9. Summary

At the beginning of the 21st century allergic diseases are a global health problem. Atopic dermatitis (AD) occurs in 20% of children and approximately 1-3% of adults, allergic rhinitis affects 20-30% of the general population. 300 million people worldwide suffer from asthma, which in 80% of children and 50% of adults is caused by allergies.

There are four immunological mechanisms responsible for the development of hypersensitivity symptoms: types I-III are humoral reactions, in which the antigen (allergen) stimulates the production of specific antibodies, type IV is a cellular response induced by T-lymphocytes. Type I immunological response mediated by IgE is used in pathogenesis of asthma, allergic rhinitis and atopic dermatitis. Type I reaction can be demonstrated by performing skin prick tests (SPT) or by determining allergen specific IgE antibodies (asIgE). According to the literature, two types of immunological reactions are important in the pathogenesis of atopic dermatitis - type I reaction, which is mediated by IgE, and type IV reaction, which is delayed and mediated by T-lymphocytes. Diagnostics of the delayed-type reaction is based on atopy patch tests (APT). These tests recreate type IV response – a sufficiently long (48-hour) contact of the allergen with the skin results in local eczema changes, the same as we see among patients with atopic dermatitis. Such identification of clinically relevant allergens enables the implementation of a strategy to reduce the exposure to these allergens, including avoiding sensitizing foods. It also allows us to qualify patients with IgE-mediated allergy to specific immunotherapy.

The aim of this study is to analyze the frequency of two types of immune reactions in the skin, immediate and late, after various applications of the same allergen among patients with atopic dermatitis, asthma and allergic rhinitis.

Atopy patch tests were used to evaluate the delayed (cellular) immune response. The IgE-mediated, immediate response was assessed by skin prick tests and allergen specific IgE (asIgE) levels in the serum. In addition, the SCORAD index was used for the clinical evaluation of patients with AD.

The research material consisted of 23312 information cards of patients hospitalized from January 1, 1996 to February 28, 2012 in the Department of Allergology and Lung Diseases of the Children's Hospital Polanki them. Maciej Płażyński LLC in Gdańsk. 830 patient information cards were selected for atopic patch tests with airborne and food allergens. After analyzing the completeness of the data contained in the information cards, the study group was narrowed down to 711 patients. It consisted of 406 girls (57.1%) and 305 boys (42.9%). The average age of the subjects was 89.9 months, the median age was 79 months. 560 children were diagnosed with atopic dermatitis (AD), 151 children suffered from asthma (A) and in 260 children allergic rhinitis (AR) was determined. Patients diagnosed with bronchial asthma and/or allergic rhinitis were classified as patients with a respiratory disease (RD). Based on clinical diagnosis the subjects were divided into four groups: group A (AD without RD) – 314 patients, group B (RD without AD) – 61 patients, group C (AD and RD) – 246 patients, group D (other diseases without AD and RD) – 90 patients. Positive APT were determined in 71.9%, positive SPT in 60.5%, positive asIgE in 54.1%, and positive SPT/asIgE in 66.2% of the patients.

Among all hospitalized children positive atopic patch tests occurred with a higher or comparable frequency as positive SPT/asIgE. The most common sensitizers were house dust mites – *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae* (positive patch tests were found in 59.8% and 57.8% of patients respectively), yolk (52.2%) and white (46.7%) of chicken egg. In group A, positive APT was found in 75.2% and SPT/asIgE in

55.1% of patients, in group B in 67.2% and in 85.5%, in group C in 79.3% and in 89.8%, in group D in 43.3% and 29.8% of patients.

Patients suffering only from atopic dermatitis (group A) had a significantly higher frequency of positive atopic patch tests than positive SPT/asIgE tests. In this group positive APT occurred from 1.37 (positive tests with at least one allergen from all allergens used for testing) to 3.57 times more (positive tests with *Cladosporium herbarum* allergens) than positive SPT/asIgE.

Positive atopy patch tests were determined significantly more frequent among patients from groups A and C (children with AD and children with both AD and RD) than in patients from group D (without AD and RD). This applies to tests with at least one allergen, with *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*, with cat, dog, grass pollen allergens (group A only) and with *Cladosporium herbarum* allergens (group C only). The most common sensitizing allergen detected with APT among our patients with AD, patients with AD and RD as well as patients with RD were house dust mites. In our work there was no indication of higher frequency of positive APTs with different food allergens (cow's milk, yolk and white of chicken egg, wheat and rye flour) in children with AD in comparison to children without this condition. There was no correlation between the SCORAD index and the positive atopic patch tests in patients with AD.

The coincidence of both types of hypersensitivity – mediated by IgE and type IV T-cell hypersensitivity was found between patients with AD (group A and C). The relative risk of positive atopic patch test is higher when SPT/asIgE is positive to the corresponding allergen and is from 1.31 for a positive atopic patch test with *Dermatophagoides pteronyssinus* to 2.42 for a positive APT with cat allergens in group A and from 1.84 for a positive APT with *Dermatophagoides pteronyssinus* to 2.46 with *Cladosporium herbarum* in group C. IgE-dependent allergy can promote allergy caused by cellular mechanisms. Langerhans cells in the skin, that are coated with specific IgE, are more effective in the capture and presentation of the allergen to specific T lymphocytes in comparison to Langerhans cells lacking specific IgE.

