

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

Department of general and clinical pharmacology

Authors:

A.V.Sennikava, senior lecturer

B.S. Yarashevich, senior lecturer

E.I. Mikhailova, head of department, DMS, prof.

**METHODOLOGICAL RECOMMENDATIONS**

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

**TOPIC 27: ANTI-INFLAMMATORY AND ANTI-GOUT DRUGS.  
ANTI-ALLERGIC DRUGS. IMMUNOMODULATORS»**

Time: 3 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**

Nonsteroidal anti-inflammatory drugs (NSAIDs) are a group of drugs with a diverse chemical structure. Their number is constantly increasing and currently this group has the largest number of drugs that differ in the characteristics of action and application. More than thirty million people in the world take NSAIDs every day, and 40% of these patients are over the age of 60.

The incidence of gout is progressively increasing from year to year. This is accompanied by a simultaneous increase in the incidence of diseases such as obesity, alcoholism, hypertension and metabolic syndrome. For rheumatologists, traumatologists, general practitioners, as well as for doctors of many other specialties who encounter patients with gout in their work, the primary tasks are adequate relief of acute and prevention of all subsequent attacks of the disease.

Allergoses are another pathology, the occurrence of which is steadily increasing. For example, from 3-5 to 30% of the general population of people suffer from atopic dermatitis. 15-20% had at least one episode of acute urticaria at least once in their life. At the same time, urticaria recurs in 75% of cases. The leading role in the treatment of allergic diseases, in particular allergic dermatoses, belongs to antihistamines.

The problem of immunotherapy also plays an important role in modern medicine. Doctors of almost all specialties have a special interest in it. This is primarily due to the steady growth of various infectious and inflammatory diseases prone to chronic and recurrent course against the background of not always effective basic therapy. An important importance in this regard is attached to the constantly increasing incidence of malignant neoplasms, autoimmune diseases, viral and fungal infections. The course of many of them leads to the development of disability, and in some cases even death of patients, often of young and socially active age.

### **Learning objective:**

- formation of scientific knowledge about the main pharmacological effects, providing therapeutic and preventive effect of drugs on the topic of the class, indications and contraindications for their use, the interaction of drugs, their combined use for use in medical and preventive activities.

### **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:**

- classification and basic characteristics of the studied drugs, pharmacodynamics and pharmacokinetics, indications and contraindications for their use, side effects;
- features of pharmacokinetics and pharmacodynamics, advantages and disadvantages of different dosage forms of these drugs;

– principles of research and testing of new drugs; information and reference and search systems;

**be able to:**

– analyze the effect of the studied drugs on the set of their pharmacological properties and the possibility of their use in medical practice; to write them in prescriptions;

– use different dosage forms of these drugs, based on the peculiarities of their pharmacodynamics and pharmacokinetics;

– work with scientific literature, search for information about the use and action of the studied drugs;

**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**

1. Metabolism and functions of phospholipids and their derivatives;
2. Participation of prostaglandins in physiological processes in the human body;
3. Types and mechanisms of development of immune reactions;
4. Features of the humoral and cellular defense systems of the human body.

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

1. Steroid anti-inflammatory drugs, classification. GC: prednisone, methylprednisolone, triamcinolone, dexamethasone, betamethasone. Mechanisms of action, the main schemes of the use of GC, side effects of GC and ways to prevent them. Comparative characteristics of systemic and local drugs. The main contraindications.

2. Nonsteroidal anti-inflammatory drugs (NSAIDs): acetylsalicylic acid, diclofenac, ibuprofen, naproxen, indomethacin, etodolac, nabumeton, meloxicam, celecoxib, etoricoxib. Classification (by chemical structure and selectivity of action on various types of COX).

3. Mechanisms of anti-inflammatory action (effect on mediators and inflammatory cells, prostaglandin synthesis processes (COX-1 and COX-2), monoamines, kinins, fibroblast proliferation, synthesis of acid mucopolysaccharides, transcription factor NF-kB, cartilage metabolism), other pharmacological effects of NSAIDs.

4. Comparative characteristics of NSAIDs. Advantages and disadvantages of non-selective COX-1 and COX-2 inhibitors, as well as agents selectively blocking COX-2. Indications and contraindications to the use of NSAIDs, side effects, their prevention.

5. Anti-gouty remedies. Classification.

Inhibitors of uric acid synthesis (allopurinol, febuxostat), uricosuric agents (sulfipyrazone, probenecid); agents used in acute gout attacks: NSAIDs, GC, colchicine. Mechanisms of action, application, side effects of anti-gouty agents.

6. Anti-allergic agents. Classification. Remedies used for allergic reactions of the immediate type.

Antihistamines (H1-histamine receptor blockers): diphenhydramine, clemastine, loratadine, cetirizine, ciproheptadine. Stabilizers of mast cell membranes (cromoglycic acid).

