

To the Problem of Fungal Pathology in the Hot Climate in Children and Adults

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ABSTRACT

Fungi are often the etiological factor of allergic diseases in both children and adults. With the help of a detailed history and modern in vitro diagnostics, it is possible to determine immunoglobulin E antibodies to various groups of allergens, including molds and yeasts, typical for a region with a hot climate, which can lead to a personalized approach in the treatment and prevention of the disease.

Keywords: allergen-specific immunoglobulin E, fungal allergens, food products, environmental factors, atopy.

INTRODUCTION

In recent years, allergic diseases have tended to grow and are one of the frequent manifestations of the pathology of immunity, caused by an excessive response of the immune system. Fungal sensitization makes a significant contribution to the increase in morbidity. The indicators of the frequency of sensitization to fungi in various allergic pathologies vary widely (from 2 to 60%) depending on the type of fungus and the patients' belonging to the risk groups for developing mycogenic allergy. At the same time, there is an underdiagnosis of sensitization to fungi, when fungi are not taken into account as an etiological factor, which leads to insufficient effectiveness of standard methods of therapy for allergic diseases [16].

In the immune system, under the influence of antigenic structures of fungi, various pathological processes are formed, including type I allergic reactions caused by IgE mechanisms, as well as type II, III, and IV allergic reactions [22]. It should be noted that allergic reactions can occur as an immune response to allergens from house dust mites, pets, pollen, and fungal spores. Allergenic properties are possessed by only about 100 species of fungi, out of more than 100,000 species of known fungi, due to the fact that fungi are able to colonize substrates almost everywhere, their spores are constantly present in the air, causing year-round symptoms in sensitized patients. Among the fungi with etiological significance in the development of allergies, representatives of the genus *Aspergillus* are one of the most important inhalation allergens in various countries. The frequency of hypersensitivity to various *Aspergillus* species in patients with allergic respiratory diseases in

different countries of the world varies from 15.3 to 38%. The most studied allergenic components of *Aspergillus*: Asp n 14 (β -xylosidase) is a professional allergen present in currently used bakery additives and causes sensitization symptoms in at least 4% of bakers. Asp n 18 (vacuolar serine protease), its homologous allergens were also isolated from *Aspergillus fumigatus* (Asp f 18) and *Penicillium* (Pench 18 and Pen about 18). Asp n 25 (3-phytase B) is a glycoprotein with a molecular weight of approximately 85 kDa, used as an enzymatic additive in the processing of foods rich in phytates, such as cereals, legumes, and also as a food additive used for better digestion of foods, rich in phytates [1, 13, 20, 23, 28, 33].

In vitro diagnostics of specific IgE to food, plant, fungal, epidermal, latex and other environmental allergens is of greater importance for severe bronchopulmonary diseases, allergic dermatoses, atopic diseases, since it has many advantages, is safe for the patient - there is no direct contact with the patient, may be carried out during the period of exacerbation of the disease, the risk of developing severe reactions during testing is excluded, there are no age restrictions.

Molds play a significant role in the development of allergic sensitization in the body. Under the action of antigenic structures of fungi, various pathological processes are formed in the immune system, including type I allergic reactions caused by IgE mechanisms, as well as other types of allergic reactions [5, 7, 10]. Constant contact with the fungus leads to colonization in the respiratory tract and can cause persistent allergenic stimulation [8].

Prolonged contact with fungal spores leads to immune reactions leading to the formation of

specific IgG and IgA [14]. Mycogenic allergization is often accompanied by polyvalent sensitization [2]. In 20–65% of people suffering from allergic pathology, fungal allergens are a causal factor, of which 20–25% of patients have bronchial asthma [3, 15, 21]. It has been proven that in about 3–6% of cases, the development of bronchial asthma is associated precisely with the sensitization of fungal spores. The increased content of fungal spores depends on the sanitary and epidemiological characteristics of the dwelling, seasonal fluctuations, ecology and geographical location. Deep penetration into the respiratory tract of fungal spores is due to their size, which ranges from 1 to 40 microns [3, 12, 14]. Studies have shown that in 76.5% of the apartments, signs of mold damage were found in the concentration of fungal spores, which exceeded the conditionally permissible norm - 500 CFU / m³. Of all the detected fungi, the highest concentration was found for *Penicillium* spp. (92.5% detectability in indoor air), *Aspergillus* spp. (81.1%), *Cladosporium* spp. (34.4%), as well as *Rhizopus* spp. (34.4%). A high correlation was found between micromycete spores in indoor air and an increased content of specific IgE to fungal allergens in the blood serum of residents of these rooms. Molds of the genera *Rhizopus* and *Cladosporium* are common components of house dust [6, 14].