On the other hand, some of the patients with AD may have a cellular immune response without the involvement of IgE antibodies. It was found that in group A (AD) positive APT simultaneous with negative SPT/asIgE occurred significantly more frequently than positive SPT/asIgE simultaneous with negative APT with corresponding allergens (this applies to *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*, dog allergens, *Alternaria tenuis* and *Cladosporium herbarum*). In 67.2% of our patients with RD (with AR or asthma – group B) positive atopic patch tests were found, and 12.7% of them had positive APT simultaneous with negative SPT/asIgE tests.

The research has shown that in children suffering from asthma or AR (group B) and in children suffering from AD and RD (group C) positive SPT/asIgE was significantly more frequent than positive APT.

Positive SPT/asIgE were significantly more frequent in patients with respiratory disease (group B) than in patients from group A (only with AD) and group D (patients with other diseases without asthma, AR and AD). Positive SPT/asIgE were also, significantly more frequent in patients with AD and RD (group C) than in patients from group A and in patients from group D. There was no indication of statistically significant difference between the frequency of positive SPT/asIgE in patients with both AD and RD as well as in the patients with RD. It was found that in patients with both AD and RD (group C) positive SPT/asIgE with simultaneously negative APT cases were more frequent than positive APT with simultaneously negative SPT/asIgE cases with corresponding allergens (it concerned cat allergens, grass pollen and birch pollen). Such results, as well as a higher frequency of positive SPT/asIgE than positive APT in groups B and C, indicate that atopy is more strongly

associated with AR and asthma than with AD. A clear relation between atopy (higher frequency of positive SPT/asIgE) and atopic dermatitis is observed when AD appears simultaneously with AR and/or asthma.

Our study showed more frequent positive atopic patch tests in children under the age of 6 years than in children over 6 years of age. The relative risk of positive APT in children under 6 compared to children over 6 years ranged from 1.26 (positive APT with at least 1 allergen) to 2.26 (positive APT with dog allergens). However, there is a prevalence of positive SPT/asIgE in children over 6 years of age compared to children under 6 years of age. The relative risk of positive SPT/asIgE was higher in this age group than in children under 6 and ranged from 1.15 (positive SPT/asIgE with at least one allergen) to 1.96 (positive SPT/asIgE with allergy to mugwort). The highest frequency of positive APT (89.3%) was found in children under the age of 3. As children grow up the frequency of positive APT decreases and amounts to 51.5% in children aged 12-14 years. In the case of positive SPT/asIgE we can observe the opposite relation – the lowest frequency (50%) is found in children under the age of 3 and as they grow the frequency increases – 77.8% in children aged 10 - 12 years.

The first stage of atopic march in children is often atopic dermatitis. There are two immunological mechanisms involved in the pathogenesis of this disease – IgE-dependent and T-lymphocytes-dependent. As the time goes by, the immune response is gradually evolving – from type IV reaction (dependent on T-lymphocytes) to type I reaction (IgE-dependent). Children grow out of atopic dermatitis, but they develop allergic rhinitis and/or asthma, which are associated with IgE-dependent allergy, hence the prevalence of positive SPT/asIgE in older children. In some patients, however, the T-cell dependent allergic response may subsist. Some authors believe that patients with allergic rhinitis and asthma with negative SPT and/or asIgE tests as well as with negative provocation tests with suspected allergens, especially those who had AD in the past, should undergo atopic patch tests with aeroallergens, in order to find a "hidden allergy".

The advantage of the polyvalent sensitization over the monovalent one was found in our patients, both by means of APT as well as SPT/asIgE.

In some patients from each group hypersensitivity wasn't determined – both atopy patch tests and SPT/asIgE were negative. In group A (AD) negative APT simultaneous with negative SPT/asIgE occurred in 15.5% of the cases, in group B (RD) in 0.2% of the cases, in group C (AD and RD) in 2.2% of the cases, in group D (other diseases) in 41.7% of the cases.

There are two types of immune responses to common environmental allergens in patients with atopic dermatitis, asthma and allergic rhinitis – IgE-dependent, immediate reaction and type IV, T lymphocytes dependent reaction. The use of both methods in diagnosing atopic diseases enables more precise identification of the factor triggering allergy symptoms e.g. using APT allergy can be detected in some patients with intrinsic form of atopic dermatitis, who would not have been diagnosed without this method.

Based on the calculations performed, it can be concluded that positive APT results are significantly more frequent than positive SPT/asIgE results in the group of patients suffering from AD only. While in the group of patients only with RD positive SPT/asIgE results are significantly more frequent than in patients only with AD and patients without both AD and RD. In the group of patients with both AD and RD as well as in the group of patients with RD the frequency of positive APT and SPT/asIgE results is similar. The frequency of positive APT decreases and the frequency of positive SPT/asIgE increases with the child's age.