism of action, indications for use and side effects of anorexigenic agents;
- diagnostic and therapeutic agents for low secretion of the stomach;
- main groups of drugs for the treatment of ulcerative disease of the stomach, their characteristics and contra-indications;
- action features gag funds Central action. Emetic drugs of plant origin. The importance in the treatment of acute poisoning.
- antiemetic drugs from the group of cholinoblockers, dopamine and serotonin receptor blockers, mechanisms of action, application.
classification and principles of actions of haereticos, cholekinetic and cholestanol-ticks;
- classification and mechanism of action of funds used in violations of the mo-toric function of the gastrointestinal tract, indications for use and selection of drugs for various violations of the evacuation function of the intestine.

The student must be able to:

- - justify the choice of the drug taking into account the absolute and relative contraindications;

- select the drug in the appropriate dosage form and dosage regimen based on age, appropriate pathology and other features;

- prescriptions for drugs studied groups.

Control question

1. Classification of substances acting on the function of the digestive system.
2. The mechanism of action of bitterness on the secretory activity of the stomach.
3. Principles of treatment of obesity with anorexigenic agents.
4. Complex therapy of diseases of the gastrointestinal tract, accompanied by a decrease in secretion and peristalsis.
- histamine: the nature and mechanism of action on gastric secretion, the use of;

- means of replacement therapy with reduced secretion of the stomach;
- prokinetics action cholinomimetics, agonists of serotonin receptors on the motility of the gastrointestinal tract.
5. Complex therapy of diseases of the gastrointestinal tract, accompanied by increased secretion and peristalsis.
- pharmacotherapy of acute gastritis: ganglioblockers, cholinoblockers, histamine H2-receptor blockers, their use in the treatment of ulcerative disease;
- features of the action of proton pump inhibitors omeprazole, lansoprazole;
- the mechanism and distinctive features of the action of funds neutralizing the acidity of gastric juice, the use of;
- gastroprotectia in the treatment of gastric ulcer; comparative characteristics of the drugs;
- group of funds and their drugs used in increased gastric motility and relieve spastic conditions of the intestine (M-holinoblokatory, Ganges-loblocator, antispasmodics myotropic actions). The principle of the depressing effect of loperamide on the intestine.

6. Mechanism of vomiting. Features of the purpose of emetic agents. Principles of treatment of chronic alcoholism. Pharmacotherapy of indomitable vomiting: drugs and the mechanism of antiemetic action.

7. The importance of choleretic drugs in the treatment of liver diseases and biliary system. Classification and principles of action of preparations of this group.

8. Hepatoprotectors and cholelitolitic funds: mechanisms of action, application.

9. Laxative. Classification. The mechanism of action of castor oil, anthraglycosides, salt and synthetic laxatives. Indications for the use of certain groups of drugs.

2.1 Means of influencing appetite.

Means that increase appetite-means that either stimulate the center of the holo-Yes, or inhibit the center of saturation.

To reflex acting stimulants include bitter - infusions, tinctures, liquid extracts of bitter herbs (wormwood, grass centaury, juice of under-roznica, dandelion root, rhizome, plantasia). Taken for 10-15 minutes before eating, they excite the receptors of the tongue and the reflex center of hunger, which leads to an increase in the first phase of gastric secretion during the subsequent meal.

To centrally acting appetite stimulants include peritol (cyprohept-DIN), which has a Central antiserotoninova, H1-gistaminblokirtee and M-holinoblokirutuyu action. Shows moderate sedative and hypnotic effects. It is indicated for neurogenic and hormonal thinness, can be prescribed to children. Contraindicated in glaucoma.

A means of reducing appetite (anorectic), are the opposite: reduce the excitability of the hunger center, or activate the satiety center, thereby reducing the psychological need for food. Used to treat obesity. Divided into 2 groups: 1) drugs affecting catecholaminergic-cal system (stimulate CNS); 2) drugs affecting the serotonergic system (CNS depress).

Table 2.1. Anorectics

Preparations	Mechanism of action	Side effects
Means affecting the catecholaminergic system		
Amphepramone	archived from the original ON	CCC: tachycardia, increased blood

(fepranon), phenylpropanolamine	release from presynaptic endings, a violation of its reverse takeover → ↓activity of hunger center.	PRESSURE, arrhythmia; CNS: anxiety, sleep disturbance, risk of drug dependence.
Means affecting the serotonergic system		
Fenfluramine, fluoxetine (prozac)	↑release of serotonin and disruption of its reuptake → → activity of the center of saturation.	Sedative effect; depression, drowsiness.
Agents affecting the noradrenergic and serotonergic systems		
Sibutramine. (Meridian)	Disruption of reuptake ON and serotonin→↓activity of the hunger center and ↑ activity of the saturation center.	Most often: dry mouth, loss of appetite, constipation; sleep disorders less often: increased blood PRESSURE, arrhythmia; headache.

2.2. Means used in violations of the function of the stomach glands.

The secretion of the gastric glands is under the control of the vagus nerve and also mountains-the Hmong of the gastrointestinal tract (gastrin, secretin, cholecystokinin). Pharmacological effect on the secretion of gastric glands can be both stimulating and inhibiting.

Means that enhance the secretion of the stomach glands.

The main components of gastric juice are hydrochloric acid (produced by the lining cells), pepsinogen (produced by the main cells), and mucin (produced by additional cells). In hypoacid and anacid gastritis, the secretion of hydrochloric acid and pepsin (Achilles) may be reduced or, accordingly, completely absent, and there may be a decrease in the secretion of hydrochloric acid and pepsin (Achilles). If the secretion of gastric juice is insufficient to improve the digestion of food, the means of substitutive te-RAPIA are prescribed - natural gastric juice, pepsin, hydrochloric acid, except-Denny. For diagnostic purposes, the following drugs are used: gastrin, histamine, which in the functional hypoacid state dramatically increase the secretion of the stomach glands, with organic lesions of the mucous membrane, increased secretion does not occur.

Means that reduce the secretion of the stomach glands.

With increased secretion of gastric glands, a syndrome associated with an increase in the production of hydrochloric acid by the lining cells develops, which results in an increase in the activity of pepsin-excretion of the main cells of the gastric mucosa. Increasing the production of hydrochloric acid and increase the activity of pepsin leads to a decrease in the production of mucin - the main component of mucus, covering the mucous membrane of the stomach and intestines. Hyperacidity, increased pepsin activity and lack of mucin predispose to damage the mucous membrane of the stomach and duodenum (inflammation, erosion, ulcers) and contribute to the development of the syndrome of increasing the activity of the acid-peptic factor. Means, pony-zhayuschie secretion of gastric glands, inhibit neurogenic and hormonal activation of the secretion of the main and parietal cells of the gastric glands, reduce the yield of hydrochloric acid and pepsin.

For pathogenetic therapy of patients with peptic ulcer disease, the following groups of drugs are mainly used (table 2.2.)

The pathophysiology of UB along with the aggressive action of Hcl and pepsin often includes contamination of Helicobacter pylori

! First-line eradication therapy includes proton pump inhibitors or ranitidine + antibacterial agent (clarithromycin, amoxicillin or metronidazole). Second-line therapy includes proton pump inhibitors, bismuth subcitrate, metronidazole, tetracycline.

The great therapeutic importance are the antacids, because of the acidity depends on the activity of pepsin and its digestive action on the gastric mucosa. The optimal pH for pepsin activity is in the range from 1, 5 to 4, 0. At pH =5, 0 pepsin is not active. Therefore, it is desirable that the antacids raised the pH not higher than 4, 0 (optimally, when taking antacids, the pH of gastric juice was 3,0-3,5), which does not violate the digestion of food. Usually, the pH of gastric contents normally ranges from 1.5 to 2.0. The pain syndrome begins to subside when the pH is more than 2. In this sense, the role of antacids is twofold.

! Systemic antacids-a means that can be absorbed, so they show their effect not only in the stomach, but also can lead to the development of Alka-vine in the body as a whole (systemic alkalosis). Non-systemic antacids are not absorbed, and therefore are able to neutralize the acidity only in the stomach, does not affect the acid-base state of the body.