GC: prednisone, methylprednisolone, triamcinolone, dexamethasone, betamethasone.

Leukotriene receptor antagonists (zafirlukast, montelukast).

Mechanisms of action of antiallergic agents, comparative characteristics, indications for use, side effects.

1. Drugs used for anaphylactic shock (epinephrine, GCS, dopamine, salbutamol, antihistamines): principles of action, ways of introduction.

2. Drugs used for delayed allergic reactions.

Basic anti-rheumatic drugs: auranofin, penicillamine, chloroquine, sulfosalazine; immunosuppressants (cyclosporine, tacrolimus, anti-lymphocytic immunoglobulins, monoclonal antibody preparations – basiliximab); cytotoxic agents – methotrexate.

3. Immunomodulators.

Immunoregulatory peptides (interferon gamma-1b and other interferons); interferogens (tilorone, arbidol); thymus preparations (thymogen): mechanisms of action, application in medicine.

4. Immunosuppressants. Immunosuppressive properties of cytostatic agents.

## **PROCESS OF THE STUDY**

### **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;
- completing the tasks on the topic of the class in the workbook;
- 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.

**The list of tasks of the SIW:**

- solving practical problems in the EEMC;
- completing the test tasks of the EEMC.

**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.

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

**Recommended forms of CIWS organization:**

- doing exercises on the topic of the class in the workbook;
- 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. Interferons are natural and recombinant. Pharmacological effects, clinical application. Interferogens.
2. Colony-stimulating factors, immunoglobulin preparations.
3. Monoclonal antibodies in the treatment of autoimmune diseases.
4. Preferential and selective COX-2 inhibitors in the treatment of inflammatory diseases of the musculoskeletal system.

**Forms of control of CIWS realization:**

- 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.

**NSAIDs are drugs with anti-inflammatory, antipyretic and analgesic effects.**

| Classification          | Non-selective COX inhibitors  | Preferential COX-2 inhibitors   | Selective COX-2 inhibitors  | Antipyretic analgesics  |
|-------------------------|---|---|---|---|
| Drugs                   | <b>1. Acetylsalicylic acid (Aspirin)</b><br><b>2. Diclofenac sodium (Voltaren, Orthofen)</b><br><b>3. Ibuprofen (Ibufen, Nurofen)</b><br><b>4. Ketoprofen (Ketonal, Ultrafasten, Fastum gel)</b><br><b>5. Indomethacin (Metindol)</b><br><b>6. Phenylbutazone (Butadione)</b>   | <b>7. Meloksikam (Movalis)</b><br><b>8. Nimesulid (Sulide, Coxtal, Sintalgin, Octaprin, Nimesil)</b><br><b>9. Eudolacus (Elderin)</b> | <b>10. Celecoxib (Celebrex)</b><br><b>11. Rofecoxib (Rofika, Denebol)</b> | <b>12. Mephenamic acid (Pomstal)</b><br><b>13. Paracetamol</b><br><b>14. Ketorolac</b><br><b>15. Metamizole (Analgin)</b> |
| Mechanism of action     | <p>1. Inhibition of COX-1 and COX-2 (1-6) or COX 2 (7-10) → suppression of prostaglandin synthesis (PG) from arachidonic acid; inhibition of thromboxane A<sub>2</sub> synthesis</p> <p>2. Affect the synthesis of PG associated with the mobilization of Ca in smooth muscle (anti-Ca mechanism of anti-inflammatory effect)</p> <p>3. Block the interaction of bradykinin with tissue receptors → Restoration of impaired microcirculation, ↓ extravasation of capillaries, ↓ exudation of plasma, its proteins, proinflammatory factors and blood cells (bradykinin mechanism of anti-inflammatory effect) (1-3, 5)</p> <p>4. Inhibit the release of histamine, serotonin and biogenic amines (antihistamine and antiserotonin component of anti-inflammatory effect)</p> <p>5. Bind to with G-protein in the cell membrane → affect the transmission of membrane signals, ↓ transport of anions, affect biological processes (membrane stabilizing component of anti-inflammatory effect)</p> <p>6. Inhibition of inflammation → ↓ pain, because inflammation in the peripheral tissues stimulates pain receptors</p> <p>7. ↓ synthesis of prostaglandins (PG E<sub>1</sub>) stimulating thermoregulation center in the hypothalamus, peripheral vasodilatation → ↓ body temperature</p> <p>8. ↓ capillary permeability → impair immunocompetent cells contact with antigen and antibodies contact with a substrate; macrophages lysosomal membranes stabilization</p> <p>9. ↓ chemotaxis of monocytes, eosinophils, lymphocytes, leukocytes</p> <p>10. Inhibition of subcortical pain centers (central action) and pain impulses transmission to the CNS (12-15)</p> |   |   |   |
| Pharmacological effects | <p>1. Anti-inflammatory effect (1-11)</p> <p>2. Analgesic effect</p> <p>3. Antipyretic effect</p> <p>4. Antiplatelet effect (1)</p> <p>5. Immunosuppressive effect (3, 5, 6)</p> <p>6. Desensitizing effect</p>   |   |   |   |
| Indications             | <p>1. Rheumatic diseases (rheumatoid arthritis, gouty and psoriatic arthritis, ankylosing spondylitis, etc.) (1-11);</p> <p>2. Non-rheumatic diseases of the musculoskeletal system (osteoarthritis, myositis, tendovaginitis, trauma, etc.);</p> <p>3. Moderate pain syndrome of various etiologies (headache and toothache, postoperative pain, algodismenorea) (12-14);</p> <p>4. Neurological diseases (neuralgia, radiculitis, etc.) (12-14);</p> <p>5. ↑ body temperature &gt;38,5°C (1,3,13,15);</p> <p>6. Prevention of "white" (arterial) thrombi formation (1).</p>   |   |   |   |