Rhizopus survives in very humid conditions and is susceptible to low humidity. *Rhizopus* spp. usually forms black mold on bread. Fungi of the genus *Cladosporium* also survive in relatively humid conditions and are especially sensitive to a lack of moisture [11, 27]. The basis of the origin of fungi is dead plants, cheeses, cereals, textiles, old window frames [18].

It should be noted that in the practice of general practitioners, therapy is often carried out empirically, without taking into account the characteristics of allergens that determine the prognostic value. A detailed and carefully collected medical history can suggest a positive mycotic history. When taking an anamnesis, you need to pay attention to the following aspects:

1. PRESENCE OF CONTACT WITH HOUSEHOLD MOLD:

Certain difficulties in assessing the importance of household contact with mold often arise due to the fact that, for example, BA with sensitization to fungi may debut years after the improvement of living conditions. At the same time, patients themselves do not inform the doctor about contact with mold, and when collecting anamnesis, they deny the fact of long-term contact with mold, since at the time of contact they already live in another living room.

Microscopic fungi actively populate living quarters, the human environment. Long-term exposure to mold spores can lead to sensitization of the body, which affects the course of bronchopulmonary diseases. Climatic conditions, geographical location have a significant impact on the composition and biochemical processes of micromycetes. Conidia of some fungi that entered the body through the respiratory tract provoke allergic reactions (*Alternaria alternata*, *Mucor* sp., *Penicillium* sp., *Aspergillus* sp.), Mycoses of internal organs (*Aspergillus flavus*, *Asp. fumigatus*, *Asp. niger*), mycotoxicosis (*Alternaria alternata*, *Aspergillus flavus*, *Asp. fumigatus*) [4, 6].

It should be noted that the growth and development of fungi in a room directly depends on the level of humidity and temperature. The most common fungi are found in leaks, in flower pots, in food storage areas, on moldy foods (bread, fruits, vegetables), on shower curtains, in old furniture upholstery, in garbage containers, on other organic substrates (for example, wool). With pronounced humidity, there are more mushrooms in wooden houses than in concrete ones. The *Aspergillus fumigatus* fungi have even been found in pillows. *Penicillium* in the form of green mold can be found on the foundations of buildings. In addition, one important feature should be noted - the subjectivity of the patient's assessment of his apartment as "damp". Often, the analysis of such objective factors as "presence of mold in the apartment" and "living on the first floor" will be much more informative than the subjective assessment of "damp apartment" [16]. *Cladosporium herbarum* is widely distributed in the environment and is the main source of inhaled fungal allergens. *C. herbarum* is one of the most abundant fungi found everywhere. It is found in abundance on wilted or already wilted leaves of herbaceous and woody plants, as a secondary invader on necrotic leaf spots, it is often found in air, food, paints, textiles, and many other substrates. It is also known that *C. herbarum* occurs on old fungal carpophores and also on fungi as a common endophyte, especially in temperate regions. In favorable climatic conditions, *C. herbarum* also lives as an epiphyte on the surface of green, healthy plant leaves [24, 25].

The wide range of allergenic proteins of *C. herbarum* can lead to sensitization and subsequent expression of a number of immune diseases. *Cladosporium* sensitization has been associated with severe life-threatening asthma. Upper respiratory symptoms may also occur with exposure to *cladosporium*, but asthma symptoms are more common. *Cladosporium* exposure can also lead to allergic bronchopulmonary

cladosporium disease, which has been described even in a child [32].

The number of mold species (from different classes and families) is estimated at at least 1 million. Some fungi with flying spores, such as *Alternaria*, *Aspergillus*, *Penicillus* and *Cladosporium*, are found throughout the world. *A. alternata*, usually inhabiting plants, belongs to imperfect fungi and is one of the most important representatives of allergenic fungi. The brown segmented mycelium has outgrowths - conidiophores, on which apical conidia spores develop, single or forming chains. The spores of imperfect fungi differ in shape, size, texture, color, number of cells, and cell wall thickness [29]. Although other *Alternaria* species are likely to be of clinical importance as well, in particular as a result of species cross-reactivity, most studies have focused on *A. alternata*.

A. alternata can be found in many plants, foods, and textiles. Its favorite habitats are soil, rotten wood, corn silage, compost, and various plants. Black spots on vegetables and nuts can be caused by *A. alternata*.