Table 2.2. Means used for the treatment of peptic ulcer disease

The drugs	Mechanism of action	Side effects
Products that reduce the function of the stomach glands		
M-holinoblokatory (a) indiscriminate effects: atropine, metacin, platyphylline b) M1-holinoblokatory: pirenzepin (gastrotsepin)	a) non-selective blockade of M-CHR stomach → ↓↓basal and nocturnal secretion of gastric juice and hydrochloric acid. b) selective blockade of M 1-XP parasympathetic ganglia of the stomach and parietal cells (G-cells) that produce gastrin → ↓basal and pentagastrin-stimulated and insulin gastric secretion.	Tachycardia; dry mucous membranes; visual impairment.
H2-histamine blockers I generation-cimetidine, II-ranitidine, III-famotidine (kvamatel, IV-nizatidine, V-roxatidine	Blockade of histamine action on parietal cells → ↓secretory activity, ↓basal and night secretion of gastric juice and hydrochloric acid.	Headache, dizziness, weakness, nausea, diarrhea, constipation, rarely – loss of consciousness. Cimetidine-negative Chrono -, inotropic and positive dromotropic effect; ↓activity of microsomal liver enzymes; antiandrogenic action; neutropenia, thrombocytopenia, anemia.
Proton pump blockers: omeprazole, lansoprazole, pantoprazole	Selective↓ activity of N+, K+ -ATPase of the proton pump of the parietal cells → ↓ night and stimulated gastric secretion.	Nausea, diarrhea, numbness of the fingers, the possibility of atrophy of the gastric mucosa.
Antacids		
Na bicarbonate, CA carbonate, Al and Mg hydroxides, magnesium oxide.	Neutralization of hydrochloric acid in the lumen of the stomach → ↓acidity of gastric juice.	Na bicarbonate-systemic alkalosis (decreased appetite, nausea, vomiting, weakness, abdominal pain, cramps and muscle cramps); see recoil (hyperacidness); Al hydroxide-nausea; constipation.
Gastroprotectia		
1) of Bismuth tripotassium dicitrate (de-knoll), sucralfate 2) misoprostol (prostaglandin E2, cytotec) 3) carbenoxolone	1) Polymerization (pH below 4) with the formation of a protective colloidal protein layer on the mucosa; activity; antimicrobial action (de-Nol). 2) ↓acidity of gastric juice, ↑motility of stomach and intestines; reparative, hypoacid action 3) ^ the allocation of gastric mucus; ^ the life of epithelial cells; ↑synthesis of glycoproteins.	1) constipation, dry mouth; 2) transient diarrhea, mild nausea, headache, abdominal pain; 3) fluid retention in the body, hypertension, hypokalemia.

2.3. Emetic and antiemetic agents.

Vomiting, on the one hand, the protective act (exemption of the stomach from poisons and toxins); on the other hand, the process, worsening the condition of the body with many types of PA-politology de partment at (toxemia cytostatic and radiation therapy, sea sickness).

Vomiting is controlled by a corresponding center of the medulla oblongata, the stimulation of which causes an act of vomiting. The emetic center receives afferent fibers from: 1) the bark of the limbic system; 2) the chemoreceptorial trigger zone, in which a significant number of dopamine and serotonin receptors are localized; 3) the solar plexus; 4) the spinal cord; 5) the vestibular system with a significant number of cholinergic and histaminergic synapses.
When poisoning in order to remove from the stomach of any chemicals or foods for the reproduction of an emetic act, emetic agents are used.

Emetic products:

1) Central action (morphine and other narcotic analgesics, apomorphine, antitumor drugs) - act directly on the chemoreceptors of the pus-kovy zone at the bottom of the IV ventricle;

2) reflex action (copper sulfate, zinc sulfate and others) - irritate the receptors of the gastric mucosa;

3) mixed action (cardiac glycosides).

As the main drug, emetic is used APO-morphine-morphine derivative, a specific agonist of d-receptors of the Central nervous system. The drug acts on the chemoreceptor area of the medulla oblongata (trigger zone), which leads to the stimulation of the emetic center.

Antiemetics

Antiemetic effect can have drugs that act on different parts of the nervous regulation of the act of vomiting:

Table 2.3. Antiemetics

The drugs	Mechanism of action	Indications	Contraindications
Astringent: *tannin, tanalin, cherry fruit*; enveloping: drugs of flax seed, rice, starch	The formation of a colloidal film on the inflamed areas of the gastric mucosa and the protection of the sensitive nerve endings in them.	Vomiting caused by local irritation of the stomach.	-
M-anticholinergics: *scopolamine, hyoscyamine*	Direct blockade Of m-cholinoreceptors of the emetic center.	Vomiting caused by vestibular disorders (prevention and treatment of sea and air diseases), Meniere's disease.	Glaucoma.
Blockers of H1-histamine receptors: diphenhydramine, promethazine, meclozine	Blockade of H1 - wastemini-mization the vomiting center.	Vomiting caused by vestibular disorders.	Hypersensitivity angle-closure glaucoma.
The drugs	Mechanism of action	Indications	Contraindications
5-HT3 serotonin receptor blockers: ondansetron	Blockade of Central and peripheral serotonin 5-HT3 – receptors.	Prevention of vomiting during chemotherapy and radiation therapy in cancer patients.	Dyspepsia, dizziness, constipation, increased blood PRES-

			SURE.
Metoclopramide	Specific blockade of dopamine (D2) and serotonin (5-HT3) receptors.	Intoxication with cardiac glycosides; prevention the side effects of cancer therapy; a violation of the diet; psoriasis of the abdomen, flatulence; vomiting of pregnant	Rarely: the phenomenon of parkinsonism, drowsiness, tinnitus, dry mouth.

2.4. Medications and remedies that dissolve gallstones

Bile plays an important role in the functioning of the gastrointestinal tract. Bile acids are stimulants of intestinal peristalsis, pancreatic juice production, emulsification and absorption of fats and fat-soluble vitamins.

In the treatment of diseases of the gallbladder and biliary tract with the purpose of correction of dis-kinetic disorders and normalizes the composition of bile is used cholagogue. In accordance with the pathogenesis of bile disruption, these preparations are divided into funds that enhance the formation of bile and funds that contribute to the allocation of bile to the intestine.

Bile salts play an important role in maintaining cholesterol in dissolved state. Increasing the concentration of cholesterol and reducing the content of bile salts can lead to the formation of cholesterol stones. Small neckalce related stones can be removed using cholelitolitic funds. Contraindications to the appointment cholelithiasis funds are:

- inflammatory diseases of the gallbladder;
- blockage of the common bile duct;
- inflammatory diseases of the liver, small intestine;
-renal failure;
- fasting and diet

In chronic and subacute hepatitis, cirrhosis of the liver; fatty liver of various origins; toxic and drug lesions of the liver parenchyma used to protect hepatocytes, preserving and restoring their functions - hepatoprotectors.

Table 2.4. Hepatotropic, choleretic and cholelitolitic funds

Drugs	Mechanism of action	Indications for use
Cholagogue		

I. Stimulating the bile production (choleretic) a)animal origin (containing bile acids) : Holohan, allohol, holenzim, liabil b) of vegetable origin: drugs of Helichrysum, peppermint, rose hips, corn silk, tansy; rhizomes with roots of Valerian C) synthetic: oksafenamid, nicodin, tsikvalon II. Stimulating bile secretion: a) holekinetiki: magnesium sulfate, preparations of barberry, polyhydric alcohols b) holespazmolitiki: atropine, platifillin, metacin, but-shpa, papaverine, oksafenamid	Stimulation of the formation of liquid bile fraction, increased blood flow in the liver. Animal choleretics: 1) compensate for the lack of bile in the intestine, 2) stimulate the secretory function of the liver, 3) promote the passage of bile through the ducts, coordinate the duration of contraction of the gallbladder and sphincter muscles of Oddi. Increased tone of the gallbladder (holekinetiki) and relaxed tone of the biliary tract (holespazmolitiki).	Cholecystitis, hepatitis, gastritis, prevention of cholelithiasis.
Hepatoprotectors		
Ademetionine (Heptral), Essentiale, legalon, Liv-52, lipoic acid (thioctacid), vitamin E, siripur, vitamin B12, vitamin B15.	Improvement of liver function, strengthening of intracellular metabolism, prevents fatty liver infiltration, stimulation of hepatocyte regeneration, restoration of damaged hepatocyte membranes.	Hepatitis, cirrhosis,fatty liver.
Cholelitolitic funds		
Henodeauxiholeva acid (henofalk), ursodeoxycholic acid (Ursofalk)	Inhibition of enzymatic synthesis of cholesterol, followed by a decrease in the concentration of cholesterol in bile, the gradual dissolution of cholesterol stones.	Cholesterol stones of the biliary tract and gallbladder with a diameter of not more than 2 cm (R-negative stones)

2.5. Means used in violation of the functions of the pancreas.

With reduced excretory function of the pancreas for correction of Exo - and endocrine insufficiency of the gland outside of exacerbations of chronic pancreatitis is used for-meticulou therapy enzymes: Pancreatin, festal (contains pancreatic enzymes-lipase, protease, amylase and major components of bile), meksaza (three-layer tablet containing enteroseptol; Pancreatin and dehydrocholic acid; the enzyme preparation bromelain), panzinorm etc.

Acute exacerbations of HP for relief of pain impose baralgin, sandista-tin (a somatostatin analogue), promedol. Protease-contrical, gordox, tra-silol inhibitors neutralize the enzyme, reduce the activity of kallikrein-kinin system, inhibit proteases, normalize the rheological

properties of blood and improve microcirculation in exacerbations of CP and acute pancreatitis. Also, the transition of pancreatic edema to necrosis is inhibited, the process of autolysis stops, exudation is reduced.

In order to prevent septic complications, it is recommended to administer semi-synthetic penicillins or cephalosporins.