|                          |   |
|--------------------------|---|
| <b>Side effects</b>      | <ol style="list-style-type: none"> <li>1. <i>NSAID-induced gastropathy</i> (inhibition of the synthesis of PG and prostacycline → ↓ pH; ↓ mucosa reparation- 1-6)</li> <li>2. <i>Nephrotoxicity</i> (vasoconstriction and deterioration of renal blood flow due to PG-E2 and prostacyclin synthesis inhibition in the kidneys → ischemic changes in the kidneys, ↓ glomerular filtration and volume of diuresis → water retention, edema, hypernatremia, hyperkalemia, ↑ serum creatinine level, ↑ blood pressure - most expressed in 1,5,6; direct influence on the renal parenchyma → interstitial nephritis - most expressed in 1,5,6,15)</li> <li>3. <i>Coagulopathy</i> (antiplatelet and moderate anticoagulant effect due to inhibition of prothrombin formation in the liver → bleeding - 1)</li> <li>4. <i>Hematotoxicity</i> (hypochromic microcytic anemia, hemolytic anemia, thrombocytopenia - 1, 5; leukopenia, agranulocytosis and thrombocytopenia due to hematopoiesis suppression in the bone marrow - 15)</li> <li>5. <i>Hepatotoxicity</i> (immunoallergic hepatitis at the beginning of the drug taking – more often 6; in long intake and high doses - toxic hepatitis more often at 2, 6)</li> <li>6. <i>Allergic reactions</i></li> <li>7. <i>Reye syndrome</i> (rapidly progressive, vitally threatening acute encephalopathy combined with liver damage and caused by the intake of NSAIDs against the background of a viral infectious disease - more often 1)</li> <li>8. Dizziness, headache</li> <li>9. Retinopathy, keratopathy (5); optic neuritis (3)</li> <li>10. Bronchospasm (more often in people with bronchial asthma - most pronounced in 1)</li> </ol> |
| <b>Contraindications</b> | <ol style="list-style-type: none"> <li>1. Erosive-ulcerative lesions of the digestive tract</li> <li>2. Severe dysfunction of the liver and kidneys</li> <li>3. Cytopenia</li> <li>4. Individual intolerance</li> <li>5. Pregnancy</li> </ol>   |
| <b>NB!</b>               | <ul style="list-style-type: none"> <li>• NSAIDs should be taken after meals and washed down with milk or alkaline water.</li> <li>• NSAIDs should be administered with caution to patients with bronchial asthma, as well as individuals who previously identified unwanted reactions when taking any other NSAIDs.</li> <li>• Patients with hypertension or heart failure should choose those NSAIDs, Which have the least effect on the renal blood flow.</li> <li>• Older people should take minimum effective doses and undergo short courses of NSAIDs.</li> </ul>   |

NSAIDs - non-steroidal anti-inflammatory drugs, COX - cyclooxygenase, GIT - gastrointestinal tract, CNS - central nervous system



