

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 12	Pseudoallergy. Drug-induced diseases
Year of study	5
Faculty	medical

Poltava 2017

1. Relevance of the topic:

In recent years, allergy is steadily increasing population of the industrialized countries. And the number is growing pseudoallergic reactions in the first place to the differential allergic to them. Allergic reactions are variety of immune responses, but their difference: first, the presence of allergies own tissue damage, and secondly, allergic reactions are the same type of clinical manifestations, regardless of the nature the allergens. 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.

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 pseudoallergic 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 claim, possible complications.
5. Conduct a differential diagnosis between allergic diseases and pseudoallergic.
6. To show the different variants of the course and complications of allergic and pseudoallergic reactions to medicines.
7. be appointed th 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 of 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
Pseudoatopic pathologists	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

haptens (For Greece Nario -.)	Semi antigens substance (mainly 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	Increased sensitivity to allergens, due to T - lymphocytes - effectors and lymphokines, IV of the type of reaction
linseed 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 anti-allergic therapy and immunotropic treatment in allergy. Specific immunotherapy, mechanism of action, indications and contraindications, forecast efficiency.
2. Crappie ence, 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. Gistaminliberatsional mechanisms of pseudoallergic 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. Immunopatogenesis, clinic, allergodiagnosics, treatment, preventive medicine.

4.3. Practical works that are performed in class:

1. To prepare a plan of examination of patients with Allergic Diseases and pseudoallergic.
2. Master the skills performed allergy tests (tests panch-).
3. Mastering these skills assessment laboratory allergy, toxic-allergic tests.
4. To be able to determine the allergen with similar antigenic determinants for drawing up recommendations for the prevention of Allergic.
5. Master the skills performed 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 pseudoallergy pathology.
9. Enforce standards of diagnosis and treatment of allergic, pseudoallergical diseases.

Content topics

Pseudoallergic reactions are only 2 stages: pathochemical and pathophysiological.

There are 3 groups of South Africa:

- 1) reactions associated with the release of mediators (mainly histamine) from mast cells or impaired histamine inactivation. Factors which release histamine: chemicals (including drugs - narcotic analgesics politsukridy - dextran, antibiotics (polymyxin B), calcium ions, enzymes (chymotrypsin), toxic substances, which come from the intestine, UV ionizing radiation Clinical signs: anaphylactoid shock, urticaria, bronchospasm, conjunctivitis.
- 2) reactions associated with deficiency of inhibitor 1 component complement (C1) and logical complement activation in an alternate path. Clinical features: angioedema.
- 3) Reactions associated with impaired metabolism of polyunsaturated fatty acids, primarily arachidonic: inhibition of lipoygenase activation and path forming excess leukotrienes (e.g., under the influence of non-steroidal antiinflammatory drugs and narcotic analgesics). Clinical manifestations: anaphylactoid shock, allergic processes in the respiratory tract (bronchospasm), hives, skin rash, itching, angioedema.

Often Similar allergic reactions have clinical appearance of hypersensitivity to the drug. In accordance with the "official enclosing it the problem commission on nomenclature eAAC" (2001), inadequate drug reactions should be referred to drug hypersensitivity. If it is mediated by immunological mechanisms - appropriate term is drug allergy. As of the dependence of on the immunological reactions, it can be immediate (antibody-mediated) or delayed (mediated by lymphocytes) type.

The vast majority of drugs is defective allergens - haptens. Just connecting the body to plasma proteins, they get the full properties of an allergen. Against such a conjugated allergen in the body it comes time between antibodies - sensitization, as well as in relation to other allergens, when re-entry of drugs into the body occurs known cascade process: interaction with antibodies to allergens - the selection of mediators - the pathophysiological reaction - clinical manifestations.

The clinic has a drug allergy and systemic manifestations predominant organ reactions:

1. Systemic reactions: anaphylaxis, serum sickness.
2. The body reactions, mainly affecting:
 - 2.1. Skin (urticaria and angioedema, vasculitis, erythema multiforme, fixed dermatitis, contact dermatitis, maculopapular rash, etc.).
 - 2.2. Blood (anemia, leukopenia, agranulocytosis, thrombocytopenia, pancytopenia, eosinophilia).
 - 2.3. Visceral organs (kidney, liver, heart, lung, etc.).