2.6. Means that affect intestinal motility.

For lowering the tone of the intestine used M-holinoblokatory, ganglioblockers Torah, antispasmodics myotropic actions. Reduce peristalsis also adsorbents (activated charcoal, cholestyramine); astringent (tannin); obvolute serving; antidiarrheal products to eliminate increased activity of the vagus nerve (reasec, Imodium). Antidiarrheals delay defecation due to the increase in tone of the sphincters of the gastrointestinal tract. In allergic and Ney-Rogen diarrhea, irritable bowel syndrome, ulcerative colitis, "traveler's diarrhea" often as symptomatic therapy on-mean Imodium (loperamide) and reasek (lomotil). The main active ingredient of these drugs are synthetic opioids that bind to opioid receptors of the intestinal wall and cause obstipation (similar to morphine). The Central morphine-like action Imodium and reasec not have (part of Rebeca also includes atropine sulfate). Contraindicated in diarrhea caused by microorganisms.
In atony of the bowel (eg, postoperative) designate M-cholinomimetics, anticholinesterase drugs, α-blockers and the hormone vasopressin, having myotropic stimulating effect.
By means of increasing the contractile activity of the intestine, include weak-tel means.
Laxative is means that accelerate the bowel movement by increasing intestinal motility and increase water excretion with the feces.

Table 2.5. Purgatives

Drugs	Localization of action	Mechanism actions	Indications application
Salt laxatives: magnesium sulfate, sodium sulfate (Glauber salt), Karlovy vary salt	Throughout the intestine.	Osmotically active substances, practically not absorbed in the intestine → ↓ water absorption, increase in the volume of intestinal contents and reflex increase peristalsis.	Acute constipation and acute enteral poisoning, to reduce the absorption of poison from the intestine and accelerate its excretion from the gastrointestinal tract.
Drugs antraglikozida-plants: Senna leaf, rhubarb root, senade	The lower parts of the colon.	Stimulation of the chemoreceptors of the intestine.	Chronic constipation.
Synthetic drugs: izafenin, phenolphthalein, Bisacodyl, guttalaks	- //-	- //-	- //-
Vaseline oil, vegetable	Predominan	Mechanical relief promoting	- //- (except castor oil).

oils (castor, almond), glycerin candles	tly the small intestine.	chyme, causing its loosening.	

Tasks for self-training

Task 1. Determine the localization of the action of bitterness and anorexigenic agents.

1.		2.		3.		4.		5.
Feels the nerve end-ings of the mucous membrane of the tongue and mouth	→	Spinal brain	→	Oblong Brain	→	Hypothalamus	→	Cortex

_____
_____
_____
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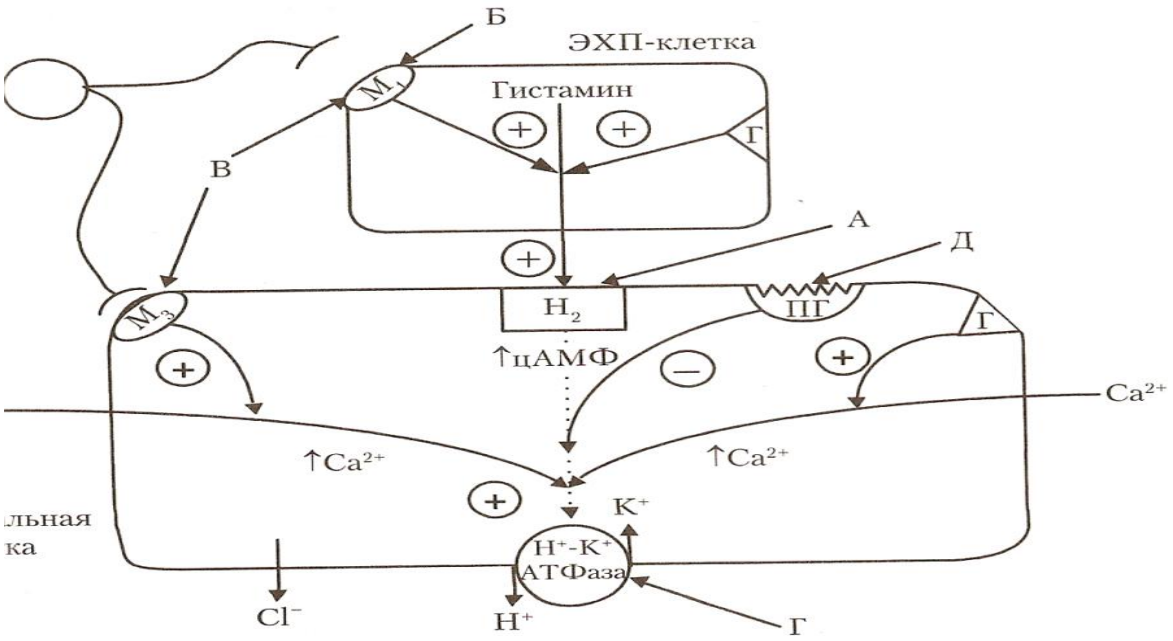
Task 2. Identify the drugs A-D applied to decrease the secretion of gastric glands (atropine, pirenzepine, roxatidine, misoprostol, pantoprazole).



Task 3. Fill in the table by entering the groups of funds that regulate the secretion of the digestive glands.

Stomach		Liver		Pancreas	
↑ secretions glands'	↓ secretions glands'	↑ secretions biles	↑ excreta biles	substitutive actions	↓ secretions
1.	1.	1.	1.		
2.	2.	2.	2.		
3.	3.	3.	3.		
	4.				
	5.				

Task 4. Complete the table by writing for any type of therapy uses the following tools: bitter, mazindol, fenfluramine, pepsin, gastrin, pirenzepin, omepra angry, allohol, contrical, metoclopramide, de-Nol, papaverine, oksafenamid, phenolphthalein, ondansetron.

Therapy	Symptomatic	Pathogenetic	Substitution	Incentive
Means				

Task 5. Identify the tools A-E to be applied when violations of the secretory activity of the gastric glands (de-Nol, nizatidin, pirenzepine, omeprazole, Al(OH)3, Mizo-prostol).

Preparations	Acid salt	Pepsin	synthesis of prostaglandins	Helicobacter Pylori
A	↓	↓	↑↑	-
B	↓↓	↓	-	-
C	↓	-	-	-
G	↓↓↓	↓	-	-
D	↓	-	↑↑	-
E	-	↓	↑↑	↓↓

Tasks for self-control

I. Note drugs used to reduce appetite:
1) amphetamine; 2) tincture of wormwood; 3) fepranon; 4) sibutramine; 5) apomorphine; 6) carnitine.

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II. Tick the group of drugs used in the treatment of ulcerative disease of the stomach:

1) M-holinoblokatory; 2) α-blockers; 3) histamine H1-receptors; 4) the histamine H2-receptors; 5) simpatolitiki; 6) Anta-cydnie funds; 7) proton pump inhibitors; 8) gastroprotectia.

_____

III. Explain the mechanism of the hypoacid action of proton pump inhibitors by putting the following statements in logical sequence:
1. Long-term Reduction of hcl secretion.
2. Covalent binding of the thiol groups sulfenamide H,K ATPase.
3. The transformation of the drug into sulfenamide.
4. Violation of the transport of hydrogen ions in the lumen of the stomach.
5. Irreversible inhibition of proton pump.

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IV. Note the main effects of ursodeoxycholic acid:
1) refers to a group of hepatoprotective funds; 2) refers to a group of cholelith-lytic tools; 3) causes the dissolution in the gallbladder cholesterol stones are small; 4) effective with prolonged use.

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V. Mark the major effects loperamide:
1) stimulates intestinal peristalsis; 2) inhibits intestinal peristalsis. 3) agonist μ-opioid receptors; 4) agonist M-holinoretseptorov; 5) used in acute and chronic diarrhea; 6) poorly penetrates the Central nervous system and does not cause drug-venous dependence**.**

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VI. Note the main effects of ademetionine:
1) has hepatoprotective activity; 2) has gastroprotective activity; 3) has choleretic activity; 4) activates the synthesis of membrane phospholipids; 5) promotes the synthesis of biologically active substances with detoxifying properties.

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VII. Note the main effects of the ondansetron:
1) has a prokinetic effect; 2) has antiemetic effect; 3) blocks the dopamine D2-receptors of the starting zone of the emetic center; 4) blocks serotonin 5-HT3-receptors in the Central nervous system and on the periphery; 5) is used to prevent and eliminate vomiting associated with chemotherapy of tumors of radiation disease-new; 6) is used for motion sickness.

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VIII. Note the main effects of salt laxatives:
1) increase the osmotic pressure in the intestinal lumen; 2) reduce the absorption in the intestine; 3) increase the volume of intestinal contents, leading to the activation of mechanoreceptors of the intestine; 4) act primarily on the thick ky-shechnik; 5) act throughout the intestine; 6) used in acute constipation; 7) used in the treatment of acute poisoning.

IX. Determine the substance: the drug of plant origin, thick syrupy liquid dark brown. It helps to increase the secretion of bile.

