

Ministry of health care of Ukraine  
Highest state scientific institution of the Ukraine  
«Ukrainian medical stomatological academy»

"Approved"

at a meeting of the Department of Experimental  
and Clinical Pharmacology with Clinical  
Immunology and Allergology

**Head of the department**

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**Methodical guidance  
for students' self-directed  
work when preparing for practical session**

Academic discipline	Clinical Immunology and Allergology
Semantic module №2	Allergic, toxic and allergic diseases
Topic <b>13</b>	<b>Allergotherapy. GMC</b>
Year of study	5
Faculty	medical

### 1. Relevance of the topic:

In recent years, allergy is steadily growing population, so the question's allergoterapie are highly relevant. Allergic diseases - this is the most affordable model, an example of which today it is easier to explain the basic principles of the pathogenesis, clinical manifestations, diagnosis and treatment of patients with immunopathology. These issues are of particular importance in the differential diagnosis pseudoallergy and allergies. Thanks to the invention, major and minor allergens antigens appeared to more reliably detect allergens, and therefore more accurately assign specific immunotherapy (SIT).

Hypersensitivity to medication plays an important role in assisting any person. In recent years much has changed the understanding of drug allergy.

### 2. Specific learning objectives:

1. To be able to determine the etiologic and pathogenetic factors of allergy and pseudo allergic diseases.
2. Conduct a survey and physical examination of patients with this pathology.
3. Understand the basics of allergy research methods (laboratory tests, skin tests, provocation tests for drugs and others.).
4. To prepare a plan of examination of patients with Allergic Diseases and pseudoallergic, to justify the use of the main specific diagnostic methods to determine the indications and contraindications for their conduct, possible complications;
5. Conduct a differential diagnosis between allergic diseases and pseudoallergic.
6. To show the different variants of the course and complications and allergic reactions to medications pseudoallergic;
7. Appoint antiallergic therapy, to evaluate its effectiveness.
8. Identify the forecast, conduct primary and secondary prevention of allergic diseases and pseudoallergic.

### 3. Basic knowledge, skills necessary for studying the subject (interdisciplinary integration)

The name of the previous disciplines	These skills
Anatomy	Knowing the structure of the thymus, lymph nodes, Peyer's patches, spleen, bone marrow. To conduct physical examination of patients.
normal physiology	To know the functioning of the central and peripheral organs of the immune system. Master the basics of clinical and laboratory studies.
Biochemistry	Learn the basics of biochemical laboratory studies. Action and effect of various cytokines groups of biologically active substances.
Microbiology and Virology	Know the immune response, the diagnosis of bacterial and viral infection. Master the basics of special microbiological methods.
Therapy	Know the pathogenesis and clinical manifestations of allergic diseases and secondary immunodeficiencies. To be able to collect immunological and allergic history.
phthisiatry	To master the mechanisms of the immune response cell dependence. The course and clinical manifestations of tuberculosis.

### 4. Tasks for work during preparation for the classes.

#### 4.1. The list of key terms, parameters, characteristics which the student is to assimilate while preparing for the class:

Term	Definition
Pseuatopic pathology	Hyperergic that have their basis in the development of the immune mechanism, and are formed by direct exposure to pathogens sources of biologically active substances

Hapten (for Greece Nario -. Attach)	Poluantigeny substances (mostly low molecular weight), do not have the immunogenic properties but able to interact specifically with antibodies and immune cells after binding to the specific molecule more such protein, so that they become immunogenic antigens
Delayed-type hypersensitivity	Hypersensitivity to the allergens, is caused by T lymphocytes - effectors and lymphokines, IV type of reaction
Essential eosinophilic syndrome	Steady increase in the number of eosinophils, 0.6 g / L in the peripheral blood with the exception of well-known causes of disease development

#### 4.2. Theoretical questions for the class:

1. Principles of antiallergic therapy and immuno- therapies in allergology. Specific immunotherapy, mechanism of action, indications and contraindications, forecast efficiency.
2. Qu Nica beers, angioedema, allergic dermatitis: etiology, immunopathogenesis, clinical allergodiagnosics basic principles immunotherapy.
3. Drug allergy: immunopatogenesis, clinic, allergodiagnosics, treatment, preventive medicine.
4. The concept of allergy and pseudoallergy, differential diagnosis. Pseudoallergic mechanisms of reactions. The principles of treatment.
5. Development pseudoallergic reactions in violation of the activation of the complement system and the metabolism of arachidonic acid. The principles of treatment.
6. Drug allergy. Immunopatogenez, clinic, allergodiagnosics, treatment.

