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Modern Approaches to Allergen-Specific Diagnostics in Children with Allergic Diseases

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Abstract Theallergen-specific diagnosis of allergic diseases is aimed at establishing the causal significance of allergens in the occurrence of allergic diseases, which is of great importance for the development of effective therapeutic and preventive programs for children suffering from allergic diseases. In recent years, the ability to diagnose allergic diseases has expanded due to the standardization of most inhaled allergens. The specific diagnosis is based on the evaluation of an allergic history, the results of skin tests for allergies, the use of tests for in vitro allergy diagnosis, and provocative tests.

Keywords: allergy, diagnosis, rasprostnanennost, children.

Conducting allergen-specific diagnostics in allergic diseases aims to establish the causal significance of allergens in the development of the disease, which is of great importance for the development of effective therapeutic and preventive programs for children with allergic pathology. The ability to diagnose allergies has expanded in recent years due to the standardization of most inhaled allergens. Specific diagnosis is based on the evaluation of the allergological history, the results of skin tests with allergens, the use of allergological diagnostic methods in in vitro and the performance of provocative tests.

Allergological anamnesis. Find out the presence of complaints from the child or his parents, the presence of allergic diseases both in the anamnesis and at the time of examination. The collection of allergy history data allows us to determine the features of its development before the manifestation of allergy manifestations, to identify the sources of sensitization and factors that caused their development. These may include excessive consumption of products with high allergenic activity by the mother during pregnancy and lactation, drug therapy of the mother during the specified period, and contact with aeroallergens. After the birth of a child, these factors can cause sensitization of the body. Information about previous allergic diseases and reactions is of great importance; their presence in the past most likely indicates the atopic genesis of a newly developed allergic disease. If a child has a history of allergic diseases and reactions, the results of a previous allergological examination, the effectiveness of anti-allergic pharmacotherapy and allergen-specific immunotherapy are determined. A positive result of anti-allergic treatment indicates the allergic nature of the disease. When collecting an allergic history, the time of occurrence and causes of the first manifestation of the disease, the frequency and causes of subsequent exacerbations, their seasonality or occurrence throughout the year are determined. The manifestation of allergy manifestations during the flowering season of plants indicates the likely development of pollinosis, their year-round presence may be due to sensitization with aeroallergens of homes. Pay attention to the relationship between the occurrence of allergic symptoms and the time of day. Children with pollinosis feel worse during daytime hours due to the increased concentration of pollen in the air



during this time period. In patients with bronchial asthma and atopic dermatitis associated with tickborne sensitization, bronchial patency disorders and allergic skin inflammation often increase in the evening and night hours.

Modern approaches to allergen-specific diagnostics in children with allergic diseases

Manifestations of bronchial asthma, allergic rhinitis, and allergic conjunctivitis caused by tickborne sensitization occur most often in the home environment, while when patients change their place of residence or are hospitalized, their condition improves. In children with allergic diseases caused by sensitization to mold allergens (bronchial asthma, allergic rhinitis), the exacerbation of the disease is usually noted when living in damp living quarters, near water bodies, in a forest with high humidity, in contact with green leaves, hay. Increasing sensitization of the body to allergens of house dust and frequent exacerbations of bronchial asthma and atopic dermatitis contributes to living in residential areas with a large number of upholstered furniture, curtains, carpets. The association of the occurrence of allergic manifestations with the intake of certain food products indicates the possible presence of food sensitization in the patient. The appearance of allergic symptoms in contact with pets, birds, or when visiting a zoo or circus indicates the development of sensitization to epidermal allergens. In case of insect allergy, the occurrence of allergic manifestations is associated with insect bites and contact with them, in particular with cockroaches. An allergic history allows you to establish a link between the development of allergic symptoms and the use of certain medications. Based on the anamnesis data, it is possible to judge the role of non-specific factors (infection, pollutants, stress, smoking, climate factors, physical exertion) in the development of exacerbations of the allergic process. An allergological history allows you to get an impression of the severity of the allergic process, differentially carry out basic (anti-inflammatory) therapy and a set of the most appropriate preventive measures, determine the scope and methods of allergological examination.