On the sharpness of the flow of drug allergy can be identified:

Acute form:

anaphylactic shock
bronchospastic syndrome
phenomena rhinitis, conjunctivitis

Blood Disorders

cutaneous manifestations.

Prolonged forms:

whey syndrome
medicinal vasculitis

Syndromes Steven - Johnson syndrome, toxic epidermal necrolysis.

Cutaneous manifestations. May include (listed in order of decreasing frequency) acute urticaria and angioedema, unclassified exanthema, polymorphic erythema, fixed dermatitis, vasculitis, contact dermatitis and some other less frequent symptoms.

Hematologic manifestations may include isolated eosinophilia, aplastic, hemolytic anemia, thrombocytopenia, agranulocytosis, pancytopenia.

Respiratory symptoms may include phenomena rhinitis, bronchospasm, allergic alveolitis.

Among the visceral lesions can occur pathological changes of the heart (myocarditis, pericarditis), gastrointestinal (enterocolitis, ulcerative-necrotic manifestations), liver, gall bladder, kidney and the like.

Drug allergies can manifest itself in the form of a serum sickness syndrome (it is based on the 3rd type of allergic reaction). Thus sensitization period lasts 7-10 days. With a slight variant on the background of increase in body temperature can occur polymorphic rash, swelling, small swollen lymph nodes. In moderate form around the site of injection drugs may form redness, rash, swelling of the regional lymph nodes occur headache, tachycardia, pain in the joints. This condition can last up to 3-4 weeks. If severe, these phenomena are more pronounced and prolonged, may decrease blood pressure, there is shortness of breath, convulsions, more changes in the blood (leucopenia with lymphocytosis, accelerated erythrocyte sedimentation rate). This course of drug allergy may be complicated by myocarditis, polyneuritis, hepatitis, encephalitis.

Several special condition is Stevens-Johnson syndrome and toxic epidermal necrolysis. In recent years, more and more experts believe that the occurrence of these syndromes occur as the toxic effects of drugs, and allergy to them. More and more authors have expressed the view that the exudative erythema multiforme, under certain conditions can progress, in the mucous membranes of the lips, tongue, the sky, the conjunctiva, the mucous membrane of the nose, genitals surface may occur bubbles with hemorrhagic content. They can be opened with the formation of ulcers, possible

bleeding, complications such as pneumonia, nephritis, pyoderma and others.

Lyell's syndrome (mainly based on the type 4 allergic reactions) or epidermal necrolysis, manifested hectic body temperature, severe intoxication, sore throat, joint pain, tachycardia. The skin of the trunk, limbs, sometimes the face is sharply hyperemic with a bluish tint, a large number of different size bubbles. The skin easily peels off, removed, forming a large eroded surface with "rags" of the skin, sores on mucous membranes. There may be toxic and infectious lesions of many organs. Mortality in Lyell's syndrome reaches 30-50%.

Extrinsic allergic alveolitis - a disease resulting from the second reaction allergic pulmonary tissue at inhalation of antigens (Ag) contained in an organic dust. Among the hypertension pathology causing the formation of this play an important role, particularly thermophilic actinomycetes, animal proteins (birds, fish, mammals), and others. Depending on the nature of the antigen, triggering its disease emit its various forms. AG, that enter the body by inhalation, causes the formation of precipitating AG relating to IgG. Repeated contact AG form circulating immune complexes that are deposited under the endothelium of the alveolar capillaries. Immune complexes activate the complement system, chemotactic factors. Circulating complexes contribute to the release of lysosomal enzymes that cause damage to the lung tissue. Because of these interactions form epithelioid cell pellets occurs between infiltration of alveolar septa lymphocytes and plasma cells, and in the final step - fibrosis. Lung tissue damage associated with the influence of sensitized lymphocytes disequilibrium between T and B cell responses. Clinical symptoms of the disease is determined by the duration and intensity of exposure to the antigen and its form. The acute form develops within a few hours after contact with the antigen. Manifested by shortness of breath, cough. Auscultation defined typical alveoli that crepitus. The chronic form of the disease characterized by progressive respiratory failure, cough, crepitus, malnourished patients. X-ray detect focal shadows, increased vascular pattern, in chronic forms - fibrotic changes. In the diagnosis of exogenous alveolitis attaches great importance to the immunological studies aimed at identifying specific antibodies or determination of cell-mediated reactions. The sensitive is the fluorescence method and radioimmunoassay test, which is used to quantify their Ia. Identification of precipitating antibodies in combination with the anamnestic data on the presence of allergen exposure and corresponding symptoms usually sufficient for diagnosis.