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X. determine the substance: the drug on the chemical structure and action close to atropine. It is used as a means of prevention of sea and air disease; reduces the tone of smooth muscles; reduces the secretion of glands; soothes the Central nervous system.

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XI. Explain the mechanism of action of magnesium sulfate, placing the following statements in logical sequence:
1.Delayed absorption of water in the intestine.
2. Increase in the volume of intestinal contents.
3. Stimulation of mechanoreceptors of the intestine.
4. Strengthening of intestinal peristalsis throughout its entire length.
5. Increased osmotic pressure in the intestinal lumen.

XII. Combine.

Drugs:	Mechanism of action:
A) Pantoprazole	1) Blocks serotonin 5-HT3-receptors.
B)Pirenzepin	2)Blocks histamine H2-receptors.
C)Ondansetron	3) Blocks M1-cholinergic receptors.
D)Roxatidine	4) Inhibits N,C-ATPase.

Situational concerns
1. A patient suffering from obesity was prescribed a drug, under the influence of which the patient's weight decreased. But he had headaches, pain in the heart, began to increase blood PRESSURE. What medication was the patient taking? Explain the mechanism of side effects.

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2. Patient suffering from ulcerative disease of the stomach, prescribed the drug. The pain decreased, but there was dry mouth, heartbeat. What medication was prescribed to the patient? What is the mechanism of action of the drug?

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3. A patient with a stomach YAB, taking an antacid for a long time, has ratified to the doctor for a feeling of overflow of the stomach, nausea, abdominal pain. When the patient was examined, a change in the acid-base balance towards alkalosis was revealed. Determine the drug that causes such a side effect.

Prescribe:
1. means to increase appetite.
2. anorectic agent.
3. a means of replacement therapy in case of insufficiency of the stomach glands.
4. proton pump inhibitor in peptic ulcer.

5. the remedy for hyperacid gastritis.
6. gastroprotective agent.
7.antiemetic.
8. a tool that stimulates the secretion of bile.
9. a tool that promotes the release of bile.
10. hepatoprotective agent.
11. a remedy for replacement therapy for chronic pancreatitis.
12. laxative for acute poisoning.
13. laxative for chronic constipation.
14. remedy for the relief of biliary colic.
15. a remedy for acute and chronic diarrhea.

To prescribe additional in the pediatric department:
1. a means for elimination of regurgitation in infants.
2. prescribe antidiarrheal medication to a newborn baby.

PRACTICAL CLASS №3

The theme of the lesson. ANTI-INFLAMMATORY DRUGS.
DRUGS AFFECTING THE IMMUNE PROCESSES.

The General purpose of the lesson. To study the classification, mechanisms of action of steroid and non-steroidal anti-inflammatory drugs, anti-allergic and immuno-tropics, pharmacokinetics and pharmacodynamics of individual pre-parates.

Specific objectives of the lesson

The student should know:
- classification of anti-inflammatory, anti-allergic and immunotropic agents;
- mechanisms of anti-inflammatory action of steroid and non-steroidal anti-inflammatory drugs;
- mechanisms of antipyretic and analgesic action of non-steroidal anti-inflammatory drugs;
- mechanisms of anti-allergic action of drugs of different groups;
- pharmacological effects and features of the action of certain groups of drugs;
- side effects and contraindications to the appointment;

The student must be able to:
- write prescriptions for drugs studied groups;
- to justify the choice of drugs for various pathological conditions;
- choose the dose and route of administration of the drug, taking into account the disease, the presence of accompanying pathology, the possible interaction of drugs.

Control question:
1. Classification of glucocorticoids.
2. Mechanisms of anti-inflammatory, anti-allergic and immunosuppressive action of glucocorticoids.

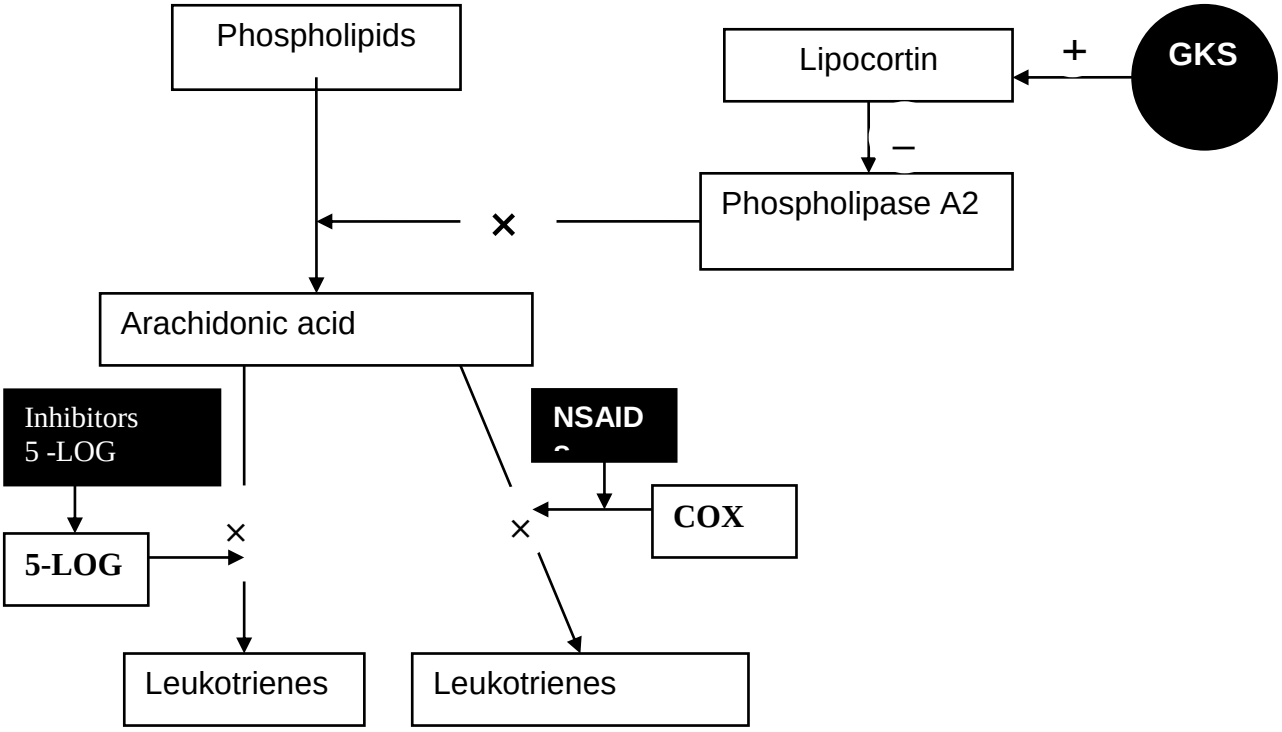
3. Pharmacological effects of glucocorticoids.
4. Dosage forms of glucocorticoids and indications for use.
5. Side effects and contraindications to the use of glucocorticoids.
6. The mechanism of anti-inflammatory, analgesic and antipyretic action of drugs.
7. Classification of non-steroidal anti-inflammatory drugs.
8. Indications for use of non-steroidal anti-inflammatory drugs.
9. Side effects, contraindications to the use of non-steroidal anti-inflammatory drugs.
10. Possibilities of prevention and correction of side effects of non-steroidal Protivovospalitelnyh drugs.
11. Groups of agents used in different types of allergic reactions.
12. Histamine H1-receptor blockers: classification, mechanism of action, application, side effects.
13. Stabilizers of membranes of fat cells: mechanism of action, application, side effects.
14. Immunotropic means: classification, mechanisms of action, application.

3.1 Glucocorticosteroids
3.2 non-Steroidal anti-inflammatory drugs
3.3 histamine H1 receptor Blockers
3.4 Immunotropic agents

Inflammation is a pathological process that develops in organs and tissues in response to the action of damaging factors. Inflammation is regulated by many endogenous biologically active substances, so-called mediators of inflammation, the most important among which are metabolites of arachidonic acid (prostaglandins and leukotrienes), platelet activation factor (PHAT), cytokines, biogenic amines, complement, bradykinin, neuropeptides. In this respect, pharmacological regulation of inflammation is directed most often to the suppression of the processes of synthesis and visualos-Denia of these mediators.

Of great interest are substances that inhibit the formation of eicosanoids-prostaglandins and leukotrienes, the common precursor of which is Ara-hidonic acid. The process of formation and metabolism of arachidonic acid, as well as the point of application of the main groups of anti-inflammatory drugs are shown in figure 3.1.

Figure 3.1. Effect of the main groups of anti-inflammatory drugs on the biosynthesis of eicosanoids



3.1. CORTICOSTEROIDS

Mechanism of action. GCS by passive diffusion penetrate through the cell membrane into the cytoplasm of the cell, where it binds to a specific receptor. The activated complex GCS receptor can penetrate into the cell nucleus, where it binds to certain areas of DNA and subsequent specific modulation of cellular effects by direct or indirect regulation of TRANS-cryption of certain target genes. These genes are responsible for the synthesis of white molecules involved in almost all parts of inflammation, while the GCS inhibit the synthesis of so-called proinflammatory substances and enhance the synthesis of proteins with anti-inflammatory activity (figure 3.2. table 3.1).