#### 4.3. Practical works that are performed in class:

1. To be able to leave the plan of inspection of patients with Allergic Diseases and pseudoallergic.
2. Master the skills to perform allergy tests leather (panch- tests).
3. Mastering these skills assessment laboratory allergy, toxic-allergic tests.
4. Master the skills to identify allergens with similar antigenic determinants to make recommendations for the prevention of Allergic.
5. Master the skills to carry out provocative allergy tests for skin allergy forms and evaluation of their performance.
6. Conduct a differential diagnosis, to justify a clinical diagnosis of major allergy, pseudoallergic diseases based on data analysis of laboratory and instrumental examination
7. To appoint treatment, determine prognosis, to conduct primary and secondary prevention of allergic diseases.
8. To render the first aid in case of acute or cr apivnitse pseudoallergic pathology.
9. Enforce standards of diagnosis and treatment of allergic, pseudoanalytic their diseases.

#### Content topics

##### Antihistamines (AGP).

Action of histamine on the nasal mucosa due to mainly its first contact with the receptor type. A warning of this contact and targeted by antihistamines. They can reduce the sneezing, itching in the nose, runny nose. Antihistamines are today quite popular among physicians and the public. In recent years, due to the many drawbacks of the first generation antihistamines (diphenhydramine, Pipolphenum etc.) applied antihistamines second and third generation worldwide. The Table shows the face of these drugs.

#### GCS for intranasal administration (In AV Emelyanov., 1999)

chemical name	Tradename	release Form	daily dose (g) the multiplicity
beclomethasone dipropionate	"Aldetsin", "Bekonaze"	Nasal spray	200-400 (50 ug / dose) twice 2

triamcinolone acetonide	"Nazokort"	Nasal spray (55 mcg / dose)	110-220 1 time
budesonide	"Rinokort"	Nasal spray st s, tour bohaler (100 mcg / dose)	200-400 1 time
fluticasone propionate	"Fliksonaze"	Nasal spray (50 mg / dose)	200-400 1 time
mometasone furoate	"Nasonex"	Nasal spray (50 mg / dose)	200-400 1 time

Due to the absence of significant side effects from antihistamines s 2-3 generations in comparison with the first-generation antihistamine drugs allow to use them for a long time without significant restrictions.

**Antileukotrienes preparations.** Numerous experiments have shown that leukotrienes LTC<sub>4</sub> and LTD<sub>3</sub> cause bronchospasm significantly stronger than histamine. This led to the creation of search and antileukotrienes preparations. In recent years, we synthesized antileukotrienes 4 groups drugs, the most widely adopted receptor antagonists Leukotriene sulfidopeptidose - zafirlukast, montelukast.

But the so-called "aspirin asthma" efficiency antileukotriene's products is quite high, given the key role of leukotrienes in this type of asthma.

**Decongestants.** Decongestants act on the regulation of tone sympathetic blood vessels, activating the adrenergic receptors, causing vasoconstriction. These include: simpadrenomimetik and (phenylephrine),  $\beta$ 2-agonists (oxymetazoline, xylometazoline, naphazoline), substances that promote release of norepinephrine (ephedrine, pseudoephedrine, phenylpropanolamine, amphetamines) and drugs, stop recycling norepinephrine (cocaine, tricyclic antidepressants, phenylpropanolamine). They are able to effectively restore nasal breathing in allergic rhinitis. Oral vasoconstrictors (phenylpropanolamine and pseudoephedrine in particular) are less able to restore nasal breathing, but have the phenomenon of "rebound" vasodilation.

Long-term use (more than 10 days), decongestants can lead to tachyphylaxis, pronounced swelling of the nasal mucosa and development of medical rhinitis. It is especially dangerous to use them for the younger children and the elderly. Regarding decongestants, over-widely used in our country (Naphthyzinum, galazolin, Sanorin etc.), we should not forget that the maximum period of application should not exceed 2 weeks, as they can cause unwanted local and general phenomena.