### Antigout agents – medicines used to treat gout.

| Classification          | Uricosuric agents   | Uricodepressive drugs   | Uric acid-specific enzymes (PEGylated uricase)  |
|-------------------------|---|---|---|
| Drugs                   | <b>1. Sulfinpyrazone (Anturan)</b><br><b>2. Probenecid (Probalan)</b><br><b>3. Benzbromarone (Normurat, Hypurik)</b>  | <b>4. Allopurinol (Milurite)</b><br><b>5. Febuxostat (Adenurik)</b>   | <b>6. Pegloticase (Krystexxa)</b>   |
| Mechanism of action     | 1. ↓ reabsorption of uric acid in the proximal renal tubules → ↑ its excretion in the urine (1-3)   | 1. Inhibits xanthine oxidase → prevents the uric acid formation from hypoxanthine and xanthine  | Metabolizes uric acid to soluble allantoin to be eliminated   |
| Pharmacological effects | 1. Antigout effect  |   |   |
| Indications             | 1. Chronic gout<br>2. Hyperuricemia   | 1. Chronic gout<br>2. Urolithiasis<br>3. Prevention of hyperuricemia in radiation therapy and chemotherapy (4)  | 1. Drug-resistant gout<br>3. High disease activity with high blood level of uric acid<br>2. Intolerance to other antigout drugs |
| Side effects            | 1. Kidney stones<br>3. Dyspepsia<br>2. Gastroduodenal ulcer (1)   | 1. <b>Acute gout attack</b><br>2. Dyspepsia<br>3. Eosinophilia  | 1. Anaphylaxis<br>2. Infusion reactions   |
| Contraindications       | 1. Hyperuricosuria<br>2. Liver and renal disfunctions<br>2. Urolithiasis<br>3. Pregnancy and lactation<br>3. Gastroduodenal ulcer (1)   | 1. Severe liver and renal disfunctions  | 1. Glucose-6-phosphate dehydrogenase deficiency (risk of hemolysis and methemoglobinemia)                                       |
| NB!                     | Acidic medium of the urine facilitates uric acid crystallization and stones formation; therefor urine alkalization is needed (12-18 g of potassium citrate orally daily). The patient is to perform urine pH dipstick tests by himself regularly. | <b>Urate</b> -lowering therapies should not be initiated during an acute attack. But in patients already receiving these agents the urate-lowering medication should be continued without interruption. | High allergic intravenous drug; premedication by anti-histamines and glucocorticoids is needed                                  |

### Treatment of acute gout attack

|   |  |   |
|---|--|---|
| <b>1. Complete rest</b><br><b>2. Elevated position of affected limbs</b><br><b>3. In acute inflammation – cold (soak limbs in cold water). After pain relief – warming.</b><br><b>4. Increased fluid consumption (alkaline mineral water)</b> |  |   |
| 1. NSAIDs   |  | <b>Diclofenac</b> 100-150 mg daily orally or i/m; or <b>ibuprofen</b> 1200-2400 mg daily orally; or <b>meloxicam</b> 15 mg daily orally or i/m; or <b>nimesulide</b> 200-400 mg daily orally; a <b>celecoxib</b> 400 mg daily orally  |
| 2. When NSAIDs are ineffective or contraindicated   | <b>Colchicine</b>                        | Colchicine prevents microtubule assembly and thereby disrupts inflammasome activation, microtubule-based inflammatory cell chemotaxis, generation of leukotrienes and cytokines, and phagocytosis. Doesn't affect uric acid metabolism.<br>1 mg (2 tab.) in the first arthritis signs, then 1 tab. one hour later<br>Maximum dose for attack is 1,5 mg/h.<br>Maximum daily dose is 4-6 mg (8-12 tab.)<br>2-3 weeks intake   |
| 3. When NSAIDs and colchicine are ineffective or contraindicated  | <b>Glucocorticoids</b>                   | <b>Prednisolone</b> 15-30 mg daily ( <b>methylprednisolone</b> 12-24 mg/ kg daily) orally the first day, followed by a decrease in the dose of 5 mg/day (4 mg/day) every subsequent day till withhold the drugs or<br><b>Betamethasone</b> 1-2 ml (5-10 mg) or <b>triamcinolone</b> 40-80 mg or <b>methylprednisolone</b> 40-80 mg ( <b>intraarticularly</b> not often than 2-3 times/year into one joint or <b>periarticularly</b> ).<br>In the hospital: you can start with i/v injections of methylprednisolone 250-500 mg daily |
| When there is gastrointestinal complications risk   | <b>4. Proton pump inhibitors</b>         | <b>Omeprazole</b> 20-40 mg daily or <b>rabeprazole</b> 20-40 mg daily, or <b>lansoprazole</b> 30-60 mg daily  |
|   | <b>5. H2 histamine receptor blockers</b> | <b>Ranitidine</b> 0.15-0.3 / day orally or <b>famotidine</b> 0.02-0.04 g / day orally   |

