

## **ANTIINFLAMMATORY, ANTIALLERGIC AND DRUGS ACTING ON THE IMMUNE SYSTEM.**

**A. Actuality.** Inflammation is a complex reaction triggered in the body to the action of various harmful factors with the involvement of several mediator systems (prostaglandins, leukotrienes, interleukins, etc.). Initially it occurs as a defense reaction, which later becomes a pathological process that requires therapeutic interventions. In these situations it is necessary to use fast-acting, symptomatic anti-inflammatory drugs that will influence the pathogenetic mechanisms of inflammation. In chronic diseases, together with treatment of acute symptoms, it will be necessary to use preparations that will influence the evolution of the disease. For these reasons, extensive knowledge in the field of anti-inflammatory drugs is required.

Allergic reactions, caused by various factors, and firstly by drugs, are various, frequent, often very serious and require emergency care. Pathogenetic mechanisms and clinical manifestations will determine the principles of rational selection of drugs in the treatment of allergic reactions. For these reasons, deep knowledge in the field of antiallergic preparations is required.

The progress of immunology in last decades has led to an increase in the incidence of diseases and conditions accompanied by primary and / or secondary disorders of the immune system. At the same time, increased the number of new drugs (leukotrienes, antileukotrienes, monoclonal antibodies, etc.) used in these situations. For this reason, deep and up-to-date knowledge in the field of preparations with an influence on immune processes is needed.

**B. The purpose of the training.** Familiarize students with the pharmacokinetic and pharmacodynamic properties of anti-inflammatory, anti-allergic and immune system drugs, as well as the selection of medications based on disease and pathological conditions.

### **C. Learning objectives:**

- a) The student needs **to know**: definition, classification, mechanism of action, effects, indications, contraindications and adverse reactions of anti-inflammatory, anti-allergic, immunomodulatory and immunosuppressive preparations.
- b) The student should **be able to**: prescribe anti-inflammatory, anti-allergic and immunomodulatory drugs in various forms of medicine, to indicate them according to diseases and pathological conditions.

### **D. Initial level of knowledge required for interdisciplinary integration:**

**Histology.** Immunological protection organs. Immune system and cellular interactions in immune reactions.

**Biochemistry.** Structure and function of immunoglobulins.

**Microbiology, virology and immunology.** Humoral and cellular immune response. Cellular cooperation and mediators of the immune response. Immunological memory. Immunological method of diagnosis. Direct serological reactions. The main indirect serological reactions. Immune status. Hypersensitivity. Immunoprophylaxis and immunotherapy of infectious diseases.

**Pathophysiology.** Inflammation. Alteration. Mediators of inflammation. Vascular reactions in the inflammatory focus. Exudation. Leukocyte migration. Phagocytosis. Proliferation and regeneration in the inflammatory focus. Allergic reactions type I, II, III, IV, V. Immunopathology. Autoimmune reactions. Nonspecific allergic reactions.

**E. Self-training questions:**

1. Classification of anti-inflammatory drugs.
2. Nonsteroidal antiinflammatory drugs. Classification. Mechanism of action, effects, indications, contraindications and adverse reactions.
3. Selective cyclooxygenase inhibitors. Mechanism of anti-inflammatory action. Effects, indications, contraindications, side effects.
4. Steroidal antiinflammatory drugs. Classification. Mechanism of anti-inflammatory action. Effects, indications and contraindications. Adverse reactions
5. Disease-modifying anti-rheumatic drugs (DMARDs). Classification. Mechanism of action. Effects, indications, contraindications and side effects of 4-aminoquinoline derivatives, gold preparations, thiol derivatives, sulfasalazine, monoclonal antibodies and cytostatics.
6. Classification of antiallergic drugs.
7. Medicines used in immediate-type of allergic reactions: anaphylactic shock, bronchial asthma, urticaria, etc. Pharmacodynamic features and indications of  $\beta$ -adrenomimetics, methylxanthines, M-cholinoblockers.
8. Glucocorticoids: antiallergic mechanism of action, effects, indications.
9. Antihistamines. Classification according to structure and generations. Mechanism of action, effects, indications, contraindications and adverse reactions.
10. Acute intoxication with H1-Antihistamines. Clinical picture. Treatment. Particularities of poisoning in children.
11. Mast cell degranulation inhibitors. Classification. Mechanism of action. Effects. Indications. Contraindications. Side effects.
12. Classification of preparations used in delayed allergic reactions.
13. Minor immunosuppressants. Classification. Mechanism of action, effects, indications, contraindications and side effects of quinoline derivatives, gold salts, thiol derivatives.
14. Major immunodepressives. Classification. Mechanism of action, effects, indications, contraindications and adverse reactions of glucocorticoids and cytostatic.
15. Classification of immunomodulatory preparations (preparations with influence on the immune system).
16. Immunostimulators of bacterial origin: classification, immunostimulatory action, indications, contraindications, adverse reactions.
17. Immunostimulators of fungal and plant origin: immunostimulatory action, indications.
18. Immunostimulants of animal and synthetic origin: immunostimulatory action, indications.