Basic principles of treatment for allergic process

Among the specific (ergenospetsific) methods of influence on allergical processes the safest and simplest is the elimination therapy, although it probably can be considered a secondary prevention methods. Success is ensured by preventing contact with the allergen. There are active method of elimination - eliminating the allergen from the environment surrounding the patient and passive elimination - patient isolation (such as changing the place of work, residence). In connection with the possibility but we can cross-reactions, especially with food allergies, are also excluded similar antigenic composition of provocative factors. Eg EP, with sensitization to chicken , exclude from the diet as chicken. It is clear that in many cases quite difficult to avoid the contact, and in some - even impossible to detect the antigen itself. There are situations when, as a result of long-term trends for the left with the development of complications or other reasons (for example, allergical independent stage of bronchial asthma), allergen plays and eliminate inefficient or even meaningless. Prolonged elimination sensitization level is reduced and may disappear.

Dangerous and difficult in the performance of a specific desensitization (one method of immunotherapy). The old name of "desensitization" does not reflect the features of the process as complete desensitization can be achieved only in the ideal case. Its essence lies in the formation of the so-called blocking antibodies in response high doses of allergen. These antibodies are IgG and quickly contacting the allergen, warned its interaction with reagin (IGE), fixed to the mast cell or basophil.

Other possible mechanisms of specific desensitization one to the formation of antibodies to reagin antiidiotipnic (obviously, also of IgG) or an increase in the activity of the T-lymphocyte suppressor that is going to reduce overproduction IGe.

Specific immunotherapy is considered one of the most effective methods, which, when done properly, prevents the emergence or strengthening of the symptoms of atopic diseases. Particularly efficiency method was in the childhood and young age - that is, in cases where the immune system has a maximum capacity for self-regulation and requires only an initial "push". The best results were observed in allergy to house dust and pollen. Along with food and fungal, these allergens are the most common.

There are various methods of specific desensitization. Classic injection method proposed in 1911, we using. In Western Europe and the United States give advantage of oral desensitization is much easier and safer.

Promising practices in a sustained second desensitization with allergen adsorbed to aluminum oxide, provides a slow release of the allergen for a long time. An example of such a drug can insintanal TP-3, which is manufactured by depositing pollen chloride and zinc of holding the slurry on aluminum hydrate and hydroxy. To improve the efficiency of the method sometimes provide direct contact "allergen-target", introducing the drug intranasally, sublingually, or the conjunctiva. These methods are not widely used in medical practice due to the complexity of selecting the minimum therapeutic dose, correspondingly, treatment regimens in each case.

To prevent unwanted reactions to the allergen used is less than its pre-dose, providing these binding reagin. Conducting therapies begin with intradermal administration of individualized doses of allergen (usually within diluted 10<sup>-9</sup>-10<sup>-6</sup>), gradually increasing the dose until a low positive reaction. Subsequently, gradually increasing dose of allergen reaching the optimum concentration. In many cases, sustainable effect continue administering maintenance doses 2-3 times a month over a prolonged time. The incidence and frequency of administration, as well as the rate of increase of the dose picked individually, guided by the standard scheme.

In adults most often used more rapid dose escalation (0,1-0,2-0,4-0,8 mL). The proposed scheme called standard as provide traditional way of administration of the allergen and the slow pace of escalating doses.

For health apply "rapid" desensitization, when due to the rapid change of divorced 4-6 minute injection comes to optimal dose of the allergen over several days. In case it is necessary the introduction of their spine when straightening serums, diphtheria, botulism, and others. (Subject to positive tests for sensitivity to the drug), this time is needed reduce to one day. Then each subsequent dose is administered through the 1.5-2 hours under the cover of parenteral application antihistamine means and glucocorticoids (Alexandre Besredka method).

During the course of injection patients receive antihistamines (children - by age doses), preferably of the 2nd generation, since 102 dilution of allergen, and when orally use - with 10-3.

In pediatrics, as well as in food allergy is common method of oral administration of allergen. For oral administration the allergen is mixed with pure glycerol: 5 drops of pure glycerol were added appropriate amount of drops (or dose) of allergen according to the selected scheme. The fluid are mixed together and take on an empty stomach 1 time per day (with a standard scheme) or more often (if fast).