Figure 3.2. Mechanism of action of GCS

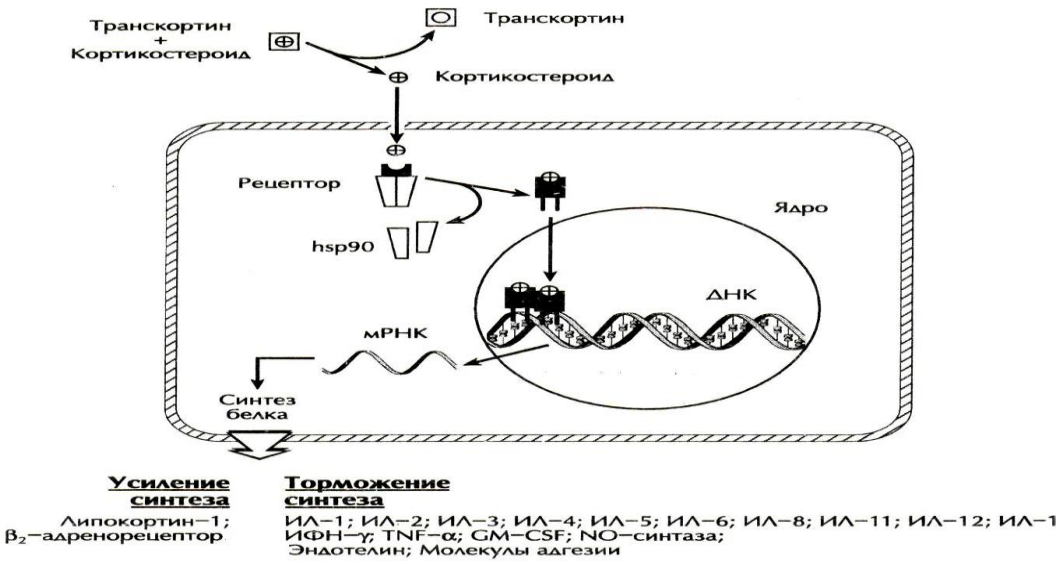


Table 3.1. The effect of GCS on the expression of genes of certain substances, the host participation in the development of inflammation

Suppression	Gain
Cytokines: IL-1, IL-2, IL-6, IL-8, TNF-α, IFN-γ, GM-CSF	Lipocortin
Elastase	Plasminogen activator inhibitor
Plasminogen activator	Vasocardin
Metalloproteinases	Neutral endopeptidase
Cyclooxygenase	Receptors for hormones and cytokines
No synthetase	Angiotensin converting enzyme
Adhesion molecules	

Anti-inflammatory effect of GCS in the focus of inflammation

Braking or suppression:

- migration of leukocytes to the inflammation site
-cytokine production
- platelet-activating factor
- IgE-dependent release of histamine and leukotrienes from basophils
- migration and degranulation of mast cells
- functions of the goblet cells and mucous glands of the epithelium

- expression of adhesion molecules
- the level of leukotriene
- the content of prostaglandins
- migration and number of eosinophils

- nitric oxide production
-capillary permeability
- permeability of lysosomal membranes
- reactivity of fibroblasts and endothelial cells

Main pharmacological effects of GCS

- Anti-inflammatory, anti-allergic (see above)
- Delay in the body of sodium and water, increased potassium secretion
- Stimulation of gluconeogenesis, hyperglycemia, glucosuria.
-Strengthening of catabolism processes, inhibition of protein synthesis
- Redistribution of subcutaneous fat on cushingoid type
- Inhibition of calcium absorption in the intestine, hypercalciuria, increased calcium release from bone
- Increased blood pressure
- Lymphopenia, monocytopenia, eosinopenia. Increasing the number of neutrophils, red blood cells, platelets.
- Skin atrophy, delayed wound healing
- Immunosuppressive action:

-reduction of the number of lymphocytes in peripheral blood
- increased apoptosis of T and b lymphocytes
- suppression of t lymphocyte proliferation
- reduced function of T-helpers and cytotoxic T-lymphocytes
- inhibition of tyrosine kinase activity
- inhibition of complement system activity
- inhibition of immune complex formation
- a decrease in the level of immunoglobulins (high-dose corticosteroids)

Table 3.3. Glucocorticosteroid preparations

Drugs	Indication	Side effects, contraindications
System GC: short-acting: *hydrocortisone hemisuccinate, prednisone, methylprednisolone*; average duration: *triamcinolone;* long-acting: *dexamethasone, betamethasone*	Acute adrenal insufficiency; acute allergic reactions (anaphylactic shock, toxicodermia, urticaria, angioedema); asthma status, bronchial asthma, bronchoobstructive syndrome; myocardial infarction complicated by cardiogenic shock, thyrotoxic crisis; malignant neoplasms; diseases of blood; rheumatic diseases; allergic and inflammatory diseases of the eye; ulcerative colitis, autoimmune diseases of the liver and kidneys, etc.	Skin atrophy, acne, impaired wound healing, myopathy, osteoporosis, unstable mood, psychosis, increased intracranial pressure, insomnia, hypertension, thromboembolism, steroid ulcers of the gastrointestinal tract, bleeding, perforation, delayed growth in children, steroid diabetes, menstrual irregularities, depression of the hypothalamic-pituitary-adrenal system, edema, hypokalemia, glaucoma, increased susceptibility to infections, opportunistische infection erased for infections, weight gain, increased appetite, Cushing's syndrome. Complications associated with the termination of treatment: exacerbation of the underlying disease, adrenal insufficiency.
Topical corticosteroids (for topical application) Inhalation: beclometasone, budesonide, fluticasone Intranasal (nasal sprays) Eye drops Ointments, creams, lotions	Bronchial asthma (prevention of attacks), chronic obstructive pulmonary disease. Allergic rhinitis, pollinosis Allergic conjunctivitis Allergic diseases of the skin	Local: candidiasis of the mouth and throat, hoarseness, paradoxical bronchospasm (requires withdrawal of the drug). Systemic (in rare cases with prolonged use of high doses): reduced adrenal cortex function, growth retardation in children, cataract, glaucoma. Hoarseness of the voice, dryness in the nose, hypersensitivity reactions, candidiasis of the nasopharynx cavity, in some cases - bloody discharge from the nose. A slight burning sensation, slight redness, lacrimation. With long - term use, secondary viral or fungal infections, the development of steroid cataracts and glaucoma are possible. In cutaneous use: itching, skin irritation, contact eczema, steroid acne, purpura. With long-term use of ointment-the development of secondary infectious lesions. When applied to large surfaces and long-term use of possible systemic manifestations.

CONTRAINDICATIONS

! There are no absolute contraindications for the appointment of glucocorticosteroids, except for individual intolerance

Relative contra-indications for glucocorticosteroid therapy:

1. Severe hypertension
2.Viral infection
3. Pronounced degenerative changes in the myocardium
4.Osteoporosis
5. Vaccination period
6.Mental illness
7.Diabetes
8. Heart failure II-III degree.
9.Cushing syndrome
10.Systemic mycosis
11.Thrombophlebitises
12.Tuberculosis
13.Ulcer
14.Childhood
15. The first trimester of pregnancy, lactation

3.2. NONSTEROIDAL ANTI-INFLAMMATORY DRUGS

Non-steroidal anti-inflammatory drugs (NSAIDs) are among the most important drugs that are widely used in clinical practice.

Table 3.4. The main effects of prostaglandins in the human body

Prostaglandin	Receptor	Effect
PGE2	EP_1	The contraction of the muscles of the bronchi and gastrointestinal tract
	EP_2	Relaxing the muscles of blood vessels, bronchi and gastrointestinal tract
	EP_3	The contraction of the muscles of the bronchi, uterus; gastroprotective action (inhibition of secretion of gastric juice, increased secretion of mucus is neutral); inhibition of lipolysis; reduced allocation of mediators in the autonomic nervous system
	-	Increase in body temperature; inhibition of proliferation of T-lymphocytes; inhibition of macrophage activation
PGE2	FP	Uterine contraction
PGI2	DP	Vasodilation (mesenteric, coronary, renal vessels) or vasoconstriction (pulmonary vessels); antiplatelet effect, relaxation of the uterus and gastrointestinal tract

PGI2 (prostacyclin)	IP	Inhibition of platelet aggregation, vasodilation
THA2 (thromboxane)	TP	Stimulation of platelet aggregation, vasoconstriction

- ! Prostaglandins are mediators of inflammatory reaction:
- cause local vasodilation, edema, exudation, migration of leukocytes and others;
- sensitize receptors to pain mediators (histamine, serotonin, bradykinin) and mechanical effects, lowering the pain sensitivity threshold;

increase the yield of enzymes from lysosomes, activate the enzymes collagenase and metalloproteinase.