Due to the importance of the problem of drug allergy health difficulties in its diagnosis is expedient to adhere to phasing in the detection and identification of drug allergy drug-allergens. According to the Ministry of Health and Medical Sciences of Ukraine the order number 127 eighteenth from 02 / 04.2002. it should be:

I stage. Clinicoanamnestic diagnostics. To be applied wherever carried prescription drugs (from obstetric points in a general hospital).

These contingents are allocated on the basis of anamnesis:

- 1) with an increased probability of allergic reactions to medications. These include:
 - Patients with adverse reactions to drugs in the past, which were apparent phenomena of drug allergy
 - Patients with allergic diseases of non-drug genesis (bronchial asthma, allergic rhinitis, urticaria, dermatitis, insect allergens, etc.);
- 2) category, having a large constant professional contact with the LP: employees of chemical companies, etc.;
- 3) patients with autoimmune diseases, as well as those who often takes a long time and drugs.

If any positive reaction to a particular drug solution, it is recorded in the patient's medical records (outpatient, inpatient card) and this drug (and its chemical analogues) is prohibited for use!

The above diagnostic technology is advisable to apply only when the first type (reaginic) allergic reactions. For etiological diagnosis in the second types only laboratory tests can be used, at the 4th type - emplast samples and laboratory tests.

Stage 4. Laboratory tests

They can be used in the presence of contraindications to each and provocative test with drugs, but the urgent need for this, controversial, questionable or difficult cases not. Literature data and own many years of experience (since the real possibilities of our health care) show that as of

such tests can be proposed reaction inhibiting leukocyte migration (micromethod in capillaries), the reaction of blast transformation of lymphocytes (micromethod) and immunotermistometria, ELISA test Shelley release histamine, etc.).

Prevention of drug allergy is divided into general and individual measures.

Measures of general include the fight against polypharmacy, change the order of operation of pharmacies, to improve the quality of drugs produced or sold by establishing institutions of health methods for early detection and prevention of drug allergy, their careful consideration, prohibition of the use of medicinal pre formulations as preservatives, conducting outreach among the population. These include improving the training of doctors on drug allergies, changing the order of prescribing in the inpatient and outpatient facilities, a thorough examination of patients to drug therapy, and the like.

Individual drug allergy prevention measures should be implemented immediately makers drugs. Patients must be aware of all the dangers of drugs and to adhere to certain measures to prevent the complications of pharmacotherapy. In doing so, they should help providers.

Pharmacotherapy of allergic diseases

We can assume that the notional principal pharmacological agent for the treatment of allergic diseases of the respiratory system are divided into the following groups:

- Medications for allergic inflammation.
- Antimediatore funds.
- symptomatic drugs.

This can result in a circuit:

Materials for students' self-directed work.

A. Tests for the self-control:

- 1). The best means of diagnosing IgE-dependent reactions:
 - a) enzyme immunoassay method for the determination of specific IgE; +
 - b) the reaction of a specific leykotsitoliz ;
 - c) skin test to allergens; +
 - g) RAST method.
- 2). What are the main mechanisms of urticaria (by Gell-Coombs)
 1. I type +
 2. II type +
 3. III type +
 4. the IV type
- 3). Food allergens can often beeches cause of atopic dermatitis?
 1. cereals, plum
 - 2 eggs, chocolate +
 3. apricots, bananas
 4. Cyrus, milk +
- 4). The most frequent cause of atopic dermatitis in children during the first years of life there?
 1. household allergens
 2. food allergens +
 3. emotional factors
 4. The physical effort
- 5). If the vast activity of Th2 helper cells predominantly produce interleukin:
 - a) 4,5,13; +
 - b) 1,2,7;
 - c) alpha-interferons, colony stimulating factor