In the absence of comorbidity and a moderate course and recommend the use of the accelerated methods given in the tables.

Indications for specific desensitization may be considered:

- identify the specific allergen hypersensitivity - pollen, household, fungal, bacterial or dietary ;
- impossibility of carrying out active or passive elimination;
- inefficiency or lack of effectiveness of funds patogenetic and symptomatic therapy;
- uncomplicated allergic diseases.

Contraindications for specific desensitization are:

- infectious processes, especially those related to the affected organ (acute or exacerbation of chronic);
- severe liver and kidney disease, causing their functional failure;
- severe respiratory failure in asthma in the interictal period;
- thyrotoxicosis;
- pregnancy;

- substance abuse.

Desensitization success is determined by the following factors:

- The quality of preparations made of of allergen and dose (efficiency second is the high end and the total dose)
- The type of sensitization;
- The type of allergen (the most effective extracts of pollen)
- clinical manifestations (rhinitis when efficiency is 70-90%, and in bronchial asthma - only 50-70%;
- presence of irreversible organic changes;
- sensitization to a single allergen or a few at a time.

Much less frequently used "cluster" desensitization when in one day is administered multiple injections followed by a multi-day break (for example, plant pollen and house dust). Mixed in the same syringe can only those allergens that belong to one group, for example, only pollen or food only. Allergens different groups of these should they about to enter different syringes, or use combinations way of introduction. For example, in pediatrics is often combined injection allergen and with house dust with oral pollen allergens.

At present, specific desensitization hardly applies with food allergies - both because of the lack of efficiency and because of the complexity of execution. In the case of recurrence of hives and swelling of angioedema it is very important to exclude pseudoallergy origin.

*Allergenonespecific (pathogenetic) therapy* involves the use of several groups of assets.

Nonsteroidal stabilizing cell membranes - ketotifen, cromolyn sodium and nedocromil sodium. These drugs do not block the action of histamine and prevent release of biologically active amines and leukotrienes from basophils and mast cells. The action of histamine already activated lasts until it is destroyed gistamindezaminazating minutes . Therefore, these drugs are used only for the prevention of clinical manifested allergies, but not to remove them. For this reason, these funds should be taken for a long time or to achieve clinical effect as well . Each of these drugs has certain features of influence that leads to their advantage in a variety of allergic diseases.

So, ketotifen (Zaditen) inherent powerful and long-lasting effect of blocking (H1-receptors), although this effect is seen only after a few days of treatment. Ketotifen to influence the clinical manifestations of allergy prevails loratadine and clemastine, but yields astemizole. Obviously, ketotifen place mainly in patients with asthma allergical(children and teenagers, as well as "fresh" asthma in adults ), and also in the treatment of other pathogenic allergic diseases (allergic rhinitis and conjunctivitis, hay fever).

Cromolyn sodium due to the impact on non-specific mechanisms of activation of mast cells, affects not only the proper components of allergic asthma, urticaria or other allergies. Therefore, the drug is effective and infectious-allergic, occupational and neuropsychiatric forms of asthma, food allergies, and at the time of specific desensitization. In allergic rhinitis, keratitis and conjunctivitis after a month of receiving cromolyn is not inferior to the majority of antihistamines on the ability to block the pathological manifestations, but it has far fewer side effects.

Nedocromil sodium powerful than cromolyn, warns forms allergic reactions for with block the biological effects of prostaglandins and leukotrienes. The only exceptions are due to neurogenic diseases options. In bronchial asthma medication more than on preventive activity drugs theophylline and (3-blockers, and not inferior to inhaled steroids. In allergic lesions of upper respiratory tract and conjunctiva nedocromil exhibit pronounced effect than cromolyn, and has the ability to enhance the effect of antihistamines, while the application .

Glucocorticoids in allergic diseases exhibit immunosuppressive, cytostatic and anti-inflammatory.

The main indications for the purpose glyukortikoids allergical their diseases are:

- acute emergency conditions caused life-threatening patients (anaphylactic shock, anaphylactoid reactions, asthma status, etc.);
- Chronic or continuously relapsing course of disease after failure of other means;
- adrenocortical insufficiency, in particular due to previous prolonged use of glucocorticoids.