### Antihistamines - drugs that block H1-histamine receptors.

| Classification          | I generation   | II generation   | III поколение   |
|-------------------------|--|---|---|
| Drugs                   | <b>1. Diphenhydramine</b><br><b>2. Clemastin (Tavegil)</b><br><b>3. Chloropyramine (Suprastin)</b><br><b>4. Mebrogroline (Diazolin)</b><br><b>5. Quifenadine (Fenkarol)</b><br><b>6. Prometazine (diprasine, Pipolphen)</b>  | <b>7. Loratadin (Claritin)</b><br><b>8. Dimethindene (Fenistil)</b><br><b>9. Ebastin (Kestin)</b><br><b>10. Azelastine (Allergodyl)</b><br><b>11. Astemizole (Gismanal)</b><br><b>12. Terfenadine (Bronal, Histadine)</b>   | <b>13. Cetirizine (Zirtek)</b><br><b>14. Fexofenadine (Telfast)</b><br><b>15. Desloratadine (Erius)</b>   |
| Mechanism of action     | Block H1-histamine receptors, as well as cholinergic and serotonin receptors   | H1-histamine receptors are blocked  |   |
| Pharmacological effects | <b>1. Antihistamine</b><br><b>2.</b> Sedative, hypnotic (1-3, 6)<br><b>3.</b> Anticholinergic (1-4, 6)<br><b>4.</b> Hypotensive (1.6)<br><b>5.</b> Resistance<br><b>6.</b> Antiemetic (1.6)  | <i>Unlike the I st generation:</i><br>1. Do not have a sedative and hypnotic effect (poorly penetrate through the blood-brain barrier)<br>2. Do not have anticholinergic and α-adrenergic blocking properties<br>3. Do not cause resistance<br><b>4.</b> Are long-acting (about 24 <b>hours</b> ) | <i>Unlike the II generation:</i><br>1. Are active metabolites of anti-histamine drugs of the previous generation.<br>2. DO NOT affect the QT interval |
| Indications             | 1. Urticaria, eczema, itchy skin, dermatitis<br>2. Allergic rhinitis and conjunctivitis<br>3. Quincke's edema<br>4. Anaphylactic reactions with cutaneous manifestations<br>5. Marine and air sickness (1.6)   |   |   |
| Side effects            | 1. Drowsiness<br>2. Dry mouth<br>3. Hypotension (1.6)<br>4. Dyspeptic phenomena  | 1. Dyspeptic phenomena<br>2. Dry mouth<br>3. Cardiotoxicity: prolongation of QT, rhythm disturbance (11, 12)  | 1. Dyspeptic phenomena<br>2. Dizziness, headache  |
| Contraindications       | 1. Closed-angle glaucoma (1-4, 6)<br>2. Hypertrophy of the prostate (1-4, 6)<br>3. Severe liver diseases, erosive-ulcerative lesions of the gastroduodenal zone<br>4. Pregnancy, breast-feeding  | 1. Pregnancy, breast-feeding  |   |
| NB!                     | 1. Drugs with sedative and hypnotic effects can’t be prescribed to drivers and other persons whose job requires a rapid mental and motor reaction.<br>2. Groups of drugs with antihistamine action: glucocorticosteroids, mast cell stabilizers, leukotriene receptor inhibitors, "universal" adrenomimetic (epinephrine). |   |   |

### Acute management of anaphylaxis

|                     |  |
|---------------------|--|
| I line management   | 1. Assess respiratory tract patency, the presence and adequacy of breathing, the level of consciousness, the state of skin.  |
|                     | 2. Adrenaline (epinephrine) 0,1% 0,3-0,5 ml i/m into the middle of the anterolateral lateral surface of the thigh or i/v   |
| II line management  | 3. Cardiopulmonary resuscitation in cardiac or respiratory arrest. Ratio of breaths to compression – 2:30  |
|                     | 4. When hypotension: lay the patient with raised lower limbs, ensure the supply of moistened oxygen (if available), the introduction of sodium chloride solution 0,9% i/v (to 20 ml/kg)  |
|                     | 5. When bronchospasm: sitting position of the patient, ensure the supply of moistened oxygen (if available), inhalation of $\beta$ 2-agonists – salbutamol 100 mkg via a metered aerosol inhaler (1-2 doses) or a nebulizer 2,5 mg/3 ml                      |
|                     | 6. If there is no response within 5-10 minutes, reapply adrenaline 0,1% 0,3-0,5 ml   |
| III line management | 7. Corticosteroids (prednisolone 90-120 mg)  |
|                     | 8. Introduction of antihistamines for the treatment of skin symptoms v/m clemastine 2 mg or chloropyramamine 20 mg or definehydramine 25-50 mg i/, i/v or orally   |
| NB!                 | <p><i>If only an angioedema or urticaria it's not anaphylaxis and management includes:</i></p> <p>1. Antihistamines v/m, v/v, clemastine 2 mg orally, chloropyramamine 20 mg, definehydramine 25-50 mg</p> <p>2. corticosteroids (prednisolone 25-30 mg)</p> |

**Immunosuppressive drugs** are drugs inhibiting or preventing activity of the immune system.

**Monoclonal antibodies** are antibodies that are made by identical immune cells that are all clones of a unique parent cell.