! General mechanism of action of all nsaids is the inhibition of cyclooxygenase

Despite the differences in the chemical structure, all NSAIDs have common therapeutic and side effects, which is explained by a single mechanism of action. In 1971, it was shown that acetylsalicylic acid inhibits the activity of the enzyme cyclooxygenase (COG) and blocks the synthesis of PG from arachidonic acid. Later it was found that there are at least two isoforms of COG. COG-1 is a "constitutional" form of the enzyme, it is constantly present in the endoplasmic reticulum of cells and provides synthesis of PG, involved in the regulation of physiological functions of the body (gastroprotection, platelet aggregation, renal blood flow, glomerular filtration, excretion of ions and water, uterine tone, spermatogenesis, etc.). COX-2 is the" induced " form of the enzyme, the activity of which increases 10-80 times in inflammation. Formed under the influence of COX-2 PG participate in the development and progression of acute and chronic inflammation. In this regard, J. R Vane (1994) formulated a hypothesis according to which the anti-inflammatory effect of NSAIDs is associated with their ability to inhibit COX-2, while the most common side effects (time-ing of the gastrointestinal tract, kidneys, platelet aggregation, etc.)-with the suppression of COX-1 activity.

Non-selective COX inhibitors (COX-1 and COX-2)

Derivatives of salicylic acid

Acetylsalicylic acid

Derivatives of Anthranilic acid

Mephenamic acid

Acid floranova

Pyrazolone derivatives

Phenylbutazone

Sodium Metamizole

Derivatives of indolacetic acid

Indomethacin

Derivatives of phenylacetic acid

Diclofenac sodium

Derivatives of phenylpropionic acid

Ibuprofen

Ketoprofen

Naphtylpropionate acid derivatives

Naproxen

Axioms

Piroxicam

Lornoxicam

Table 3.5 non-Steroidal anti-inflammatory drugs

Drugs	Mechanism of action and pharmacological effects	Indications application	Side effects, contraindications
Non-selective COX inhibitors	*Anti-inflammatory effect:* - inhibition of COX → inhibition of PG synthesis - COX-independent mechanisms of anti-inflammatory action of NSAIDs: suppression of synthesis and expression of adhesion molecules, stabilization of lysocom, antioxidant effect, suppression of nitric oxide (NO) synthesis. *Analgesic effect:* - violation of the synthesis of prostaglandins; - violation of the processes of release and activation of pain mediators; - - decrease in the activity of proteolytic enzymes. *Antipyretic effect:* - suppression of the activity of COX-2 → a decrease in the synthesis ПГЕ2 → rebalancing of the centers of heat production and heat loss; - vasodilatation of the skin and increase teplootdelenie.	Rheumatic diseases, non-rheumatic diseases of the musculoskeletal system, inflammation, pain syndrome of medium intensity (head, toothache, dysmenorrhea, etc.), renal and hepatic co-faces, fever, as an antiplatelet (acetyl-LIC acid).	Hemorrhagic syndrome, defeat of the gastrointestinal mucosa, bronchospasm, impaired renal function, liver, violation of labor, oppression of hematopoiesis (pyrazolone derivatives).
Selective Inhibitors COG-2: Meloxicam, Nimesulide, Celecoxib	Selectively inhibits COX-2, suppresses the synthesis of PG in the focus of inflammation. Inhibits lipid peroxidation, inhibits the release of myeloperoxidase. Does not affect hemostasis.	Rheumatoid arthritis, reactive arthritis, osteoarthritis, bursitis, tendinitis; pain of medium intensity.	Dyspepsia, nausea, vomiting, abdominal pain, esophagitis, Gast-routinely ulcers, constipation, diarrhoea, flatulence; dizziness, headache, sleep, him getting; swelling, increased blood pressure, increased creatinine and/or urea in the serum, depression of Trovatore-tion, photosensitization, al-liricheskie reaction.

3.3. Antiallergic agents

Allergy (hypersensitivity)-a phenomenon based on the damage caused by my immune response to allergens. Thus, Allergy b includes all the main signs of inflammation with one fundamental difference: allergic inflammation has a specific orientation against a certain pathogenic agent (allergen). In this case, there is a combination of a universal reaction of inflammation with an immunological reaction that provides specific antigenic recognition and elimination of the allergen.
Pharmacotherapy of allergic diseases is based on the use of the following groups of drugs: glucocorticosteroids, H1-histamine receptor blockers, membrane stabilizers of mast cells, antileukotriene drugs. The symptoms of allergic diseases are caused by razlichnymi IU-diatreme, but only histamine through stimulation of H1-receptors is involved in almost all manifestations of this disease are shown, which allowed to consider this material as one of the most important mediators of Allergy.
Antihistamines block histamine-sensitive receptors in the tissues and hinder the development of mediator-induced spasm of the smooth muskulatur-ture of the bronchi and intestines, prevent vasodilation and increase their Pro-Nichelatti, reduce itching, reduce the secretory activity of the glands.

Table 3.6. H1-histamine receptor blockers

Drugs	Mechanism of action Pharmacological effects	Side effects, contraindications
First generation*: diphenhydramine (diphenhydramine), clemastine (tavegil), promethazine (pipolfen), chloropyramine (suprastin) mebhydrolin (diazo-Lin), quifenadine (fenkarol)*	Blockade of H1-histamine receptors → increased tone and decreased vascular permeability, reducing the intensity of itching, lowering the tone of smooth muscles of the bronchi and intestines. Pharmacodynamic features: partial binding to H1-receptors at therapeutic doses; the short duration of action; the binding of M-cholinergic receptors, 5HT receptor α - adrenergic receptors, D-receptors; and hinidinopodobny local anesthetic effect; sedative effect; stimulation of appetite; dysfunction of the gastrointestinal tract; addictive	Dizziness, drowsiness, dry mouth, coordination disorders, nausea, diarrhea, gastralgia, irritation of the gastric mucosa, paresthesia, increased fatigue. *Contraindications*: hypersensitivity, prostatic hypertrophy, angle-closure glaucoma, peptic ulcer, inflammatory diseases of the gastrointestinal tract in the acute phase.
Second generation: *loratadine (claritin), acrivastine (semprex), cetirizine (zyrtec, cethrin), ebastine (kestin)* III generation: *cetirizine (xyzal), desloratadine (aerius), Fexofenadine (Telfast)*	Pharmacodynamic features: very high specificity and affinity to H1-receptors; rapid onset of action; sufficient duration of the main effect; no blockade of other types of receptors; impenetrability through the blood-brain barrier in therapeutic doses; no connection with absorption of food intake; no addiction	In rare cases-nausea, dry mouth, fatigue, headache, sedation, cough, allergic reactions - possible skin rash. *Contraindications.* Hypersensitivity, pregnancy, lactation, childhood (up to 2-6 years).

3.4. Immunotropic agents

Table 3.7. Immunomodulators (immunostimulators)

Preparation	Mechanism of action and pharmacological effects
Likopid	Stimulation of effector functions of phagocytes; stimulation of leukopoiesis
Polyoxidonium	Stimulation of tissue and circulating monocytes/macrophages activity; antioxidant and detoxifying effect
Taktivin.	Increased migration of t-cell precursors and their maturation in the thymus
Interferons	Stimulation of the Th1 response; the blockade of the signaling pathways of growth factors of tumors; the blockade of the Assembly of the virus
Colony stimulating	Induction of differentiation of progenitor cells in the bone marrow and the yield of leukocytes in the blood

Table 3.8. Immunosuppressants

Group	Mechanism of action	Side effect
Cytostatics (methotrexate, cyclophosphamide, etc.), see section " Anticancer agents»	Antiproliferative effect on lymphocytes	Oppression of hematopoiesis, oppression of reparative processes in the gastrointestinal tract, reproductive system
Intravenous immunoglobulins (human normal immunoglobulin)	The lower titers of autoantibodies, neutralization of circulating antibodies, inhibition of the synthesis of immunoglobulins	Individual intolerance, influenza-like syndrome
Cyclosporine A	Violation of the synthesis of T-helper cells by Il-2 and expression of the receptor of IL-2 in T-effectors	Nephrotoxicity, increased blood pressure, tremor, paresthesia, hepatotoxicity, pneumosclerosis

Preparations of this group are used to treat severe autoimmune processes, severe atopy, tumors, to prevent transplant rejection. The most common side effect of all drugs, with the exception of intravenous immunoglobulins, is secondary immunodeficiency.

Table 3.8. Therapeutic monoclonal antibodies

Preparation	Mechanism	Target	Indications for use	Side action
Infliximab	actions Chemical antagonism	Fnoa.	Rheumatoid arthritis, Crohn's disease	Allergic reactions, pyrogenic reactions
Omalizumab		IgE	Bronchial asthma	
Daclizumab		Receptor to IL-2	Graft rejection, autoimmune diseases	

Tasks for self-training:

Task 1. Specify the side effects of systemic and topical corticosteroids

Preparation Side effect	GCS for oral administration	ICS	GKS – ointment
The level of glucose in blood plasma			
Fat redistribution			
Protein synthesis and breakdown			
Reabsorption of sodium			
Secretion of potassium			
Water retention			
Glaucoma			
Ulceration of the gas-trointestinal mucosa			
Immune system			
Neutrophils			
Monocytes			
Lymphocytes			

Use the following notation:
+ - the existence of the effect; - no effect; ↓ - decrease (of numbers, functions);
↑ - gain.

