

## THE ROLE OF MOLD FUNGI *ALTERNARIA ALTERNATA* IN THE DEVELOPMENT OF ALLERGIES

**Zoabi Tamer, Myronchenko S.**

*National University of Pharmacy,*

*Kharkiv, Ukraine*

s.mironchenko@ukr.net

The greatest influence on the development of allergic pathologies has air allergens, which are quite large particles of a complex structure (pollen, molds, algae, micro-mites, particles of insects and plants, epidermis of animals). An important feature of these aeroallergens is their year-round persistence. They are present in the environment, in residential and industrial premises. Of the aforementioned air allergens, the least studied are spores of fungi, which play an important role in the occurrence of allergic processes.

*Alternaria alternata* is one of the main allergens of fungi. Sensitization to *Alternaria* can be detected in patients with severe bronchial asthma, allergic rhinoconjunctivitis. The spores of the fungus are found in the air year-round, with a peak concentration in late summer and autumn.

*Alternaria alternata* is a spore-forming fungus that grows primarily on plant substrates. A typical habitat of the fungus is dead parts of plants (fallen foliage, rotten wood, bird nests), soil, seeds of grain crops. The environmental peak is associated with a seasonal peak in the concentration of fungal spores in the surrounding air - the end of summer and the beginning of autumn (leaf fall). Wind spores spread hundreds of kilometers, so that they and other elements of the fungus can be contained both in the outside air and as part of house dust. Allergens *Alternaria alternata* can be found in high concentrations in the environment of enterprises that process agricultural products - for example, the processing of wood, grain, as well as engaged in the processing of fur, and in the air of greenhouses.

In a temperate climate, *alternaria* spores are found from May to November, with peaks of concentration in late summer and autumn. Dispersion of spores occurs in dry periods, characterized by a higher wind speed and lower relative humidity, and reaches a maximum in the sunny afternoon. This is one of the most common types of mold found in house dust in North America and Europe. In this case, *alternaria* is mainly external hygrophilous mold and enters the premises mainly from the external environment. Modern buildings can help create an enabling environment for alternative growth. It was reported that the *alternaria* present in the air conditioner pan caused allergic rhinitis and asthma in a sensitized person.

The amount of allergens in extracts of *A. alternata* can vary from 10 to 30, and many allergens are not present in all studied extracts. The presence of specific allergens, including major ones, largely depends on external conditions and can vary during the fungal growth cycle from day to day. In this case, secreted proteins are the major allergens, while other allergens are intracellular proteins and are found in the immune system in the form of spores that are too large to reach the lung alveoli. In addition, spore germination significantly increases the release of the allergen (although not all spores release allergens). For example, the content of Alt a 1, a major

allergen, may be insignificant in total amount of allergens released from the spores, unless the spores germinate. Alt a 1 is the main allergen of alternaria, causing sensitization in asthmatics. Of 43 patients with asthma / rhinitis who had an antibody level of alternaria > 0.7 kUA / l, 93% of asthmatics found specific IgE for Alt a 1, while only 47% of patients with atopic dermatitis found specific IgE for Alt a 1, and their levels were lower than in patients with asthma. Alt a 2 appears to be a major allergen. This is shown in a study in which rAlt a 2 binds to serum IgE antibodies in 16 of 26 (61%) individuals allergic to *A. alternata*. Alt a 3 was associated with IgE in approximately 5% of individuals with sensitization to alternaria. Alt a 5, enolase, binds to IgE in sera from 20% to 50% of individuals sensitized to alternaria. Nevertheless, when conducting skin tests with recombinant enolase in 7 patients with an allergy to alternaria, only 2 patients had a positive result, which indicates that rAlt a 5 may not have the same reactivity as the native allergen. Alt a 6 was associated with IgE in the sera of 7% of individuals with sensitization to alternaria. Alt a 7 was associated with IgE in 7% of persons with sensitization to alternaria. However, skin tests with recombinant rAlt a 7 in 7 people with allergies to alternaria did not reveal a positive result. Alt a 10 was associated with IgE in the sera of 2% of patients with sensitization to alternaria. Alt a 70kD accounts for 13% of the dry weight of alternaria extracts and causes positive skin test results in 87% (14/16) of patients sensitized to alternaria. This protein is believed to be different from Alt a 1 because significant fluctuations were observed in the air samples during their measurement, suggesting that these glycoproteins are released under different conditions. In a study on the assessment of the sera of a large cohort of monozygous and dizygotic twins, scientists concluded that there is a pronounced genetic predisposition to IgE reactivity to a mixture of alternaria allergens, and a weaker one to IgE reactivity to its individual allergic components.

The presence of wide cross-reactivity between individual species of the genus is assumed. The Alt 2 homologue was found in 6 other alternaria strains. Enolase is a common allergen present in many types of mold, and has been shown to have pronounced cross-reactivity with other fungal enolases. In particular, the enolases of *Alternaria alternata* and *Cladosporium herbarum* are major allergens, and the sera of about 50% of patients respond to both cladosporium and alternaria. Cross IgE reactivity between the enolases of *A. fumigatus*, *P. citrinum*, and *A. alternata* was also reported. It was shown that there is a wide cross-reactivity between the enolases of *C. herbarum*, *A. alternata*, *S. cerevisiae*, *C. albicans*, and *A. fumigatus*.

Sensitization to alternaria has also been studied in European studies. In an epidemiological study at 30 centers across Europe, the incidence of mold sensitization (*Alternaria alternata* and/or *Cladosporium herbarum*) increased significantly with increasing severity of asthma in all studied regions, despite differences in the incidence of sensitization. Several studies have proven the relationship of hypersensitivity to antigens of the fungus *Alternaria alternata* with the development and severity of bronchial asthma, allergic rhinitis and atopic dermatitis.

The widespread prevalence of allergen in the environment necessitates the diagnosis of hypersensitivity to develop effective measures to prevent the development and prevention of exacerbations of allergic diseases.