19. Recombinant immunostimulators and interferons: immunostimulatory action, indications.
20. Entomological preparations as immunomodulators.

**F. Independent work** (is done in written form while preparing for the lesson)

**1.) Brief characteristics of the compulsory drugs:**

**Down:** Drug name. 1. Diclofenac. 2. Indomethacin. 3. Ibuprofen. 4. Meloxicam. 5. Nimesulide. 6. Mefenamic acid. 7. Celecoxib. 8. Auranofin. 9. Diphenhydramine. 10. Mebidroline. 11. Cetirizine. 12. Clemastine. 13. Loratadine. 14. Levamisole. 15. Chloroquine. 16. Azathioprine. 17. Interferon. 18. Infliximab. 19. Imupurin. 20. Sodium cromoglicate. 21. Ketotifen. 22. Dexamethazone.

**Across:** 1. Medicinal form. 2. Way of administration. 3. Doses (therapeutic, maximum for one intake and for 24 hours). 4. Mechanism of action. 5. Indications and contraindications. 6. Adverse reactions.

**2.) Questions on medical prescription.**

**To prescribe** the following drugs in all possible medicinal forms: 1. Diclofenac. 2. Indomethacin. 3. Ibuprofen. 4. Meloxicam. 5. Nimesulide. 6. Mefenamic acid. 7. Celecoxib. 8. Auranofin. 9. Diphenhydramine. 10. Mebidroline. 11. Cetirizine. 12. Clemastine. 13. Loratadine. 14. Levamisole. 15. Chloroquine. 16. Azathioprine. 17. Interferon. 18. Infliximab. 19. Imupurin. 20. Sodium cromoglicate. 21. Ketotifen. 22. Dexamethazone.

**Drugs used in (for):** Rheumatoid arthritis, ankylosing spondylitis, acute gout, deforming osteoarthritis, myositis, fever, arthralgia, neuralgia, collagenosis, lupus erythematosus, pollinosis, urticaria, postoperative vomiting, motion sickness, asthma attack, treatment of bronchial asthma, , anaphylactic shock, contact dermatitis, chronic infections, prophylaxis of transplant rejection, immunodeficiency, prophylaxis of recurrent respiratory infection.

**3.) Tests** (Guidelines for Laboratory Work in Pharmacology).

**4.) Clinical case** (Guideline for laboratory work in pharmacology).

**5.) Virtual Situations** (Guidelines for Laboratory Work in Pharmacology).

**6.) Virtual didactic movie**

**7.) Tables**

*Table N1*

**Selective action of COX inhibitors**

Cyclooxygenase inhibitors	Cyclooxygenase I	Cyclooxygenase II
Acetylsalicylic acid in small dose (0.1 - 0.125)		
Acetylsalicylic acid in usually doses		
Indomethacine		
Diclofenac		
Ibuprofen		

Meloxicam		
Celecoxib		

Note. the presence of the effect marked with the "+" sign.

*Table N2*

**The basic effects of non-steroidal anti-inflammatory drugs and the mechanisms of their occurrence**

Effects	Mechanisms of action
a) Analgesic	1. Blocking the synthesis of prostaglandins of group E from the hypothalamus.
	2. Blocking the synthesis of prostaglandins in the inflammatory focus and preventing hyperalgesia.
	3. Stabilization of the lysosomal membrane and prevention of the release of hydrolytic ferments: proteases, lipases, hydrolases and others.
b) Antipyretic	4. Antioxidant action.
	5. Deregulation of ATP production in the inflammatory focus.
c) Anti-inflammatory	6. Antiproliferative action in the inflammatory focus (decreased activity of fibroblasts).
	7. Blocking the formation of group E prostaglandins in brain structures, participating in the transmission of pain impulses.
	8. Blocking the synthesis of prostaglandins and other mediators of inflammation.
	9. Blocking adhesion of neutrophils and monocytes to endothelial cells.