Task 2. Specify the groups of funds in accordance with the indications for use:

Indications	Funds group
Rheumatic disease	
Headache, toothache	
Fever	
Diseases of joints of non-rheumatic nature	
Renal colic	
Bronchial asthma	
Allergic reaction	

Task 3. Side effects of NSAIDs

Side	Acid acetyls-	Metamizole	Income-Tatsinska	Ibupro-hairdryer	Diclofenac Sodium's	Proxy-kam	Celecoxi b

	salicylic		ya				
effect							
Bronchospasm							
The defeat of the gastrointestinal mucosa							
The Reye's Syndrome							
Kidney damage							

The frequency of side effect: + - rare species; ++ - common; + + + very frequent; ± - possible

Tasks for self-control

I. inhalation glucocorticosteroids include all except:
1) budesonide; 2) kromoglikata sodium; 3) beclomethasone; 4) flunisolide.

_____

II. The main mechanism of action of non-steroidal anti-inflammatory drugs is:
1) antiprostaglandin; 2) antibacterial; 3) antihistamine; 4) inhibition of antigen-antibody reaction

_____

III. The main side effects of all non-steroidal anti-inflammatory drugs are:
1) gastrotoxic; 2) hepatotoxic; 3) nephrotoxic; 4) cardiotoxic.

_____

IV. The mineralocorticoid effect is most pronounced in:
1) prednisolone; 2) polcortolone; 3) dexamethasone; 4) triamcinolone

_____

V. what is the impact of corticosteroids on the cellular composition of blood?
1) increase the number of lymphocytes; 2) reduce the number of lymphocytes; 3) increase the number of neutrophils; 4) reduce the number of neutrophils; 5) increase the number of eosi-nofils; 6) reduce the number of eosinophils.

_____

VI. Mark the answers corresponding to the questions:
1. A means of inhibiting phospholipase A2
2. Means whose anti-inflammatory effect is associated with the selective suppression of the activity of COG-2
3.The agent has the most pronounced anti-inflammatory effect
4. Means, non-selectively inhibiting COX-1 and COX-2
5. The tool has the most pronounced hepatotoxic effect

A. Indomethacin
B. Prednisone
B. Meloxicam
G Metamizole sodium
D. Diclofenac-sodium
E. Celecoxib
J. Acetylsalicylic Acid

VII. Side effects of acetylsalicylic acid:
1) hearing impairment; 2) allergic reactions; 3) leukopenia; 4) dyspepsia; 5) ulceration of the gastrointestinal tract; 6) gastric bleeding;
7) swelling; 8) respiratory depression.

VIII. Note the features of celecoxib compared to sodium diclofenac:
1) more selectively, in comparison with diclofenac, inhibits COX-2; 2) equally inhibits COX-1 and COX-2; 3) by anti-inflammatory activity of copos-tavim with diclofenac; 4) by anti-inflammatory activity inferior to diklof-NAC; 5) less likely to cause damage to the mucous of the gastrointestinal tract; 6) more often causes a violation of liver function.

IX. In the treatment of pyrazolone derivatives, the following side effects develop:
1) hearing impairment; 2) allergic reactions; 3) leukopenia; 4) dyspepsia; 5) ulceration of the gastrointestinal tract; 6) gastric bleeding;
7) swelling; 8) respiratory depression.

X. histamine H1-receptor Blockers block the following effects by histamine;
1) vasodilatation; 2) increased gastric secretion; 3) itching of the skin; 4) lowering blood PRESSURE; 5) increased capillary permeability; 6) bronchial spasm.

XI. In allergic reactions of delayed type used:
1) cromoglicate sodium; 2) blockers of H1-histamine receptors; 3) glucocorticoid; 4) β2-adrenomimetiki; 5) drugs; 6) preparations of interferons.

XII. Note the side effects that can be observed when using anti-histamine drugs of the first generation:
1) dry mouth; 2) General weakness; 3) dizziness; 4) cardiac arrhythmias; 5) bronchospasm; 6) lowering blood PRESSURE; 7) sedative effect.

XIII. Advantages of antihistamines of the 2nd generation:

1) high affinity to H1-receptors; 2) high permeability through the hemato-encephalic barrier; 3) no sedative action; 4) no habit; 5) simultaneous blockade of M-cholinoreceptors; 6) all of the above.

_____

XIV. Determine the drug by the following properties:
1) belongs to the group of antiallergic agents; 2) blocks H1 receptors; 3) good solubility in fats; 4) has a marked sedative effect; 5) with ne-redazione may cause Central nervous system excitation and seizures.

_____

XV. Determine the drug by the following properties:
1) increases the migration of predecessors of T-lymphocytes and their maturation in the thymus; 2) has immunostimulating, antistress and analgesic activity; 3) used in infectious, purulent-septic and autoimmune processes; 4) can cause "flu-like" syndrome.

_____

Situational concerns

1. Patient T., 40 years old, entered the clinic with gastric bleeding. From anamnesis it became known that the patient suffers from gastric ulcer and duodenal ulcer for 10 years. A week before hospitalization took to reduce the temperature of the drug X. the Drug of which group could take the patient? What is the mechanism of damage to the gastric mucosa?

_____

_____

2. A patient with rheumatoid arthritis, who received appropriate anti-inflammatory therapy for six months, began to note sleep disorders, weight gain. The examination revealed hypertension, hyperglycemia, lymphocytopenia, eosinopenia. What medication was the patient taking? What are the causes of complications?

_____

Prescribe:
1. Anti-inflammatory agent for rheumatoid arthritis.
2. Anti-inflammatory agent for patients with gastric ulcer and duodenal ulcer.
3. A blocker of histamine H1-receptors, CNS depressants.
4. Non-steroidal means of basic therapy of bronchial asthma for inhalation.
5. A means to prevent influenza.
6. A means to suppress the reaction of graft rejection.
7. Emergency treatment for anaphylactic shock.
8. Immunomodulator - preparation of the thymus gland.

To prescribe additional in the pediatric Department:

1. The drug is from the group of non-steroidal anti-inflammatory drugs in rheumatoid arthritis in a child of 6 years.

PRACTICAL LESSON № 4

The theme of the lesson. TOOLS THAT AFFECT THE TONE AND CONTRACTILE ACTIVITY OF THE MYOMETRIUM.
DRUGS AFFECTING THE BLOOD.

The General purpose of the lesson. To study the classification, mechanisms of action of drugs that affect the tone and contractile activity of myometrium and drugs that affect hematopoiesis, especially pharmacokinetics and pharmacodynamics of individual obstacles.

Specific objectives of the lesson

The student should know:

- classification of agents that affect the tone and contractile activity of the myometrium, agents that affect hematopoiesis;
- mechanisms of action of drugs of these groups;
- pharmacological effects and features of the action and use of individual drugs;
- side effects and contraindications to the appointment.

The student must be able to:

- write prescriptions for drugs studied groups;
- to justify the choice of drugs for various pathological conditions;
- choose the dose and route of administration of the drug, taking into account the disease, the presence of comorbidities, possible drug interactions.

Control question:

1. Classification of agents affecting myometrium.
2. Means that increase the tone and contractile activity of the myometrium. Class-fiction, the mechanism of action. Differences in the effect on the uterus and the use of drugs hormones of the posterior pituitary and preparations of prostaglandins. Side effect.
3. Means that increase mainly the tone of the myometrium. Classification and application.
4. A means of reducing the tonus of the uterine cervix. Application.
5. Means that reduce the tone and contractile activity of the myometrium. Mechanisms of action and application.
6. Classification of agents affecting erythropoiesis.
7. Iron preparation. Classification. Indications for use. Side effects and ways of correction.
8. The mechanisms of pharmacological actions of cyanocobalamin and acid fo-leeway with hyperchromic anemia. Differences in indications for use.
9. Preparations erythropoietin.
10. Means, depressing erythropoiesis.
11. Agents that stimulate leucopoiesis. Characteristics of drugs, application.
12. The agents suppressing the blood.

4.1 MEANS OF INFLUENCING THE TONE AND CONTRACTILE ACTIVITY OF THE MYOMETRIUM

The uterus is a smooth muscle organ, contractile activity and tone of which are regulated by complex neurohumoral mechanisms.

On the surface membranes of smooth muscle cells of the myometrium located M3-cholinergic receptors, the α-adrenergic receptors, the stimulation of which leads to increased uterine activity and β2-adrenergic receptors, which upon excitation of the contractile activity decreases.

Humoral regulation is carried out:

- Circulating catecholamines: stimulation of β2-adrenoreceptors → reduction of rhythmic contractions of myometrium;
- Oxytocin: increases tone and contractile activity of myometrium;
-Prostaglandins E2 and F2α: increase the tone and rhythmic contractions of Biomet-dence and reduce the tonus of the uterine cervix.