Skin tests. Skin tests are an informative method of allergological examination. Setting up skin tests aims to confirm the significance of allergens in the development of the disease, to which, according to the anamnesis, hypersensitivity is assumed, to identify causal allergens with which the history of exacerbations of the disease was not traced. The results of skin tests make it possible to assess the level of sensitization and evaluate the possibilities of allergen-specific immunotherapy. Skin allergic reactions of type 1 (IgE-mediated reactions), type 3 (arthus-like reactions), and type 4 (delayed type reactions) may occur on allergen extracts administered during skin testing. IgEmediated skin reactions occur immediately (15-20 minutes after the test is performed). An immediate skin reaction to an allergen is a highly sensitive biological method for detecting specific allergic antibodies. Histamine released from mast cells during exposure to the allergen in the skin causes dilation of capillaries with the development of hyperemia and edema (papules). The skin reaction that occurs after 15-20 minutes can quickly fade or persist for 1 hour. Skin infiltration with eosinophils and polymorphonuclear leukocytes is observed at the site of allergen administration. Such reactions most often occur on house dust allergens, mite, pollen and epidermal allergens. Arthritic-like reactions occur 3-6 hours after the sample is set up, with a maximum of manifestations 8-12 hours after the introduction of the antigen and subsequent reverse development by the end of the day after the sample is set up. Artemis-like reactions are based on an immunocomplex mechanism of development, leading to local inflammation of the skin. The occurrence of such reactions is possible to food, fungal, bacterial antigens. Delayed-type reactions often occur when intradermal tests with allergens are performed. They are manifested by hyperemia and infiltration of the skin 12-48 hours after the introduction of the antigen and often develop when setting skin tests with bacterial and fungal allergens.



Positive results of skin tests indicate the developed sensitization of the body. It is possible to make a judgment about the causal significance of certain groups of allergens only if the results of positive skin tests coincide with the data of an allergic history. When evaluating the results of skin tests, the possibility of false-positive and false-negative reactions should be taken into account. False positive reactions can be caused by preservatives present in the solvent. In this regard, the control (sample with a solvent) for the skin test is mandatory. False positive results of skin tests may be due to the use of high concentrations of allergen and excessive травматизациейskin trauma. False negative results of skin tests are possible when taking antihistamines. For this reason, be sure to put a skin test with histamine. A negative result of a skin test may also be due to the low allergenic activity of the drug. Allergens for skin testing are selected in accordance with the data of an allergic history. Allergic pathology in children is often caused by polyvalent sensitization. In this regard, in cases of allergic diseases with year-round exacerbations, skin testing with food, pollen, epidermal allergens, as well as with allergens of house dust, Dermatophagoides pteronyssinus, Dermatophagoides farinae, mold fungi is indicated. Finding out the spectrum of sensitization by allergens helps to correctly build an elimination regime and conduct allergen-specific immunotherapy in a timely manner. If there are indications of the occurrence of allergy symptoms only in contact with pets, birds kept in apartments, it is indicated to stop contact with them. In such cases, setting up skin tests with epidermal allergens is not mandatory. Expediency in their implementation occurs when the parents refuse to remove the animal or bird from the dwelling. A positive result of skin tests in children helps in such cases to convince parents of the need for these measures.

Skin tests with food allergens are not informative enough, and the positive result of the tests is taken into account when confirming anamnestic data. Skin testing is performed during remission of allergic diseases. It is not recommended to perform skin tests in the presence of their clinical manifestations. To determine the causal significance of allergens, scarification tests, prick test, pricktest, and intradermal tests are used. Scarification tests and the priktest are quite informative, and in most cases, intradermal testing is not required. Scarification tests, the prick test, and the pricktest are safer than intradermal tests, although there is a risk of developing systemic allergic reactions with any method of conducting skin tests. Scarification tests, a prick test, and a pricktest are performed either on the front surface of the forearm or on the skin of the middle part of the back. Intradermal tests are performed only on the anterior surface of the forearms. Samples are placed on an undamaged and unaltered area of skin previously treated with alcohol at a distance of 3 cm from each other. At the same time, samples are taken with 1% histamine solution intended for scarification tests, pre-test, and 0.01% solution for intradermal tests for positive control, as well as a sample with a solvent (negative control). cnpo6, 3-5% water extracts of allergens are used for setting up scarification samples, a pricktest, and glycerin is often added to them. When performing these tests, 1 drop of the allergen used is applied to the skin. Scarification tests can be performed with a scalpel, needle, or scarifier. Make notches of the surface layers of the skin with a length of 0.3-0.6 cm, without damaging the blood vessels. The results of skin tests are evaluated after 15-20 minutes. The test is considered positive if a papule occurs at the site of administration of the tested allergen. A number of allergens, in particular food allergens, can cause non-specific skin irritation reactions when performing tests. The advantage of scarification tests is a simpler technique and the ability to remove the allergen in the event of a severe skin reaction. The injection test is performed with a sterile needle, which is inserted through a drop of allergen with a tip into the surface layers of the skin. An injection or puncture test is considered to be 5 times more sensitive than scarification tests, and approximately 100 times less sensitive than intradermal tests. A type of prick test is abite test, in which, after inserting a needle at an oblique angle through a drop into the surface layers of the skin, it is lifted with a sharp end. The Priktest is quite specific, its results correlate with the level of