Modern buildings can help create a favorable environment for the growth of *Alternaria*. It has been reported that *Alternaria* present in the air conditioner tray caused allergic rhinitis and asthma in a sensitized individual [17]. *Alternaria* spores are present in the Sydney atmosphere all year round, with several peaks during the spring, summer and fall. A number of meteorological factors, including mean, minimum and maximum temperature, dew point and atmospheric pressure, correlate significantly with the concentration of *Alternaria* spores in the atmosphere. Some of these meteorological variables (air temperature and dew point) show significant correlations with changes in spore concentration both during the day and with 1-, 2- and 3-day lags [26].

Alternaria is one of the main causal allergens in children. In temperate climates, *Alternaria* spores are found from May to November, with peaks in late summer and autumn [31]. Dispersion of spores occurs during dry periods, characterized by higher wind speed and lower relative humidity, and reaches a maximum during the solar noon [19]. Despite the relatively large size of the spores, they can be dispersed hundreds of miles from the source. The number of *Alternaria* on dry, windy days ranges from 500 to 1000 spores per cubic meter in areas where grasses or weeds grow. Outdoor spores of up to 7500 per cubic meter were associated with indoor spores ranging from 0 to 280 per cubic meter [30].

2. PROFESSIONAL CONTACT WITH MOLD:

It can be noted that fungi are ubiquitous, they are widely used in the food industry, livestock, poultry, flour mills, winemaking, breweries, cheese, feed yeast, enzyme preparations, and is also often used by agricultural workers, foresters, gardeners and pharmacists. In most patients with allergic diseases with sensitization to fungi, attacks of suffocation or exacerbation of the disease occur when visiting damp rooms, basements, vegetable stores, archives, swimming pools, autumn forest, and certain metro stations [9].

3. THE PRESENCE OF ATOPY:

Atopy in the genus or the presence of an "atopic march" in children and adults.

4. SEASONALITY OF THE DISEASE:

There is a deterioration in the condition of patients with respiratory diseases, especially in the autumn-spring period (sporulation of fungi), as well as in those who are often ill and have a history of mycotic infection (candidiasis, detection of fungi in sputum crops, nasal swabs, fecal analyzes, onychomycosis, dermatophytosis and etc.).

Before the development of typical clinical manifestations of mycogenic asthma, as a rule, patients have a history of frequent colds, rhinosinusitis, periodic "bronchitis," including obstructive ones. In patients who have lived in a room with mold or on the ground floor since childhood (or for a rather long time in childhood), the extracts from children's outpatient records often include the diagnoses of "asthmatic bronchitis" or "bronchitis with an asthmoid component". In most patients, asthma debuts as a clinical picture of recurrent obstructive bronchitis [9, 16].

5. PSYCHO-EMOTIONAL LABILITY AND SUSCEPTIBILITY TO STRESS:

There is a marked decrease in the immune response under stresses of various origins, which contribute to an increase in the negative effects of pathogenic microorganisms, including fungi.

6. FOOD HISTORY:

Violation of the rules for storing food and eating. Improper storage and violation of hygiene rules and transportation conditions lead to the formation and increase of various pathogenic fungi in food products, in particular, *Candida* is often found in dairy products, *Rhizopus* - in the form of black mold on bread, vegetables, especially often on onions. *Alternaria alternata* can appear as blackheads on tomatoes. Gray mold on strawberries, grapes, cabbage, lettuce, tomatoes is *Botrytis cinerea*. *Aspergillus*

mushrooms are found in tea bags, black pepper powder, coffee, fruits, and confectionery. After the use of atropics and sensitized patients, there is a worsening of the condition after the use in children of stale dairy products, moldy cheese, spoiled fruits and vegetables, yeast-based bakery products, home canned products, and in adults - vegetables, jam, beer, champagne, kvass (i.e. fermentation products), yeast dough, the use of moldy products (old bread, etc.).

Allergic reactions can be caused by fungi of the genus *Candida*, *Alternaria*, *Aspergillus*. Allergic reactions to the intake of kefir, baked goods, kvass and other products, in the preparation of which mushrooms were used, are noted.

With the enteral intake of the allergen (with the use of foods containing molds and foods based on yeast fermentation), symptoms from the gastrointestinal tract, skin and respiratory system are observed. When fungi come into contact with the skin and mucous membranes, urticaria, angioedema, atopic dermatitis (with this disease, sensitization to *Candida* and *Malassezia* inhabiting the skin also occurs) and other skin manifestations can develop [16].