| Classification          | For cancer   | For organ transplantation  | For autoimmune diseases   | For infectious, allergic diseases and other diseases   |
|-------------------------|--|--|---|--|
| Drugs                   | <b>1. Avastin (Bevacizumab)</b><br><b>2. Herceptin (Trastuzumab)</b><br><b>3. MabThera (Rituximab)</b><br><b>4. Erbitux (Cetuximab)</b>  | <b>5. Simulekt (Baziliximab)</b>   | <b>6. Actemra (Tocilizumab)</b><br><b>7. Humirah (Adalumumab)</b><br><b>8. Remicade (Infliximab)</b>  | <b>9. Xolar (Omalizumab)</b><br><b>10. Lucentis (Ranibizumab)</b>  |
| Mechanism of action     | 1. Selectively binds to the growth factor of the endothelial vessels and neutralizes it → violation of an-giogenesis, ↓ vascularization and depression of growth of the tumor (1)<br>2. Blocks human epidermal growth factor receptor type 2 (HER-2) on tumor cells → ↓ division of malignant cells (2)<br>3. ↓ level of circulating CD20 + B-lymphocytes (3)<br>4. Blocks epidermal growth factor receptor (EGFR) → tumor growth inhibition (4) | 1. Blocks the $\alpha$ -chain of the interleukin-2 receptor (CD25) → ↓ T cell proliferation (5)  | 1. Suppresses receptors of inter-leukin-6 (6)<br>2. Inhibit tumor necrosis factor- $\alpha$ (TNF- $\alpha$ ) (7.8)  | 1. It binds to Ig E and prevents its interaction with Fc-R1 → ↓ Ig E (9)<br>2. Prevents the interaction of endothelial growth factor of the vessels (VEGF-A) with receptors on the surface of endothelial cells → ↓ neovascularization and vascular proliferation (10) |
| Pharmacological effects | 1. Antitumor effect  | 1. Immunodepressive effect   | 1. Immunodepressive effect<br>2. Anti-inflammatory effect   | 1. Antiallergic effect (9)<br>2. Antiproliferative effect (10)   |
| Indications             | 1. Metastatic colorectal cancer (1.4)<br>2. Breast and pulmonary cancer (1,2)<br>3. Renal cell carcinoma (1)<br>4. Stomach cancer (2)<br>5. Squamous cell carcinoma of the head and neck (4)<br>6. B-cell CD20-positive non-Hodgkin's lymphomas, chronic lymphocytic leukemia (3)  | 1. Prevention of kidney transplant rejection   | 1. Rheumatoid arthritis<br>2. Ulcerative colitis and Crohn's disease (7.8)<br>3. Plaque psoriasis in children (7)   | 1. Atopic bronchial asthma (9)<br>2. Chronic idiopathic urticaria (9)<br>3. Neovascular (wet) form of age-related macular degeneration (10)  |
| Side effects            | 1. Perforation of gastrointestinal tract (1)<br>2. Bleeding, thromboembolism (1)<br>3. Neutropenia, leukopenia, thrombocytopenia (1-3)<br>4. Hypertension<br>5. Diarrhea, nausea, vomiting, abdominal pain<br>6. Heart failure, tachyarrhythmia (1-3)<br>7. Upper respiratory and urinary infections<br>8. Allergic reactions  | 1. Diarrhea, nausea, vomiting, abdominal pain<br>2. Hypertension, headache<br>3. Hyperkalemia, hypercholesterolemia, hypophosphatemia<br>4. Upper respiratory and urinary infections<br>5. Allergy | 1. Upper respiratory infections<br>2. Hypertension, headache<br>3. Leukopenia, neutropenia<br>4. ↑ hepatic enzyme activity<br>5. Benign tumors (7)<br>6. Allergic reactions | 1. Upper respiratory and urinary infections (10)<br>2. Anemia (10)<br>3. Intraocular inflammation, visual disturbances (10)<br>4. Headache<br>5. Allergic reactions  |
| Contraindications       | 1. Hypersensitivity<br>2. Patients with dyspnea at rest (2)  | 1. Hypersensitivity  | 1. Hypersensitivity<br>2. Sepsis, active tuberculosis   | 1. Hypersensitivity<br>2. Eye infections (10)  |
| NB!                     | Other drugs with immunosuppressive action: cytostatics, glucocorticoids, immunoglobulins (antitumocyte immunoglobulin)   |  |   |  |