specific IgE in the blood serum when determining them by the RAST method. Allergen-coated lancets (phasets) can be used for the prik test. Prequest it is considered positive if a papule with a diameter of 3 mm or more occurs. Experts of the European Academy of Allergy and Clinical Immunology, WHO recommend using the skin pricktest as the main method for diagnosing IgEmediated allergic diseases. Indications for setting intradermal tests are indications in the anamnesis of the causal significance of certain groups of allergens in case of negative or doubtful results of scarification skin tests, or a prick test, or a prick test. The intradermal test has the highest sensitivity compared to other skin tests. When this test is made, 0.01-0.02 ml of the allergen is injected intradermally with a tuberculin syringe in a dilution of 1: 1000, using short 27-gauge needles with a beveled tip. An indicator of sufficient administration of the allergen solution is the formation of a papule with a diameter of 3 mm at the site of its introduction. Local reactions usually occur during intradermal tests, in some cases general and systemic allergic reactions may develop, and therefore an memergency kit should be provided in the allergist's office. If a high level of sensitization is assumed, it is advisable to start intradermal testing with large dilutions of the allergen. The results of the tests are taken into account after 15-20 minutes and after 24 hours. If the allergen is injected too deeply into the skin, a negative result may occur. With intradermal injection of an air bubble, skin hyperemia develops, which can be mistaken for a positive result. In the case of intradermal administration of allergens at a distance of less than 2.5 cm, with the development of a strong reaction, assessment may not be possible due to papule fusion. Do not put more than 15-20 skin samples at the same time. Before setting up skin tests, it is necessary to find out whether the patient had systemic allergic reactions in the past, whether the labeling of allergens was observed. Skin tests should not be given to patients taking antihistamines and sympathomimetic agents, as they have the ability to inhibit the development of reactions caused by histamine and allergens. Skin tests can be performed only 48 hours after the withdrawal of these drugs. Cromones and glucocorticosteroids do not significantly affect the severity of the tests. The results of skin tests with allergens are taken into account for a positive reaction to histamine and a negative reaction to solvent. Scarification and intradermal tests are considered positive if the resulting papule has a size of 5 mm or more. The severity of skin tests may depend on the age of the examined children. In children of the first two years of life, the reaction to an allergen usually manifests itself in the form of erythema, and older children develop both erythema and papula. Positive skin tests with allergens indicate the presence of sensitization of the body, expressed the higher, the greater the skin reaction to them. At the same time, it should be borne in mind that allergens can be considered causally significant in the development of the disease only if there are indications in the anamnesis of the relationship of its exacerbations with them. In children with a suspected high level of sensitization to causally significant allergens, skin testing may be initiated by setting up epicutaneous tests. samples [drip tests – applying a drop of allergen to the skin of the inner surface of the forearm or using aluminum cameras (patch-test)]. Application skin tests used for the specific diagnosis of food allergies need to be standardized.

Allergodiagnostics in in vitro The structure of allergic morbidity in children is dominated by atopic diseases (bronchial asthma, atopic dermatitis, allergic rhinitis). Their pathogenetic basis consists of IgE-mediated allergic reactions to exogenous allergens that occur in children and adolescents with a hereditary predisposition to allergic diseases. The IgE-mediated mechanism underlies the pathogenesis of pollinosis, insect allergy and is involved in the development of urticaria, angioedema, food and drug allergies. Detection of specific IgE antibodies in the blood serum to certain allergens in these groups of patients indicates that they have developed sensitization of the body and, in the presence of anamnestic confirmation, indicates the causal significance of these allergens. The level of allergen -specific IgE has an important diagnostic significance and is