Classification

I. **Means affecting the contractile activity of the myometrium**

Enhancing contractile activity

Hormones and preparations of the posterior lobe of the pituitary gland

Oxytocin

Pituitrin

Prostaglandin preparations

Dinoprost (prostaglandin F2A)

Dinoprostone (prostaglandin E2)

Weakening contractile activity

β2-adrenomimetics

Salbutamol

Fenoterol

Means to narcosis

Sodium oxybutyrate

Different

Magnesium sulfate

II. Means, increasing mainly the tone of myometrium

Preparations of plant origin (alkaloids and ergot preparations)

Ergometrine maleate

Ergotamine tartrate

Ergot extract, thick

Ergotal.

III. Tools, lowering the tone of the cervix

Atropine sulfate

Dinoprost

Dinoprostone

Table 4.1. Drugs that affect the contractile activity of the myometrium

Preparation	Mechanism of action	Application	Side effects, contraindications
Posterior pituitary hormones: oxytocin, pituitrin		Stimulation of labor; postpartum uterine bleeding, acceleration of postpartum uterine involution, stimulation of lactation	Fetal hypoxia, placental abruption, uterine rupture.
Preparations of prostaglandins: dinoprost (prostaglandin F2A), dinoprostone (prostaglandin E2)	Activation of specific receptors → increased myometrial contractility and relaxation of the cervix regardless of the pregnancy period	Artificial abortion, stimulation of labor.	Pituitrin – increase in blood pressure. Contraindications: abnormal presentation of the fetus, narrow pelvis, uterine scars.
β2-agonists: fenoterol, salbutamol	Stimulation of β2-adrenergic receptors → relaxation of the smooth muscles of the uterus.	The threat of preterm birth, short-term cessation of labor in case of excessively fast labor with strong uterine contractions and high frequency of labor.	Nausea, vomiting, diarrhea, headache, phlebitis.
Means for anesthesia: sodium oxybutyrate	Stimulation of GABA-ergic excitation transmission in the Central nervous system → relaxation of uterine muscles		Dinoprost – fluctuations in pressure, arrhythmia. Dinoprostone-fever, hypotension. Contraindications: fetal presentation abnormalities, narrow pelvis, uterine scars, glaucoma, liver, kidney, cardiovascular system.
Magnesium sulfate	Violation of the current of calcium ions into the cell → the relaxation of smooth muscles of the uterus.		Tachycardia, lowering diastolic blood PRESSURE, fetal hyperglycemia, hypokalemia, tremor, headache, dizziness. Contraindications: heart disease, arrhythmia, IHD, decompensated diabetes, thyrotoxicosis, glaucoma, I trimester of pregnancy.
Alkaloids and ergot preparations	Stimulation of α-adrenoceptors and 5-HT3 receptors → increased myometrial tone	Uterine bleeding, acceleration of uterine involution in the postpartum period	Arousal, nausea, vomiting, respiratory depression, seizures. Contraindications: toxicosis of the second half of pregnancy, hypokalemia, myasthenia gravis.

4.2. DRUGS AFFECTING HEMATOPOIESIS

Table 4.2. Drugs that affect blood formation

Drugs	Mechanism Action	Indications	Side effects
Stimulants of erythropoiesis			
Iron preparations: iron sulfate, iron lactate, ferrum-Lek	Remedying of iron deficiency → stimulation of proliferation and differentiation of red blood cells and the production of hemoglobin	Elimination of iron deficiency → stimulation of erythrocyte proliferation and differentiation and hemoglobin production	Itchy skin, metallic taste in the mouth, nausea, vomiting, constipation, stool staining in black.
Vitamins: cyanocobalamin, folic acid	Stimulation of erythrocyte proliferation and differentiation	Stimulation of erythrocyte proliferation and differentiation	
Erythropoietin		Elimination of iron deficiency → stimulation of erythrocyte proliferation and differentiation and hemoglobin production	Headache, arthralgia, hyperkalemia, skin rash
Means, depressing erythropoiesis			
Solution of sodium phosphate labeled with phosphorus-32	Inhibition of erythropoiesis → reduction in the number of red blood cells	Erythremias	
Stimulants leykopoeza			
Sodium nucleinate, pentoxyl, methyluracil	Stimulate the formation of leukocytes in the bone marrow	Light forms of leukopenia	Dyspeptic disorders
Recombinant human GM-CSF *Recombinant human G-CSF*	↑ proliferation, differentiation and function of granulocytes and monocytes	Expressed disorders of leukopoiesis associated with chemotherapy and radiation therapy, infections, bone marrow transplantation, AIDS	Nausea, vomiting, anorexia, fever, myalgia, edema, allergic reactions

Tasks For Self-Control

I. Which of the following drugs are used in hypochromic anemia:
1) iron lactate; 2) folic acid; 3) iron sulfate; 4) cyanocobalamin; 5) erythropoietin.

II. For the treatment of iron deficiency anemia with iron preparations, it is necessary:
1) complete protein nutrition; 2) enrichment of the diet with products containing ascorbic acid;
3) wash down medicines with soda solution; 4) long-term value of the drug.

III. Side effects of iron preparations:
1) metallic taste; 2) constipation; 3) diarrhea; 4) nausea, vomiting; 5) arrhythmia; 6) abdominal pain.

_____

IV. Determine the drug properties: blood stimulator, is a com-Plex drug of cobalt and nicotinamide, used for the treatment of hypochromic anemia.

_____

V. In eritremii control system uses:
1) pentoxy; 2) methyluracil; 3) a solution of sodium phosphate labeled with phosphorus-32; 4) sodium nucleinate; 5) Hamid.

_____

VI. Leukopoiesis stimulators are contraindicated in:
1) agranulocytosis; 2) malignant diseases of the blood; 3) sluggish cancer, burns, fractures.

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VII. To determine the drug properties: is a stimulant of leukopoiesis, stimulates the proliferation and differentiation of precursors of granulocytes and the activity of neutrophils.

_____

VIII. To call means stimulating the muscles of the uterus:
1) ergotal; 2) dinoprost; 3) fenoterol; 4) oxytocin; 5) cotarnine chloride; 6) amine-zine; 7) methylergoline.

_____

IX. What dreams are used to enhance the rhythmic activity of myometrium:
1) oxytocin; 2) pituitrin; 3) ergotal; 4) ergometrin; 5) dihydroergotoxin.

X. what side effects are possible when using prostaglandins to stimulate uterine contractions:
1) bronchospasm; 2) phlebitis; 3) collapse; 4) nausea, vomiting.

XI. Specify the tool to be used in threatening premature birth:
1) oxytocin; 2) phenoterol; 3) dinoprostone; 4) ergometrine.

_____

XII. Which drugs have the following set of properties: cause relaxation of myometrium, improve utero-placental blood flow, among the side effects-tremor, tachycardia, diastolic blood PRESSURE, hyperglycemia.

Situational Tasks

1. A 23-year-old woman was taken to the maternity hospital because of the birth activity. In childbirth, there are rare short-term uterine contractions. The weakness of labor activity was diagnosed. What drugs can be included in the drug scheme of stimulation of labor. Give the rationale for the answer.

_____
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2. The woman in labor is 25 years old, the Department arrived in connection with the beginning of labor activity. Childbirth was accompanied by a large blood loss. What drugs can be considered as a means of emergency care? Give the rationale for the answer.

_____
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3. A 30-year-old woman entered the maternity hospital due to the appearance of pain sensations in the lower abdomen. Term pregnancy 31-32 weeks. The tone of the uterus elevated. The diagnosis was "first-time, 30 years, threatening preterm birth". What drugs will be justified in this situation? Give a justification for the answer.

_____
_____

Prescribe

1. A treatment for iron deficiency anemia.
2. A treatment for anemia associated with chronic renal insufficiency.
3. A treatment for pernicious anemia.
4. A treatment for macrocytic anemia.
5. A means of stimulating leukopoiesis.
6. Means for induction and stimulation of labor.
7. A means to stop abnormal uterine bleeding.
8. The tool, which increases mainly the tone of myometrium.

PRACTICAL CLASS № 5

The theme of the lesson. VITAMINS

The General purpose of the lesson. To study the classification, mechanisms of action of drugs that affect the tone and contractile activity of myometrium and drugs that affect hematopoiesis, especially pharmacokinetics and pharmacodynamics of individual obstacles.

Specific objectives of the lesson

The student should know:

- classification tools that have an impact on the tone and contractile activity of Biomet-dence, agents that affect hematopoiesis;
- mechanisms of action of drugs of these groups;
- pharmacological effects and features of the action and application of individual pre-parates;
- side effects and contraindications to the appointment.

The student must be able to:

- write prescriptions for drugs studied groups;
- to justify the choice of drugs for various pathological conditions;
- choose the dose and route of administration of the drug, taking into account the disease, the presence of accompanying pathology, the possible interaction of drugs.

Control question:

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11. Agents that stimulate leucopoiesis. Characteristics of drugs, application.
12. The agents suppressing the blood.

FOR THE RECIPE

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