| Classification          | Interferons   | Interferon inducers   | Interleukins  | Colony-stimulating factors  |
|-------------------------|---|---|---|---|
| Drugs                   | <i>Natural:</i><br><b>1. Human leukocyte interferon (<math>\alpha</math>-feron)</b><br><b>2. Velferon (<math>\alpha</math>-feron)</b><br><b>3. Toraferon (<math>\beta</math>-feron)</b><br><i>Recombinant:</i><br><b>4. Reaferon, Viferon (<math>\alpha</math>2A-interferon)</b><br><b>5. Intron-A, Laferon (<math>\alpha</math>2B-interferon)</b><br><b>6. Betaferon, Fron (<math>\beta</math>-feron)</b><br><b>7. Gammaferon, Immukin (<math>\gamma</math>-feron)</b>                 | <b>8. Amiksin</b><br><b>9. Poludan</b><br><b>10. Arbidol</b><br><b>11. Ingavirin</b>  | <b>12. Interleukin-2 (Roncoleukin)</b><br><b>13. Interleukin 1<math>\beta</math> (Betaleikin)</b>   | <b>14. Filgrastim (Mylagra)</b><br><b>15. Molragostim (Leicomax)</b><br><b>16. Lenograstim (Granocyte)</b>  |
| Mechanism of action     | <ol style="list-style-type: none"> <li>↑ expression of Antigens of histocompatibility classes I и II; activate cytotoxic effector cells</li> <li>↓ the effect of tumor growth factors, ↓ The formation of new vessels in the tumor, inhibit metastasis</li> <li>Activate latent endoribonuclease which destroys viral RNA; ↓ Synthesis of viral matrix RNA, ↓ synthesis of viral envelope proteins</li> <li>Disrupt the metabolism of the bacterial cell and cause its death</li> </ol> | <ol style="list-style-type: none"> <li>Stimulate the synthesis of endogenous interferon in the body</li> </ol>                      | <ol style="list-style-type: none"> <li>↑ The amount of lymphocytes and their cytotoxicity, the activity of cell-killer killers, and the activity of tumor necrosis factor</li> </ol>  | <ol style="list-style-type: none"> <li>↑ expression of class II histocompatibility antigens on human monocytes and ↑ production of antibodies; ↑ phagocytosis of bacteria, activate cytotoxic effector cells</li> <li>Activates the maturation of myeloid and lymphoid cells</li> </ol> |
| Pharmacological effects | <b>1. Immunomodulating</b><br><b>2. Antineoplastic</b><br><b>3. Antiviral</b><br><b>4. Antibacterial</b>  | <b>1. Immunomodulating</b><br><b>2. Antiviral</b>   | <b>1. Immunomodulating</b>  |   |
| Indications             | <ol style="list-style-type: none"> <li>Influenza, ARVI (1)</li> <li>Hepatitis B and C (1-7)</li> <li>Severe bacterial infections (7)</li> <li>AIDS-associated Kaposi's sarcoma (1, 4, 5)</li> <li>Hairy cell leukemia (1,2, 4)</li> <li>Chronic myelogenous leukemia (1, 2, 5)</li> <li>Kidney cancer (1, 2, 4, 5)</li> <li>Multiple sclerosis (1. 6, 4)</li> <li>Larynx papillomatosis (2, 4)</li> </ol>   | <ol style="list-style-type: none"> <li>Influenza, ARVI</li> <li>Hepatitis A, B and C (8)</li> <li>Keratitis, uveitis (9)</li> </ol> | <ol style="list-style-type: none"> <li>Septic conditions accompanied by immunosuppression</li> <li>Renal cell carcinoma (12)</li> <li>Pulmonary tuberculosis (12, 13)</li> <li>Toxic leukopenia of 2-4 grade complicating chemo- and radiotherapy of malignant tumors (13)</li> </ol> | <ol style="list-style-type: none"> <li>Antitumor agents-induced neutropenia; HIV infection</li> <li>Neutropenia in patients with myelodysplastic syndrome (15)</li> <li>Bone marrow transplantation</li> </ol>  |

|                          |   |  |  |   |
|--------------------------|---|--|--|---|
| <b>Side effects</b>      | <ol style="list-style-type: none"> <li>1. Asthenovegetative syndrome</li> <li>2. Flu-like syndrome</li> <li>3. Nausea, diarrhea, anorexia</li> <li>4. Thrombocyto-, leukopenia (2-7)</li> <li>5. Hepatotoxicity</li> <li>6. Nephrotoxicity (2-7)</li> <li>7. Convulsive syndrome (2-6)</li> <li>8. Depression (1-6)</li> <li>9. Cardiotoxicity (2-7)</li> </ol> | <ol style="list-style-type: none"> <li>1. Dyspeptic phenomena</li> <li>2. Short-term chills (8)</li> </ol> | <ol style="list-style-type: none"> <li>1. Flu-like syndrome</li> <li>2. Dyspeptic phenomena</li> <li>3. Hematotoxicity (anemia, thrombocytopenia, leukopenia), cardio-toxicity (myocardial ischemia, atrial arrhythmias), arterial hypertension (12)</li> <li>4. Neurotoxicity (drowsiness, delirium)</li> </ol> | <ol style="list-style-type: none"> <li>1. Anorexia, nausea, vomiting, diarrhea, abdominal pain</li> <li>2. Headache, dizziness</li> <li>3. Hypotension, arrhythmia, heart failure</li> <li>4. Bronchospasm</li> </ol> |
| <b>Contraindications</b> | <ol style="list-style-type: none"> <li>1. Hypersensitivity</li> <li>2. Expressed violations of the liver, kidney, heart functions, hematopoiesis system</li> <li>3. Epilepsy, mental illness</li> </ol>   | <ol style="list-style-type: none"> <li>1. Hypersensitivity</li> <li>2. Childhood</li> </ol>                | <ol style="list-style-type: none"> <li>1. Hypersensitivity</li> <li>2. Autoimmune diseases</li> <li>3. Severe cardiovascular diseases</li> </ol>   | <ol style="list-style-type: none"> <li>1. Hypersensitivity</li> <li>2. Myeloid leukemia</li> </ol>  |