## **Materials for students' self-directed work.**

### **A. Tests for the self-control:**

1. Possible causes of chronic non-allergic rhinitis:
  - a) chronic bacterial sinusitis;
  - b) medications to control blood pressure;
  - c) long-term use of vasoconstrictive drops;
  - d) year-round allergic rhinitis.
2. The standards of treatment of perennial allergic rhinitis are not heavy flow following drugs are used:
  - a) Nasonex;
  - b) bekonaze;
  - c) Claritin;
  - g) kromogeksal;
  - d) Fliksotid.
3. What is the specific symptom of asthma radiographic unlike other lung diseases:
  - 1) The deformation of lung pattern on peribronchial type
  - 2) Increased transparency of the lung fields (emphysema)
  - 3) The flattening of the diaphragm
  - 4) The increase in the diameter of the pulmonary artery at the level of the intermediate bronchus
  - 5) All of the above features
  - 6) The signs are absent.
4. of essential eosinophilic syndrome is characterized by:
  1. The average age of patients
  2. The young age of the patients
  3. Women with postmenopausal syndrome.
5. In what clinical situation allows the presence of dyspnea suspected acute interstitial pneumonitis:
  1. Acute development of fever up to 39 ° C, unproductive cough, shortness of breath, bronchial breathing land in the right subscapular region.
  2. Long-term, for several years, a cough with purulent sputum, cyanosis, shortness of breath at light load
  3. The sudden development of dyspnea in patients with a history of prolonged cough, easing breathing right, cyanosis.
  4. The sudden appearance of dyspnea in patients with signs of pulmonary heart disease and the appearance of Q wave in standard lead III.
6. When you are allergic to pollens of grasses can be allergic to:
  - a) to millet;
  - b) to apples;
  - c) to cabbage;
  - g) to tomatoes.
7. In the emergency department team of SMP delivered to the victim, which in the root of the tongue was bitten by a bee. Status heavy stricken. Psychomotor agitation. Breathing hard, both on inhalation and exhalation, whistling. Skin pale cyanotic, mucous - cyanotic. Recovery method airway immediately shows the patient?
  - A inhaled bronchodilators
  - B average tracheostomy
  - C mechanical ventilation
  - D criedconictomia
  - E antispasmodics
8. The sequence of clinical manifestations of hay fever (for the reduction of frequency) are:
  - A rhinitis, conjunctivitis, bronchospasm phenomenon, enteritis, dermatitis
  - B enteritis, dermatitis, urethritis, rhinitis
  - C bronchoconstriction phenomena dermatitis, enteritis, conjunctivitis.
9. A woman of 30 years for 4 years in August, complaining of nasal congestion, mucous discharge from it, sneezing, itchy eyelids, watery eyes. When used Claritin these symptoms

disappear. What allergic reaction occurs?

- A anaphylactic;
- B cytotoxic;
- C immunocomplex;
- D delayed type hypersensitivity.

10. What are the options of anaphylactic shock are known to you:

- A cerebral pain;
- B visceral, cardiac;
- C nephrotic, Banti.

11. If anaphylactic shock introduction of antihistamines:

- A impractical;
- B is always advisable;
- C is recommended only under normal blood pressure;
- D advisable only generation III drugs.

12. The late allergic reactions usually occur through:

- A 15-20 min .;
- B 1-2 h .;
- C 4-6 hr .;
- D 24-48 hours.

13. After a bee sting in a patient appeared itching, hoarseness, barking cough, anxiety, OBJECTIVE: swelling of the lips, eyelids, cyanosis. Which of the following medications are used in the first place?

- A Lasix.
- B Crank.
- C eufillin.
- D prednisone.
- E Seduxen.

14. Typically, the primary allergy examination of th allergies primarily used:

- a) scarificational tests;
- b) intradermal tests;
- c) application tests;
- g) provocative tests.

17. Normally provocative allergy tests are used in the case of:

- a) providing a positive skin tests with negative history
- b) negative history and negative skin tests;
- c) lack of medical history data indicating an allergy;
- d) positive anamnesis.