Note! Join the action mechanism figures with the corresponding effects.

*Table N3*

**Comparative feature of non-steroidal anti-inflammatory drugs from various chemical groups**

Effects	Paraceta mol	Acetylsalicylic acid	Indomethac in	Diclofen ac	Meloxicam
Analgesic					
Antipyretic					
Antiinflam matory					
Antiplatelet					
Ulcerogenic					

Note. mark the degree of effect expression with the following symbols:

"++" - maximum effect

"+" - less than maximum effect

"-" - lack of effect.

*Table N4*

**The side effects of steroidal anti-inflammatory drugs**

Adverse effects	Manifestations	Mechanism of appearance	Prophylaxis and correction of complications
Cushing syndrome			
Steroid Diabetes			
Sodium and water retention			
Osteoporosis			
Steroid ulcer			
Decrease in immunity			
Intensifying of blood coagulation			
Decreasing of the regeneration process			
Psychic disturbances			
Arterial hypertension			
Cataract			
Blood disorders			
Myopathy			
Adrenal gland atrophy due to long-term administration			

*Table N5*

**Comparative feature of mast cell degranulation inhibitors**

Comparative	Sodium	Nedocromil	Ketotifen
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parameters	cromoglycate		
Rout of administration and medicinal form			
Peculiarities of mechanism of action			
Indications			
Advers reactions			

*Table N6*

**Comparative feature of H1 histamine receptor blockers**

Comparative parameters	Diphenhydramine	Chloropyramine	Promethazine	Astemizole	Cetirizine	Loratadine
The medium therapeutic dose (mg)						
Duration of action (hours)						
The sedative effect (high/ low)						
M-cholinoblocking effect						
Ganglioblocking effect						
Alpha-adrenoblocking effect						
Irritating action						
The cardiotoxic action (+/-)						

Note. The presence of the effect marked with the "+"

Table N7

**Mechanism of action of immunodepressives**

Mechanisms of action	Cyclo-phosphamide	Azathioprine	Prednisolone	Cyclosporine
Deregulation of the DNA structure				
Deregulation of the DNA synthesis				
Inhibition of transcription interleukin genome-1				
Decreased expression of interleukin receptors -2				
Formation of "T-lymphocyte-antibody" complex				

Note. The presence of the effect is marked with the "+" sign.

Table N8

**Indications of immunostimulating drugs**

Indications	Prodigiosa n	Ribomunyl	Timalin	Levamisole	Molgramostim
Prophylaxis of viral infection					
Treatment of viral infections					

Treatment of chronic infectious inflammatory process					
Treatment of chronic respiratory infectious disorders					
Autoimmune disorders					
Leukopenia, caused by antitumor chemotherapy					
Leukopenia in HIV infection					
Stimulation of leukopoiesis in the bone marrow transplantation					

Note. The presence of the effect is signed with the "+"

*Table N9*

**The adverse effects of immunosuppressants**

Side effects	Cyclophosphamide	Azathioprine	Prednisolone	Cyclosporine
Nausea, vomiting				
Deregulation of haematopoie				

s				
Secondary infections				
Cushing syndrome				
Hepatotoxicity				
Nephrotoxicity				

**8.) Solve the case:**

**Case 1.** Two patients with acute respiratory diseases were treated with drugs A and B with antipyretic properties. After 10 days of treatment, anaemia, leukopenia and thrombocytopenia have been reported in a patient who has used A-drug, and haemorrhages, haematuria and duration of coagulation have increased in the patient who has used B-drug.

**Determine the medications and indicate the cause of complications.**

**Case 2.** A driver came to the doctor with phenomena of urticaria. After the examination, the doctor prescribed a medicine. On the background of the reduction of hives, the patient reported a weakness, drowsiness, decreasing attention and concentration.

**What preparation did the doctor indicate?**

**What was the cause of the complications highlighted above?**

**Enumerate pharmacological effects of the drug.**