### Immunomodulators (continued)

| Classification          | Thymus preparations   | Synthetic drugs  | Substances of bacterial origin   | Vegetable drugs  |
|-------------------------|---|--|--|--|
| Drugs                   | <b>1. Timalin (Timosin)</b><br><b>2. Tactivin</b><br><b>3. Timopentin</b>   | <b>4. Levamisol (Decaris)</b><br><b>5. Leakadine</b><br><b>6. Berloperitin</b>   | <b>7. Prodigiosan</b><br><b>8. Ribomunil</b><br><b>9. Broncho Munal</b><br><b>10. Imudon</b>   | <b>11. Echinacea purpurea</b>  |
| Mechanism of action     | 1. Regulates the number of T- and B-lymphocytes, enhances the response of cellular immunity and phagocytosis, as well as the regeneration and hemopoiesis processes in case of their inhibition (1)<br>2. ↑ $\alpha$ - and $\gamma$ -interferons, restores the activity of T-killers, normalizes immunity indices (2)<br>3. ↑ number of T-lymphocytes (3) | 1. Stimulates the function of T-lymphocytes, macrophages, strengthens cellular immunity mainly, and also disrupts the bioenergetic processes of helminthes (4)<br>2. ↓ level of T-suppressors, normalizes the ratio of T-helpers and T-suppressors, ↑ cytotoxicity of natural killers and monocytes, inhibits tumor growth (5)<br>3. ↑ the proliferation and differentiation of bone marrow stem cells without increase in pathological immune responses (6) | 1. Activates T-lymphocytes and adrenal cortex function, ↑ formation of endogenous interferon (7)<br>2. Stimulates the formation of specific antibodies to the antigens of klebsiella and streptococci, activates T and B lymphocytes, the formation of interleukin-1 and interferon- $\alpha$ (8,9)<br>3. Stimulate local humoral immunity, ↑ the production of IgA in the mucus-stern of the upper respiratory tract and ↑ the content of lysozyme (10) | 1. Activates leukopoiesis and ↑ phagocytic activity of macrophages → ↓ bacterial growth and helps to kill pathogenic bacteria. |
| Pharmacological effects | <b>1. Immunomodulating</b>  | <b>1. Immunomodulating</b><br>2. Antiparasitic (4)<br>3. Antineoplastic (5)  | <b>1. Immunomodulating</b>   | <b>1. Immunomodulating</b><br><b>2. Antiviral</b><br><b>3. Antibacterial</b>   |
| Indications             | 1. Acute and chronic bacterial and viral infections<br>2. Malignancies (2,3)<br>3. Chronic viral hepatitis (2,3)  | 1. Auxiliary postoperative cancer treatment (4)<br>2. Nematodeases (4)<br>3. Kaposi's sarcoma, skin lymphoma (5)<br>4. Psoriasis (5)<br>5. Immunodeficiency in HIV / AIDS (6)  | 1. Decreased immunity due to chronic inflammatory diseases, after operations (7)<br>2. Chronic bronchitis, tracheitis, rhinitis (8,9,11)<br>3. Gingivitis, periodontitis, stomatitis (10)  | 1. Uncomplicated viral and bacterial diseases of the respiratory tract.  |
| Side effects            | 1. Allergy  | 1. Nausea, vomiting, diarrhea<br>2. Risk of agranulocytosis (4)<br>3. Thrombocytopenia (5)<br>4. ↑ blood pressure (5)<br>5. Burning pain at the injection site (6)   | 1. Headache (7)<br>2. ↑ body temperature (7)<br>3. Allergic reactions<br>4. Nausea, vomiting   | 1. Allergy   |
| Contraindications       | 1. Hypersensitivity<br>2. Atopic asthma (2)   | 1. Hypersensitivity<br>2. Agranulocytosis (4)<br>3. Thrombocytopenia (5)<br>4. The gastroduodenal ulcer (5)  | 1. Central nervous system lesions (7)<br>2. Myocardial infarction (7)<br>3. Autoimmune diseases (8)  | 1. Hypersensitivity<br>2. Autoimmune diseases  |
| NB!                     | Bacillus Calmette–Guérin (BCG) vaccine is also an bacterial immunomodulator (vaccine against tuberculosis)  |  |  |  |