16. A woman of 20 years for 8 years in August - September there rhinitis, conjunctivitis, and last year joined asthma or cough with shortness of breath. If skin testing revealed sensitivity to ragweed pollen. What IL is crucial in the synthesis of antibodies, causing the disease?

- a) of I L 4;                      g) of I L 3;
- b) the I L 1;                      e) of I L 6.
- c) the I L 2;

17. The man of 32 years complains of heartburn and aching pain in epigastrii 2-3 hours after a meal. Aggravation - in spring and autumn. Food intolerance eggs and fish. OBJECTIVE: palpation of the abdomen - pain in the gastroduodenal area. Ulcer 5 mm on the front wall of the duodenum. Positive urease test. What is the most likely host disease development mechanism?

- A Helicobacter pylori infection
- B Food allergies
- C Production of autoantibodies
- D Reduced synthesis of prostaglandins
- E Violation of gastric motility.

18. The best means of diagnosis of IgE-dependent reactions:

- a) enzyme immunoassay method for the determination of specific IgE;



- b) reactions tion specific leykotsitoliza ;
  - c) skin test to allergens;
  - g) RAST method.
19. With the predominance of Th2 helper cells are produced in the majority of interleukins:
- a) 3,4,5,6,10;
  - b) 1,2,7,9;
  - c) gamma-interferons, colony stimulating factor.
20. The patient who underwent surgery for acute appendicitis during the third ligation surgeons found severe inflammation of the skin around the surgical wound, the presence in the outbreak of blisters and erosions. Focal lesion is clearly limited. Put a clinical diagnosis.
- a) contact dermatitis
  - b) acute eczema
  - g) atopic dermatitis.
21. The child after drinking strawberry dish originated skin rash, itching. Previously, when the child used the small amount of strawberries, these phenomena were not. The doctor has appointed Claritin and forbidden to eat strawberries. True did the doctor?
- a) the most likely reaction is the formation pseudoallergy due to the fact that histamine release strawberries themselves contain it in large amounts. Therefore it should be advised not to drink large amounts of strawberries;
  - b) a food allergy to strawberries. The doctor did everything right;
  - c) the child digestion defect.;
  - d) the child has a food allergy to strawberries. It is necessary to carry out specific immunotherapy;
  - d) optionally, strawberries may be well washed, and there is food poisoning.
22. The patient 35 years complains of choking and rhinorrhea. An hour before this took aspirin. From history we know that sick rhinosinusitis. Underwent polypectomy. According to put the diagnosis.
- a) aspirin triad;
  - b) chronic bronchitis;
  - c) cystic fibrosis,
  - g) allergic rhinitis.
23. The anti-inflammatory drugs for the treatment of asthma are:
- a) inhaled corticosteroids;
  - b) drugs cromoglicive acid
  - c) antagonists lekotrien;
  - g) Theophylline;
  - d) selective beta-2 agonists, short-acting.
24. lekotrieno antagonists in include:
- a) akolat;
  - b) the singular;
  - c) Zaditen;
  - d) none of the above.
25. In a patient with a normal state when the food suddenly appeared crowing breathing, loss of consciousness, expressed hypoxia symptoms. What are the most probable cause:
- A tumor of the larynx or trachea.
  - B attack of asthma.
  - C foreign body larynx or trachea.
  - D acute constrictive laryngotracheitis.
  - E epileptic seizures.
26. The most powerful food allergens include:
- A rice, bananas, buckwheat, red currants
  - B milk, fish, chicken, eggs;
  - C lamb, plums, almonds, potatoes.
27. The patient complains of intense itching of the skin of both hands, monomorphic rash.

From the history of the disease it is known that she was using a new detergent. Your diagnosis?

- A scabies;
- B a pleasing dermatitis
- C eczema;
- D epidermofitia;
- E neurodermatitis.

28. pseudoallergic reactions actually everything except :

- a) absence of specific immunoglobulin IgE;
- b) a manifestation of intolerance reactions after administration of different chemical

structure of substances;

- c) the occurrence of reactions after the first administration of the drug;

29. The main point of action of thymic preparations:

- A antibody response
- B myelopoiesis
- C activity of B-lymphocyte
- T lymphocytes activity

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