comparable in its informative value to skin samples. Modern in in vitro allergodiagnostics is based on the use of methods for determining specific IgE in blood serum. These research methods include the radioaller gosorbent test (ELISE), combined allergosorbent test (MAST), and immuno CAP. The advantage of immunological methods for determining specific IgE in comparison with skin tests is the ability to perform allergodiagnostics in the acute period of allergic diseases (exacerbation of atopic dermatitis, allergic rhinitis, partially controlled or uncontrolled course of bronchial asthma, chronic urticaria), the results of these tests are not affected by pharmacotherapy. The results of these methods in of in vitro allergodiagnostics correlate with the results of skin tests, the severity of the allergic process, and the level of total IgE in blood serum. For practical purposes, the determination of specific IgE antibodies can determine the presence of sensitization to house dust allergens.Dermatophagoides pteronyssinus, Dermatophagoides farinae, food, plant pollen, mold spores, insects, animals, birds, latex, penicillin, aspirin, and some food coloring agents. Analysis of the results in of in vitro allergodiagnostics using immunological methods for determining specific IgE in blood serum indicates that they are detected in most, but not all, patients who had clinical confirmation of the significance of allergens to which IgE antibodies were detected. The sensitivity of immunological methods of allergodiagnostics when compared with the priktest is 70-75%. Determination of specific IgE antibodies to insect poisons with a positive test result is not considered absolutely conclusive when predicting the probability of developing anaphylactic sensitization to allergens of insect poisons. In this situation, it is advisable to take skin tests. Defining specific iges immunological methods are more preferable than setting up skin tests in patients with severe dermography, in children with allergic diseases who have been treated with antihistamines for a long time, when assessing cross-reactivity between insect poisons, for judging the activity of bronchopulmonary aspergillosis, and in cases when, after collecting data from an allergic history, the doctor gets the impression that the risk of anaphylaxis is significant in the presence of setting up skin It is not recommended to IgE determine indications for allergen-specific immunotherapy tests. based on the determination of specific IgE in blood serum alone. In such cases, a comprehensive allergological examination with skin tests should be performed; positive results of skin tests, if they coincide with the anamnesis data, are decisive for allergen-specific immunotherapy. The clinical determination of total IgE serum IgE and its interpretation are of less value than the determination of specific IgE. A high level of IgE can be detected in diseases such as allergic bronchopulmonary aspergillosis, eczema, hyper-IgE syndrome, HIV infection, myeloma, interstitial nephritis, as well as in patients who have undergone organ transplantation, parasitic diseases, and immunodeficiency. In recent years, the use of methods for determining specific IgG antibodies to food products in order to diagnose food allergies has become widespread, but their involvement in its pathogenesis remains unclear. In this regard, the diagnostic significance of this method requires further clarification by conducting appropriate studies.

Provocative tests Provocative tests (conjunctival, nasal, inhalation) are used to confirm the causal significance of the allergen in cases of discrepancies between the anamnesis and intradermal samples. With positive test results, symptoms of allergic rhinitis, allergic conjunctivitis, and bronchial asthma occur. Provocative tests can only be performed during the period of remission of the disease. Conjunctival tests are more sensitive than scarification tests and less sensitive than intradermal tests. You can perform the test in children over 5 years of age. Nasal tests are considered quite informative, and the results of these tests correlate with the results of skin tests and RAST. Inhalation provocation test is performed with an aerosol of the allergen. It is put in cases where there is an occurrence of attacks of bronchial asthma throughout the year. Indications for the delivery of an inhalation test are the inability to establish the causal significance of allergens by other diagnostic methods, and the identification of the most important allergens in the development of the disease.