6). Medication often has kidney failure genesis:
a) toxic; + B) allergic; c) infection; d) Autoimmune

7). By leukotrien antagonists one can include:
a) albuterol;
b) the singular;
c) Zafirlukast;
d) none of the above

8). What are the underlying mechanisms are not typical for the development of urticaria (by Gell-Coombs)?

1. the I type
2. II type
3. III type
4. the I Type V +

9). cause of urticaria in children during the first years of life there?

1. household allergens
2. food allergens +
3. emotional factors
4. The physical effort

10. How many pathophysiological stages of development tend to have allergic reactions on AD Ado?

1. two
2. Three +
3. four
4. five

B. Tasks for monitoring :

1. 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.

2. A man 37 years old during pyelography via urografin appeared itching, swelling of the face, dizziness, fear of death. BP - 70/40 mm Hg, RB - 130 bpm . min. Breath rattling, wheezing could be heard in the distance, on auscultation breathing weakened, single dry rales. The drug must enter the patient first?

- a) + epinephrine;
- b) prednisone;
- c) salbutamol;
- g) suprastin;
- d) eufillin.

3. The baby 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? Whether in this case, are allergic to strawberries?

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;
- g) cartload can, strawberries not been well washed, and there is food poisoning.

4. Patient A., 48 years old. Fell ill suddenly, the morning of March 18, when the first felt itchy thighs, buttocks and eyelids, after 15 minutes . there were rashes in the form of bubbles (reminded tunately nettles). After another 30 minutes, a rash appeared on the body, and in places contradict calculus above, merged, acquired a kind of "geographical map". From history we know: 11 March she felt disuria disorder (frequent urge, cramps). I have addressed to the doctor, was appointed Biseptol 480 Table 2. twice a day and furazolidone of 0.1 to 4 times a day. She took medication 7 days (March 12-17). Objectively: on the skin of the whole body unit and drain the bubbles with enlightenment in the center and on the periphery of the Viennese hyperemia, edema of the eyelids, periorbital hyperemia. Body temperature 36,90S. HR - 72 in 11 AD - 120/80 mm Hg. Art. Language moist, overlaid with light gray coating. Abdomen soft, liver protruded from the costal arch to 1.5 cm , the spleen is not enlarged.

1. What is the preliminary diagnosis in patient.?
2. The doctor Tactics (assign the examination and treatment plan).
3. Dif. diagnostics?

5. Patient J., 60 years old. Worried weakness, dizziness, swelling in this body, especially the face and joints, rash on the body in the form of urticaria. History: 10 days ago the patient was bitten homeless cat . The day turned to the doctor, was appointed to in keeping antirabich ESC on the first serum. On the 7th day the rash appeared, first in the entry, and then - all over the body, in the following were listed symptoms.

Question :

1. Diagnosis?
2. Tactics doctor.

B. Situation tasks:

Task №1.

- 1) Allergy medicines in the form of a generalized acute urticaria.
- 2) Plan Survey: complete blood count, urinalysis, liver function tests, determination allergical dependence basophil degranulation with furazolidone and Biseptol, urine culture on the flora and fungi, feces on a dysbacteriosis.

Treatment plan: to cancel Biseptol and furazolidone; antihistamine drugs; diphenhydramine 1% - 1.0 ml / m across 8:00; prednisolone 30 mg / in to saline or 5% glucose - 400.0 ml chelators; diuretics (furosemide 40 mg).

- 3) Acute infections: measles, rubella, infectious mononucleosis.

Task №2 .

1. Serum sickness.
2. Hospitalization. Cancel the introduction of anti-rabies serum; Diphenhydramine 1.0 - 1% №3; prednisolone 30 mg / m; epinephrine hydrochloride 0.1% - 0.5 n / a under the control of blood pressure; diuretics in low doses.

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