7. MEDICAL HISTORY:

Young children, due to the anatomical and physiological characteristics of the body and, in particular, the respiratory tract, can be exposed to respiratory diseases. Frequent, long-term and uncontrolled use of antibiotic therapy and glucocorticoids can lead to complications such as disruption of the intestinal microbiota, which is accompanied in the future in the form of difficulty breathing and typical attacks of bronchial asthma.

If a positive fungal history is detected, patients need to conduct a specific allergological examination. However, due to the objective difficulties in diagnosing this type of allergy (see above), mycoallergy cannot be ruled out in the case of negative allergy data with fungal allergens, but in the presence of clear clinical signs of fungal sensitization and constant or prolonged contact with fungi in the past or present [nine].

The study of specific immunoglobulins E to mold and yeast is relevant, since allergic bronchopulmonary diseases in children associated with fungal sensitization are characterized by a high complication rate, severe and chronic course, refractoriness and ineffectiveness of conventional treatment regimens [9, 16].

The successes of in vitro laboratory diagnostics using immunoblot panels in our republic allowed us to identify causally significant fungal

(*Cladosporium herbarum*, *Penicillium notatum*, *Candida albicans*, *Alternaria alternata*, *Aspergillus flavus*, *Aspergillus fumigatus*, *Aspergillus niger*, *Aspergillus niger* on the basis of which the traditional ideas about the role of IgE-mediated reactions in bronchopulmonary diseases have significantly expanded. The developed tests for in vitro diagnostics of allergic bronchopulmonary diseases allow timely implementation of therapeutic measures in children, pregnant women, lactating mothers and patients of different ages.

Timely diagnosis and therapy for allergic bronchopulmonary pathology to environmental factors is an urgent problem in the work of pulmonologists, allergists, pediatricians, therapists and clinical immunologists. The urgency of the problem and the need to develop preventive, diagnostic and therapeutic programs aimed at preventing and reducing the prevalence of allergic bronchopulmonary pathology to environmental factors with fungal sensitization requires a special approach.

REFERENCES

1. A.A. Bayazitova N.I., Glushko S.A., Lisovskaya E.V. et al. Allergens of *Aspergillus niger* and *Aspergillus fumigatus*. Practical medicine 3 (95) 2016.P. 73-76
2. Berzhets VM, Koreneva EA, Khalgatyán SV, et al. Identification of fungal sensitization in children with atopic diseases // Medical immunology. - 2011. - v. 13. - No. (4-5). - P.349.
3. Berzhets VM, Khalgatyán SV, Koreneva EA, et al. Study of the prevalence of sensitization to molds in residents of Moscow and the Moscow region // Immunopathology, Allergology, Infectology. - 2012. - v. 3. - P.18-22.
4. Gurina O. P. and others. Sensitization to *Aspergillus niger* in recurrent bronchitis in children // Problems of medical mycology, 2011, Vol.13, No. 2.-P.72
5. O.P. Gurina, E.A. Dementieva, A.E. Blinov, O. N. Varlamov, V.I. Timokhina IgE-hypersensitivity to allergens of the fungi *Rhizopus Nigricans* and *Cladosporium herbarum* in children with respiratory allergies // Pediatrician-2016.-Vol. 7, issue 4, P.61-66.
6. Dorshakova E.V. and others. Micromycetes in their natural habitat and indoors - their potential danger to human health // Problems of medical mycology, 2012, Vol.14, No. 3.-P.53-58.
7. Kozlova Ya.I., Vasilyeva NV, Chilina GA, et al. Mycogenic allergy in residents of premises affected by micromycetes // Problems of medical mycology. - 2008. - v. 10. - No. 2. - P.17-21.
8. Kozlova Ya.I., Frolova EV, Filipova LV, et al. Mycogenic sensitization in patients with bronchial