Conducting provocative inhalation tests is contraindicated with a high level of sensitization of the body and the presence of bronchopulmonary infection. Tests can be performed in children over 5 years of age, not earlier than 12 hours after taking sympathomimetic and methylxanthine drugs and not earlier than 1-4 days after the last intake of antihistamines, not earlier than 24 hours after taking intal and 2 weeks after the last intake of glucocorticosteroids. A provocative inhalation test is evaluated as positive if FEV1 decreases by 20% 15-20 minutes after inhalation of the allergen or bronchospasm occurs; symptoms of bronchospasm may also occur 6-8 hours after the test is performed as a manifestation of the late phase of the allergic response. Inhalation provocation tests can only be performed in a hospital setting. Provocative conjunctival, endonasal and inhalation tests are performed with allergens at a concentration of at least 1: 1000. An oral provocation test is used to diagnose food allergies. When setting up an open provocative test, the suspected food product is excluded from the diet, and after the symptoms disappear, it is reintroduced into the child's diet. In cases of exacerbation of the allergic process after taking a suspected food product, this product can be considered as the cause of its intolerance. A provocative oral food sample performed by the blind method is more reliable. The suspected food product is given to the examined patient in native or dried form, dissolved in liquid, or prescribed in the form of capsules. Concealment of exposure can be achieved by tinting the food product with juice. A clear positive reaction during loading with such a food product, carried out by a double-blind method, confirms the diagnosis of food intolerance. Anamnesis of the clinical picture of the disease and the results of subsequent allergological examination help to clarify whether IgE-mediated food allergy occurs, or it is mediated by other immunopathological reactions, or is associated with enzymatic insufficiency.

Features of specific diagnosis of drug allergy in children Drug allergy in children is characterized by polymorphism of clinical forms, the participation of various types of immunopathological reactions in its development. Conducting a specific diagnosis in patients with drug allergies is complicated by the lack of standard diagnostic allergens. When collecting data from allergological and pharmacological anamnesis, the presence of hereditary burden of allergic reactions and diseases, previous and present allergic pathology in the child is determined. They collect information about all previously used medications, previous reactions to medications, their clinical manifestations, and the time interval between the prescription of the drug and the occurrence of adverse reactions to it. In cases of detection of certain allergic reactions and diseases in a child, information is collected about the results of a previously conducted allergological examination.

The diagnosis of drug allergy is made based on the evaluation of allergologicaland pharmacological history data and the results of an allergological examination. Skin tests for patients with drug intolerance can only be performed with standard drug allergens to detect IgE-mediated allergic reactions. Application tests (patch-test) are used to identify medicinal compounds that cause contact dermatitis in adolescents. It is not recommended to use them in children. Provocative tests using increasing doses of the drug can only be performed by doctors who have the appropriate training. Contraindications for provocative tests are an increased risk of drug allergies due to concomitant diseases (acute infectious diseases, cardiovascular diseases, kidney and liver diseases, uncontrolled bronchial asthma; a history of drug reactions in the form of generalized blistering rashes, toxic epidermal necrolysis, Stevenson-Johnson syndrome, exfoliative dermatitis, allergic reactions with the use of drugs). increased eosinophilia, systemic vasculitis, anaphylactic shock, cytopenia, autoimmune diseases) [1].

Skin and provocative tests with medications can be dangerous for patients. For this reason, they can only be used if it is impossible to do without their appointment (insulin in children with diabetes, anti-tuberculosis drugs in patients with tuberculosis, anticonvulsants in patients with epilepsy, cytostatics in cancer patients). Pathogenetically justified methods for the diagnosis of drug



allergy are such methods as the determination of specific IgE antibodies (radioimmune, enzymelinked immunosorbent assays), T-lymphocyte stimulation tests in response to exposure to an allergen, setting up a test for the release of histamine from basophils, and determination of histamine and tryptase in blood plasma. Radioimmune methods have significantly expanded the understanding of the mechanisms of penicillin allergy development. Penicillin introduced into the body, combining with the body's proteins, forms a complex called penicilloyl, which is the main antigenic determinant. Penicillin causes immediate allergic reactions. RAST can detect specific IgE antibodies to penicillin. The radioallergosorbent test for detecting penicillin allergy is highly informative [2]. It is possible to use a radioallergosorbent test to determine specific IgE antibodies to aspirin. The method of enzyme-linked immunosorbent assay (ELISA) is considered more sensitive and reproducible for detecting antibodies of various classes, including specific IgE in patients with drug allergies [3]. It is possible to use the test of inhibition of natural leukocyte emigration (TTEEL) in the oral cavity to diagnose drug allergies to penicillin, cephalosporin, aminoglycosides, macrolides, tetracycline, sulfonamides, and local anesthetics [4]. The reaction of inhibition of natural leukocyte emigration makes it possible to diagnose cell-mediated hypersensitivity to drugs [2,3,5,6]. The reverse development of allergy manifestations after elimination of the suspected drug indirectly indicates its causal significance in the occurrence of the allergic process. It should be borne in mind that negative results of laboratory tests do not completely exclude drug allergy, while the identification of a positive result of laboratory tests does not serve as an indisputable confirmation of it.

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