- asthma in St. Petersburg // Medical Immunology. - 2015. - No. 17. - P.67.
9. Mizernitskiy Yu.L., Minenkova TA, et al. Clinical and immunological features of allergic bronchopulmonary diseases in children with fungal sensitization // Russian Bulletin of Perinatology and Pediatrics, No. 1.-2012.-P.90-96
10. Mitin Yu.A., Pastushenkov V.L., Uglina O.A. Characteristics of the features of the clinical course, changes in the immune system in children with acute dysentery, who had colonization of the intestines with *Aspergillus flavus* fungi // Medical Immunology. - 2015. - No. 17. - P.119-120.
11. Mitrofanov V.S., Kozlova Ya.I. Molds in the house (review) // Problems of medical mycology. - 2004. - vol. 6. - No. 2. - P.10-18.
12. Müller E., Loeffler V. Mycology: textbook. - M.: Mir, 1995.
13. Patterson R., Grammer L.K., Greenberger P.A. Allergic diseases: diagnosis and treatment. - GEOTAR MEDICINE, 2000.P.768.
14. Titova N.D. Diversity of mechanisms of mycogenic allergy in atopic bronchial asthma // asthma. - 2011. - v. 12. - No. 1. - P.5-10.
15. Titova N.D., Novikov P.D. Analysis of mycogenic sensitization in patients with bronchial asthma // Medical Immunology. - 2011. - v. 13. - No. 4-5. - P.357.
16. S.V. Tsarev Allergy to fungi: features of clinical manifestations and diagnostics // Asthma and Allergy.-2015.-№3.-C.3-6.Fung F, Tappen D, Wood G. Alternaria-associated asthma. Appl Occup Environ Hyg. 2000;15(12):924-7.
17. Fung F, Hunghton WG. Health effects of indoor fungal bioaerosol exposure. Appl Occup Environ Hyg. 2003;18 (7):535-544. doi: 10.1080/10473220301451.
18. O'Hollaren, M. T., J. W. Yunginger, K. P. Offord, M. J. Somers, et al. Exposure to an aeroallergen as a possible precipitating factor in respiratory arrest in young patients with asthma. N Engl J Med 1991;324:359-363
19. Lockey R.F. Allergens and allergen immunotherapy. — CRC Press, 2004. — P.750.
20. Mari A, Schneider P, Wally V. Sensitization to fungi: epidemiology, comparative skin tests, and IgE reactivity of fungal extracts. Clin Exp Allergy. 2003;33:1429-1438. doi: 10.1046/j.1365-2222.2003.01783.x.
21. Mitin YuA, Pastushenkov VL, Uglina OA. The characteristic features of clinical course, changes in immune system in children, patients with acute dysentery, which had colonization of gut fungi *Aspergillus flavus*. Meditsinskaya immunologiya. 2015;(17):119-120.
22. Sander I. et al. Allergy to *Aspergillus*-derived enzymes in the baking industry: identification of β -xylosidase from *Aspergillus niger* as a new allergen (Asp n 14) // Journal of allergy and clinical immunology. — 1998. — T. 102, №2. — P. 256-264.
23. Solomon WR, Matthews KP. Aerobiology and inhalant allergens. In: Middleton E, Reed CE, Ellis EF, Adkinson NF, et al, eds. Allergy: Principles and Practice. 3rd ed. St. Louis: The CV Mosby Co., 1989:312-72
24. Schubert K, Groenewald JZ, Braun U, Dijksterhuis J, Starink M, Hill CF, Zalar P, de Hoog GS, Crous PW. Biodiversity in the *Cladosporium herbarum* complex (Davidiellaceae, Capnodiales), with standardisation of methods for *Cladosporium* taxonomy and diagnostics. Stud Mycol 2007;58:105-56
25. Stennett PJ, Beggs PJ. Alternaria spores in the atmosphere of Sydney, Australia, and relationships with meteorological factors. Int J Biometeorol 2004;49(2):98-105
26. Takatory K, Saito A, Yasueda H. The effect of house design and environment on fungal movement in homes of bronchial asthma patients. Mycopathologia. 2000;152:41-49. doi: 10.1023/A:1011933627275.
27. Vermani M., Vijayan V.K., Agarwal M.K. Identification of *Aspergillus* (*A. flavus* and *A. niger*) Allergens and Heterogeneity of Allergic Patients' IgE Response // Iranian Journal of Allergy, Asthma and Immunology. — 2015. — T. 14, №4. — P.361
28. Vijay HM, Kurup VP. Fungal allergens. Clin Allergy Immunol 2004;18:223-49.
29. Vija HM, Thaker AJ, Banerjee B, Kurup VP. Mold allergens. In Lockey RF, Bukantz SC, editors. Allergens and allergen immunotherapy. New York: Marcel Dekker; 1999:113-54
30. Weber RW. Alternaria alternata. Ann Allergy Asthma Immunol 2001;87(5):A-4
31. Weber RW. Species of *Cladosporium*. Ann Allergy Asthma Immunol 2002;89(6):A-6
32. [http://www.fao.org/fileadmin/user_upload/agns/pdf/CTAPhytase from_Aspgillus_Niger_Final.pdf](http://www.fao.org/fileadmin/user_upload/agns/pdf/CTAPhytase_from_Aspgillus_Niger_Final.pdf) (13.04.2016)